ARS TOSCANA
agenzia regionale di sanità

DECRETO DEL DIRETTORE

n° 13 del 28/02/2017

Oggetto: Accordo di collaborazione tra l'Istituto di Fisiologia Clinica del CNR e l'Agenzia Regionale di Sanita' per il supporto alla realizzazione delle attività previste dal WP2 "Building EUROlinkCAT Central Results Repository" nell'ambito del progetto europeo denominato "EUROlinkCAT: Establishing a linked European Cohort of Children with Congenital Anomalies" – Approvazione

IL DIRETTORE

Vista la legge regionale 24 febbraio 2005, n. 40 "*Disciplina del servizio sanitario regionale*" e successive modificazioni ed integrazioni;

Visto il Regolamento generale di organizzazione dell'ARS, approvato dalla Giunta regionale con propria deliberazione n. 29 del 21/01/2008;

Visto il decreto del Presidente della Giunta Regionale n. 162 dell'8 novembre 2016, con il quale il sottoscritto è stato nominato Direttore dell'ARS;

Visto e richiamato l'accordo quadro sottoscritto in data 18/02/2010 fra l'Agenzia Regionale di Sanità (ARS) e l'Istituto di Fisiologia Clinica del CNR (IFC-CNR), successivamente prorogato fino al 17/02/2019, con l'obiettivo di garantire una stretta collaborazione su tematiche d'interesse comune all'interno di eventuali progetti regionali, nazionali ed internazionali;

Dato atto che in data 12 dicembre 2016 è stato sottoscritto con la Commissione Europea il Grant Agreement (GA) n. 733001 per la realizzazione del progetto "EUROlinkCAT - *Establishing a linked European Cohort of Children with Congenital Anomalies*" finanziato dalla Commissione Europea, al quale IFC-CNR partecipa in qualità di Partner, e che avrà durata di 60 mesi a partire dal 01/01/2017;

Considerato che, all'interno del progetto EUROlinkCAT, ARS è individuata quale Terza Parte (Linked Third Party ex Art. 14 del GA) del Partner IFC-CNR, che pertanto le riconosce una quota di finanziamento pari ad € 44.856,25;

Visto lo schema di accordo di collaborazione con IFC-CNR (Allegato A) per il supporto da parte di ARS, in qualità di Terza Parte, alla realizzazione delle attività previste dal WP2 "*Building EUROlinkCAT Central Results Repository*" (coordinatore: partner 2 University of Ulster) così come descritte nel Grant Agreement (Allegato B), che in dettaglio prevede la realizzazione delle seguenti azioni:

- censimento dei dati disponibili su mortalità, morbosità, prescrizioni farmaceutiche per i casi di bambini con difetti congeniti nati nel periodo 1995-2014;
- traduzione dall'italiano all'inglese la descrizione delle variabili;
- standardizzazione delle variabili per l'analisi della mortalità e della morbosità;
- *data linkage* del Registro Toscano Difetti Congeniti con i flussi sanitari correnti relativi a mortalità, schede dimissione ospedaliera e prescrizioni farmaceutiche, utilizzando come chiave di ricerca il codice identificativo universale IDUNI;
- creazione di *linked dataset*;
- produzione di un report sui *linkage* effettuati (*linkage report*);
- produzione di tabelle con dati aggregati necessari allo svolgimento delle attività del progetto;

Valutata l'opportunità rappresentata dal Coordinatore dell'Osservatorio di epidemiologia di provvedere alla sottoscrizione con IFC-CNR di uno specifico accordo di collaborazione che definisca i rapporti fra i due enti e le azioni da

intraprendere per la realizzazione delle attività necessarie all'attuazione dei compiti assegnati ad IFC-CNR all'interno del progetto;

Tutto ciò premesso e considerato;

DECRETA

2. di approvare, con le motivazioni espresse in narrativa, lo schema di accordo di collaborazione con IFC-CNR (Allegato A) per il supporto da parte di ARS, in qualità di Terza Parte, alla realizzazione delle attività previste dal WP2 "*Building EUROlinkCAT Central Results Repository*" (coordinatore: partner 2 University of Ulster) nell'ambito del progetto europeo denominato "EUROlinkCAT: Establishing a linked European Cohort of Children with Congenital Anomalies", così come descritte nel Grant Agreement (Allegato B), che in dettaglio prevede la realizzazione delle seguenti azioni:

    - censimento dei dati disponibili su mortalità, morbosità, prescrizioni farmaceutiche per i casi di bambini con difetti congeniti nati nel periodo 1995-2014;
    - traduzione dall'italiano all'inglese la descrizione delle variabili;
    - standardizzazione delle variabili per l'analisi della mortalità e della morbosità;
    - *data linkage* del Registro Toscano Difetti Congeniti con i flussi sanitari correnti relativi a mortalità, schede dimissione ospedaliera e prescrizioni farmaceutiche, utilizzando come chiave di ricerca il codice identificativo universale IDUNI;
    - creazione di *linked dataset*;
    - produzione di un report sui *linkage* effettuati (*linkage report*);
    - produzione di tabelle con dati aggregati necessari allo svolgimento delle attività del progetto;

3. di dare atto che il sottoscritto, in quanto rappresentante legale di ARS, provvederà alla sottoscrizione dell'Accordo di collaborazione con IFC-CNR, nominando quale Responsabile delle suddette attività, nonché del trattamento dei dati personali ai sensi del D.Lgs. 196/2003, il Coordinatore dell'Osservatorio di Epidemiologia, Dott. Fabio Voller;

4. di dare atto che, per la realizzazione delle attività di cui al predetto Accordo di collaborazione, ARS si impegna ad attivare risorse umane, base di dati e strumentazioni interne all'Agenzia, e riceverà da IFC-CNR una quota di finanziamento pari ad € 44.856,25;

5. di assicurare la pubblicità integrale del presente provvedimento mediante inserimento nella sezione "*Amministrazione trasparente*" sul sito web dell'ARS (www.ars.toscana.it)

Il Direttore
VANNUCCI ANDREA
(firmato digitalmente*)

Allegato A

Progetto "EUROlinkCAT: Establishing a linked European Cohort of Children with Congenital Anomalies" finanziato dalla Commissione Europea Grant Agreement n. 733001

TRA

Consiglio Nazionale delle Ricerche - **Istituto di Fisiologia Clinica** (di seguito **CNR-IFC**) codice fiscale 80054330586, P. IVA n. 02118311006, con sede legale in Via Moruzzi 1 – 56124 Pisa, rappresentata dal Dott. Giorgio Iervasi in qualità di Direttore, nato a Livorno il 30 Maggio 1954 e domiciliato per la carica presso la sede;

E

Agenzia Regionale di Sanità (di seguito **ARS**) codice fiscale/P. IVA 04992010480, con sede in Via Pietro Dazzi, 1 – 50141 Firenze, rappresentata dal Dott. Andrea Vannucci, in qualità di Direttore, nato a Firenze il 06/02/1952 e domiciliato ove sopra per la carica,

PREMESSO CHE

- ✓ la Commissione Europea, nell'ambito del Programma Horizon 2020, ha emanato in data 14 ottobre 2015 il Bando H2020-SC1-2016-2017 (Personalized Medicine), Topic SC1-PM-04-2016 "Networking and optimising the use of population and patient cohorts at EU level";
- ✓ per il predetto progetto "Establishing a linked European Cohort of Children with Congenital Anomalies" finanziato dalla Commissione Europea (Acronimo EUROlinkCAT) è stato autorizzato un finanziamento da parte della Commissione Europea pari ad euro 7.348.072,75 (fuori del campo di applicazione IVA);
- ✓ in data 12 dicembre 2016 è stato sottoscritto con la Commissione Europea il Grant Agreement n. 733001;
- ✓ CNR-IFC, Principal Investigator Dott.ssa Anna Pierini, partecipa al progetto in qualità di partner (CNR-IFC è partner n. 07);
- ✓ ARS è Terza Parte - Linked Third Party Art. 14 – di CNR-IFC all'interno del progetto EUROlinkCAT;
- ✓ La quota di finanziamento di CNR-IFC per il progetto ammonta ad euro 200.462,50 di cui euro 44.856,25 imputati a ARS;
- ✓ CNR-IFC e ARS collaborano dal 2010 per la realizzazione di attività di interesse comune in tema di epidemiologia e verifica di qualità dei servizi sanitari come da Convenzione stipulatata in data 18 febbraio 2010 – Agenzia Regionale di Sanità Reg. n. 438/R – e prorogata fino al 17 febbraio 2019 - Agenzia Regionale di Sanità Prot. n. 436/SC

SI CONVIENE E SI STIPULA QUANTO SEGUE

ARTICOLO 1
Oggetto dell'accordo

Oggetto della presente convenzione è la definizione dei rapporti tra CNR-IFC e ARS per lo svolgimento delle attività necessarie all'attuazione del progetto.

ARTICOLO 2
Attività di ricerca e responsabilità

Le parti intendono collaborare entro i termini e le condizioni indicate nella presente convenzione per la realizzazione delle attività previste dal WP2 "Building EUROlinkCAT Central Results Repository" (coordinatore: partner 2 University of Ulster) così come descritte nel Grant Agreement

Il lavoro deve essere effettuato in conformità con quanto stabilito nel Grant Agreement e in tutti i suoi allegati.
Il Grant Agreement è allegato alla presente convenzione e ne costituisce parte integrante (Allegato 1).

ARS si impegna a consentire lo svolgimento dell'attività di ricerca nella sede prescelta per il periodo relativo all'attuazione del progetto, e nello specifico dovrà:

- ✓ effettuare il censimento dei dati disponibili su mortalità, morbosità, prescrizioni farmaceutiche per i casi di bambini con difetti congeniti nati nel periodo 1995-2014;
- ✓ tradurre dall'italiano all'inglese la descrizione delle variabili;
- ✓ standardizzare lle variabili per l'analisi della mortalità e della morbosità (standardisation of variables);
- ✓ incrociare i dati (data linkage) del Registro Toscano Difetti Congeniti con i flussi sanitari correnti relativi a mortalità, schede dimissione ospedaliera e prescrizioni farmaceutiche utilizzando come chiave di ricerca il codice identificativo universale IDUNI;
- ✓ creare linked dataset;
- ✓ produrre un report sui linkage effettuati (linkage report);
- ✓ produrre tabelle con dati aggregati necessari allo svolgimento delle attività del progetto.

Relativamente alla gestione amministrativa delle attività sopra descritte, ARS si impegna formalmente:

- ✓ alla gestione amministrativo-contabile del finanziamento secondo la propria normativa e nel rispetto delle regole comunitarie;
- ✓ ad attenersi alla previsione di budget allegato alla presente convenzione (Allegato 2);
- ✓ a fornire rendiconto economico del sopra citato budget alle scadenze prefissate (cfr. Articolo 3 della presente convenzione) ed alle scadenze dei periodi di rendicontazione stabiliti dalla Commissione Europea (cfr. Articolo 20 "Reporting, Payments requests" del Grant Agreement).

Responsabili del progetto sono la Dott.ssa Anna Pierini per CNR-IFC e la Dott.ssa Rosa Gini per ARS.

ARTICOLO 3
Durata del progetto e modalità di finanziamento

Il progetto, oggetto della presente convenzione, ha durata di 60 mesi, con data di inizio 1 gennaio 2017 individuata secondo le modalità di cui all'art. 3 del Grant Agreement stipulato con la Commissione Europea.

Nello specifico, CNR-IFC e ARS collaborano alla realizzazione delle attività previste dal WP2 "Building EUROlinkCAT Central Results Repository" le cui attività iniziano al mese 1 e terminano al mese 60.

Il finanziamento sarà erogato dalla Commissione Europea a IFC CNR, tramite il coordinatore del progetto, QUEEN MARY UNIVERSITY OF LONDON - QMUL (Regno Unito).
Il prefinanziamento ammonta al 35% del contributo (EC contribution).

Parte del contributo complessivo erogato a CNR-IFC, per un importo pari a euro 44.856,25, sarà destinato ad ARS per le attività così come dettagliate nell'articolo 2 della presente convenzione con le seguenti

modalità:

Prima tranche
IFC erogherà ad ARS il 35% del contributo previsto solo a seguito del pagamento da parte della Commissione Europea del pre-finanziamento e dopo aver realizzato le seguenti attività:

- ✓ censimento dei dati disponibili su mortalità, morbosità, prescrizioni farmaceutiche per i casi di bambini con difetti congeniti nati nel periodo 1994-2014;
- ✓ traduzione dall'italiano all'inglese della descrizione delle variabili e standardizzazione delle variabili (Standardisation of variables).

L'ARS dovrà presentare a IFC una relazione sull'attività svolta e solo dopo valutazione positiva della suddetta relazione da parte del responsabile scientifico IFC, avverrà l'erogazione della tranche.

Seconda tranche
IFC erogherà ad ARS fino al 50% del contributo previsto solo a seguito del pagamento da parte della Commissione Europea della rendicontazione del Period 1 (M1-M18, 01/01/2017-30/06/2018) e fermo restando una valutazione positiva dei costi da parte della Commissione; la rendicontazione finanziaria presentata da ARS dovrà coprire almeno l'85% del contributo complessivo previsto per ARS.

Saldo
IFC erogherà ad ARS il saldo del contributo previsto solo a seguito del pagamento da parte della Commissione Europea del saldo del progetto e fermo restando una valutazione positiva dei costi da parte della Commissione.
Si precisa che tale attività di collaborazione scientifica rientra tra i fini istituzionali delle rispettive parti e pertanto l'erogazione di tale contributo è fuori campo di applicazione IVA in quanto le parti per le attività in essere sono carenti dei requisiti oggettivi e soggettivi di cui agli articoli 1 e 2 del D.P.R. 633/1972.

Il versamento verrà effettuato da CNR-IFC mediante accrediti sul seguente c/c IBAN IT03D0100003245311300306629 presso la Banca D'Italia intestato ad Agenzia Regionale di Sanità con le modalità sopra descritte, dopo che IFC avrà ricevuto l'incasso degli importi spettanti da parte della Commissione Europea.

ARTICOLO 5
Confidenzialità

Tutti i dati e le informazioni messe a disposizione dalle parti singolarmente e/o collettivamente per lo svolgimento delle attività del progetto, così come tutti i dati e le informazioni utilizzate per la definizione delle attività sono da considerarsi confidenziali e le parti si impegnano a non divulgarle all'esterno per tutta la durata del progetto.

Per tutte le questioni non trattate nel presente articolo si fa riferimento a quanto stabilito nel Consortium Agreement (Allegato 3)

ARTICOLO 5
Foro competente

Per qualsiasi controversia derivante o connessa alla presente Convenzione, ove CNR-IFC sia attore o convenuto, è competente il Foro di Roma, con espressa rinuncia a qualsiasi altro.

ARTICOLO 6
Norme di rinvio

Per tutto quanto non espressamente previsto dalla presente Convenzione, si rinvia alla legislazione comunitaria, nazionale e regionale vigente.

ARTICOLO 7
Durata e registrazione della Convenzione

La presente Convenzione, firmata digitalmente, ha inizio dalla data ultima di sottoscrizione del presente atto fino alla scadenza del progetto così come da art. 4.
La presente Convenzione è soggetta a registrazione in caso d'uso con applicazione dell'imposta di registro in misura fissa, ai sensi del D.P.R. 26/4/86 n. 131.
L'eventuale registrazione e le relative spese sono a carico della parte richiedente.

ARTICOLO 8
Allegati

Fanno parte integrante della presente convenzione i seguenti allegati:

- ✓ Allegato 1 Grant Agreement del progetto EUROlinkCAT
- ✓ Allegato 2 Piano finanziario (Partner CNR-IFC e Linked Third Party ARS)
- ✓ Allegato 3 Consortium Agreement del progetto EUROlinkCAT

Letto, approvato e sottoscritto

CONSIGLIO NAZIONALE DELLE RICERCHE - ISTITUTO DI FISIOLOGIA CLINICA

Il Direttore
Dott. Giorgio Iervasi*

AGENZIA REGIONALE DI SANITA'

Il Direttore
Dott. Andrea Vannucci*

* "Documento informatico sottoscritto con firma digitale ai sensi del D.Lgs n. 82/2005. L'originale informatico è stato predisposto e conservato presso ARS in conformità alle regole tecniche di cui all'art. 71 del D. Lgs n. 82/2005. Nella copia analogica la sottoscrizione con firma autografa è sostituita dall'indicazione a stampa del nominativo del soggetto responsabile secondo le disposizioni di cui all'art. 3 del D.Lgs n. 39/1993."

EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR RESEARCH & INNOVATION

Health
Non-communicable diseases and the challenge of healthy ageing

GRANT AGREEMENT

NUMBER — 733001 — EUROlinkCAT

This **Agreement** ('the Agreement') is **between** the following parties:

on the one part,

*the **European Union** ('the EU'), represented by the European Commission ('the Commission')*[1],

represented for the purposes of signature of this Agreement by the Head of Unit, DIRECTORATE-GENERAL FOR RESEARCH & INNOVATION, Health, Administration and finance, Mila BAS SANCHEZ,

and

on the other part,

1. 'the coordinator ':

QUEEN MARY UNIVERSITY OF LONDON (QMUL) GB22, RC000710, established in 327 MILE END ROAD, LONDON E1 4NS, United Kingdom, VAT number GB248837911, represented for the purposes of signing the Agreement by Research Operations Manager, Jan CLARKE

and the following other beneficiaries, if they sign their 'Accession Form' (see Annex 3 and Article 56):

2. **UNIVERSITY OF ULSTER (UU)** GB22, RC000726, established in CROMORE ROAD, COLERAINE BT52 1SA, United Kingdom, VAT number GB672390524,

3. **REGION SYDDANMARK (RSD)**, 29190909, established in DAMHAVEN 12, VEJLE 7100, Denmark, VAT number DK29190909,

4. **UNIVERSITY OF NEWCASTLE UPON TYNE (UNEW)**, established in KINGS GATE, NEWCASTLE UPON TYNE NE1 7RU, United Kingdom, VAT number GB499672470,

5. **UNIVERSITA DEGLI STUDI DI FERRARA (UNIFE)**, established in VIA ARIOSTO 35, FERRARA 44121, Italy, VAT number IT00434690384,

6. **KLINIKA ZA DJECJE BOLESTI ZAGREB (KDB)** HR6, 080797139, established in KLAICEVA 16, ZAGREB HR-10000, Croatia, VAT number HR70641763756,

7. **CONSIGLIO NAZIONALE DELLE RICERCHE (CNR-IFC)**, 80054330586, established in PIAZZALE ALDO MORO 7, ROMA 00185, Italy, VAT number IT02118311006,

8. **ACADEMISCH ZIEKENHUIS GRONINGEN (UMCG)**, 01169570, established in HANZEPLEIN 1, GRONINGEN 9713 GZ, Netherlands, VAT number NL800866393B01,

9. **PUBLIC HEALTH WALES NATIONAL HEALTH SERVICE TRUST (PHW NHS)**, -, established in CHARNWOOD COURT UNIT 1 PARC, CARDIFF CF11 9LJ, United Kingdom, VAT number GB654439854,

1 Text in *italics* shows the options of the Model Grant Agreement that are applicable to this Agreement.

10. **INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM)**, 180036048, established in RUE DE TOLBIAC 101, PARIS 75654, France, VAT number FR31180036048,

11. **FUNDACION PARA EL FOMENTO DE LA INVESTIGACION SANITARIA Y BIOMEDICA DELA COMUNITAT VALENCIANA (FISABIO)** ES3, 501V, established in CALLE MICER MASCO 31, VALENCIA 46010, Spain, VAT number ESG98073760,

12. **UNIWERSYTET MEDYCZNY IM KAROLA MARCINKOWSKIEGO W POZNANIU (PUMS)**, established in UL. FREDRY 10, POZNAN 61 701, Poland, VAT number PL7770003104,

13. **TERVEYDEN JA HYVINVOINNIN LAITOS (THL)**, 22295006, established in MANNERHEIMINTIE 166, HELSINKI 00271, Finland, VAT number FI22295006,

14. **INTERNATIONAL CHARITABLE FUND OMNI-NET FOR CHILDREN (OMNI NET)** UA5, 33334985, established in 16 LYPNYA ST 36, RIVNE 33028, Ukraine,

15. **OTTO-VON-GUERICKE-UNIVERSITAET MAGDEBURG (OVGU)**, GESETZ 07/10/1993, established in UNIVERSITAETSPLATZ 2, MAGDEBURG 39106, Germany, VAT number DE139238413,

16. **INSTITUTO NACIONAL DE SAUDE DR. RICARDO JORGE (INSA)**, 271, established in AVENIDA PADRE CRUZ, LISBOA 1600 560, Portugal, VAT number PT501427511,

17. **CENTRE HOSPITALIER UNIVERSITAIRE DE LA REUNION (CHURéunion)**, 200030013, established in BELLEPIERRE, ALL DES TOPAZES, SAINT-DENIS 97400, France,

18. **PROVINCIAAL INSTITUUT VOOR HYGIENE (PIH)**, established in KRONENBURGSTRAAT 45, ANTWERPEN 2000, Belgium,

19. **ASOCIACION INSTITUTO BIODONOSTIA (BIOEF)** ES5, AS/G/15251/2010, established in Paseo Dr. Beguiristain s/n, DONOSTIA-SAN SEBASTIAN 20014, Spain, VAT number ES G-75020313,

20. **BIOMEDICAL COMPUTING LIMITED (BIOMED)** LTD, 03148645, established in INNOVATION CENTRE HIGHFIELD DRIVE CHURCHFIELDS, ST LEONARDS ON SEA EAST SUSSEX TN38 9UH, United Kingdom, VAT number GB724664328,

21. **REDBURN SOLUTIONS LIMITED (Redburn)** LTD, NI611699, established in INNOVATION CENTRE NOTHERN IRELAND SCIENCE PARK, BELFAST BT3 9DT, United Kingdom, VAT number GB136893870,

22. **SWANSEA UNIVERSITY (SU)** GB22, established in SINGLETON PARK, SWANSEA SA2 8PP, United Kingdom, VAT number GB123853477,

Unless otherwise specified, references to ‘beneficiary’ or ‘beneficiaries’ include the coordinator.

The parties referred to above have agreed to enter into the Agreement under the terms and conditions below.

By signing the Agreement or the Accession Form , the beneficiaries accept the grant and agree to implement it under their own responsibility and in accordance with the Agreement, with all the obligations and conditions it sets out.

The Agreement is composed of:

Terms and Conditions

Annex 1 Description of the action

Annex 2 Estimated budget for the action

Annex 3 Accession Forms

Annex 4 Model for the financial statements

Annex 5 Model for the certificate on the financial statements

Annex 6 Model for the certificate on the methodology

TERMS AND CONDITIONS

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CHAPTER 1 GENERAL

ARTICLE 1 — SUBJECT OF THE AGREEMENT

This Agreement sets out the rights and obligations and the terms and conditions applicable to the grant awarded to the beneficiaries for implementing the action set out in Chapter 2.

CHAPTER 2 ACTION

ARTICLE 2 — ACTION TO BE IMPLEMENTED

The grant is awarded for the action entitled '***EUROlinkCAT: Establishing a linked European Cohort of Children with Congenital Anomalies — EUROlinkCAT***' **('action')**, as described in Annex 1.

ARTICLE 3 — DURATION AND STARTING DATE OF THE ACTION

The duration of the action will be ***60*** **months** as of *1 January 2017* ('**starting date of the action**').

ARTICLE 4 — ESTIMATED BUDGET AND BUDGET TRANSFERS

4.1 Estimated budget

The '**estimated budget**' for the action is set out in Annex 2.

It contains the estimated eligible costs and the forms of costs, broken down by beneficiary *(and linked third party)* and budget category (see Articles 5, 6*, and 14*).

4.2 Budget transfers

The estimated budget breakdown indicated in Annex 2 may be adjusted by transfers of amounts between beneficiaries or between budget categories (or both). This does not require an amendment according to Article 55, if the action is implemented as described in Annex 1.

However, the beneficiaries may not add costs relating to subcontracts not provided for in Annex 1, unless such additional subcontracts are approved by an amendment or in accordance with Article 13.

CHAPTER 3 GRANT

ARTICLE 5 — GRANT AMOUNT, FORM OF GRANT, REIMBURSEMENT RATES AND FORMS OF COSTS

5.1 Maximum grant amount

The '**maximum grant amount**' is **EUR 7,348,072.75** (seven million three hundred and forty eight thousand seventy two EURO and seventy five eurocents).

5.2 Form of grant, reimbursement rates and forms of costs

The grant reimburses ***100% of the action's eligible costs*** (see Article 6) ('**reimbursement of eligible costs grant**') (see Annex 2).

The estimated eligible costs of the action are EUR **7,348,072.75** (seven million three hundred and forty eight thousand seventy two EURO and seventy five eurocents).

Eligible costs (see Article 6) must be declared under the following forms ('**forms of costs**'):

(a) for **direct personnel costs**:

- as actually incurred costs ('**actual costs**') or
- on the basis of an amount per unit calculated by the beneficiary in accordance with its usual cost accounting practices ('**unit costs**').

Personnel **costs for SME owners** or **beneficiaries that are natural persons** not receiving a salary (see Article 6.2, Points A.4 and A.5) must be declared on the basis of the amount per unit set out in Annex 2 (**unit costs**);

(b) for **direct costs for subcontracting**: as actually incurred costs (**actual costs**);

(c) for **direct costs of providing financial support to third parties**: *not applicable;*

(d) for **other direct costs**: as actually incurred costs (**actual costs**);

(e) for **indirect costs**: on the basis of a flat-rate applied as set out in Article 6.2, Point E ('**flat-rate costs**');

(f) ***specific cost category(ies):*** *not applicable.*

5.3 Final grant amount — Calculation

The '**final grant amount**' depends on the actual extent to which the action is implemented in accordance with the Agreement's terms and conditions.

This amount is calculated by the *Commission* — when the payment of the balance is made (see Article 21.4) — in the following steps:

Step 1 – Application of the reimbursement rates to the eligible costs

Step 2 – Limit to the maximum grant amount

Step 3 – Reduction due to the no-profit rule

Step 4 – Reduction due to improper implementation or breach of other obligations

5.3.1 Step 1 — Application of the reimbursement rates to the eligible costs

The reimbursement rate(s) (see Article 5.2) are applied to the eligible costs (actual costs, unit costs and flat-rate costs; see Article 6) declared by the beneficiaries *and linked third parties* (see Article 20) and approved by the *Commission* (see Article 21).

5.3.2 Step 2 — Limit to the maximum grant amount

If the amount obtained following Step 1 is higher than the maximum grant amount set out in Article 5.1, it will be limited to the latter.

5.3.3 Step 3 — Reduction due to the no-profit rule

The grant must not produce a profit.

'**Profit**' means the surplus of the amount obtained following Steps 1 and 2 plus the action's total receipts, over the action's total eligible costs.

The '**action's total eligible costs**' are the consolidated total eligible costs approved by the *Commission*.

The '**action's total receipts**' are the consolidated total receipts generated during its duration (see Article 3).

The following are considered **receipts**:

(a) income generated by the action; if the income is generated from selling equipment or other assets purchased under the Agreement, the receipt is up to the amount declared as eligible under the Agreement;

(b) financial contributions given by third parties to the beneficiary *or to a linked third party* specifically to be used for the action, and

(c) in-kind contributions provided by third parties free of charge and specifically to be used for the action, if they have been declared as eligible costs.

The following are however not considered receipts:

(a) income generated by exploiting the action's results (see Article 28);

(b) financial contributions by third parties, if they may be used to cover costs other than the eligible costs (see Article 6);

(c) financial contributions by third parties with no obligation to repay any amount unused at the end of the period set out in Article 3.

If there is a profit, it will be deducted from the amount obtained following Steps 1 and 2.

5.3.4 Step 4 — Reduction due to improper implementation or breach of other obligations — Reduced grant amount — Calculation

If the grant is reduced (see Article 43), the *Commission* will calculate the reduced grant amount by deducting the amount of the reduction (calculated in proportion to the improper implementation of the action or to the seriousness of the breach of obligations in accordance with Article 43.2) from the maximum grant amount set out in Article 5.1.

The final grant amount will be the lower of the following two:

- the amount obtained following Steps 1 to 3 or

- the reduced grant amount following Step 4.

5.4 Revised final grant amount — Calculation

If — after the payment of the balance (in particular, after checks, reviews, audits or investigations; see Article 22) — the *Commission* rejects costs (see Article 42) or reduces the grant (see Article 43), it will calculate the '**revised final grant amount**' for the beneficiary concerned by the findings.

This amount is calculated by the *Commission* on the basis of the findings, as follows:

- in case of **rejection of costs**: by applying the reimbursement rate to the revised eligible costs approved by the *Commission* for the beneficiary concerned;

- in case of **reduction of the grant**: by calculating the concerned beneficiary's share in the grant amount reduced in proportion to its improper implementation of the action or to the seriousness of its breach of obligations (see Article 43.2).

In case of **rejection of costs and reduction of the grant**, the revised final grant amount for the beneficiary concerned will be the lower of the two amounts above.

ARTICLE 6 — ELIGIBLE AND INELIGIBLE COSTS

6.1 General conditions for costs to be eligible

'**Eligible costs**' are costs that meet the following criteria:

(a) for **actual costs**:

(i) they must be actually incurred by the beneficiary;

(ii) they must be incurred in the period set out in Article 3, with the exception of costs relating to the submission of the periodic report for the last reporting period and the final report (see Article 20);

(iii) they must be indicated in the estimated budget set out in Annex 2;

(iv) they must be incurred in connection with the action as described in Annex 1 and necessary for its implementation;

(v) they must be identifiable and verifiable, in particular recorded in the beneficiary's accounts in accordance with the accounting standards applicable in the country where the beneficiary is established and with the beneficiary's usual cost accounting practices;

(vi) they must comply with the applicable national law on taxes, labour and social security, and

(vii) they must be reasonable, justified and must comply with the principle of sound financial management, in particular regarding economy and efficiency;

(b) for **unit costs**:

(i) they must be calculated as follows:

{amounts per unit set out in Annex 2 or calculated by the beneficiary in accordance with its usual cost accounting practices (see Article 6.2, Point A)

multiplied by

the number of actual units};

(ii) the number of actual units must comply with the following conditions:

- the units must be actually used or produced in the period set out in Article 3;
- the units must be necessary for implementing the action or produced by it, and
- the number of units must be identifiable and verifiable, in particular supported by records and documentation (see Article 18);

(c) for **flat-rate costs**:

(i) they must be calculated by applying the flat-rate set out in Annex 2, and

(ii) the costs (actual costs or unit costs) to which the flat-rate is applied must comply with the conditions for eligibility set out in this Article.

6.2 Specific conditions for costs to be eligible

Costs are eligible if they comply with the general conditions (see above) and the specific conditions set out below for each of the following budget categories:

A. direct personnel costs;
B. direct costs of subcontracting;
C. *not applicable;*
D. other direct costs;
E. indirect costs;
F. *not applicable.*

'Direct costs' are costs that are directly linked to the action implementation and can therefore be attributed to it directly. They must not include any indirect costs (see Point E below).

'Indirect costs' are costs that are not directly linked to the action implementation and therefore cannot be attributed directly to it.

A. Direct personnel costs

Types of eligible personnel costs

A.1 **Personnel costs** are eligible, if they are related to personnel working for the beneficiary under an employment contract (or equivalent appointing act) and assigned to the action ('**costs for employees (or equivalent)**'). They must be limited to salaries (including during parental leave), social security contributions, taxes and other costs included in the **remuneration**, if they arise from national law or the employment contract (or equivalent appointing act).

Beneficiaries that are non-profit legal entities[2] may also declare as personnel costs **additional remuneration** for personnel assigned to the action (including payments on the basis of supplementary contracts regardless of their nature), if:

(a) it is part of the beneficiary's usual remuneration practices and is paid in a consistent manner whenever the same kind of work or expertise is required;

(b) the criteria used to calculate the supplementary payments are objective and generally applied by the beneficiary, regardless of the source of funding used.

Additional remuneration for personnel assigned to the action is eligible up to the following amount:

(a) if the person works full time and exclusively on the action during the full year: up to EUR 8 000;

(b) if the person works exclusively on the action but not full-time or not for the full year: up to the corresponding pro-rata amount of EUR 8 000, or

(c) if the person does not work exclusively on the action: up to a pro-rata amount calculated as follows:

{{EUR 8 000

divided by

the number of annual productive hours (see below)},

multiplied by

the number of hours that the person has worked on the action during the year}.

A.2 The **costs for natural persons working under a direct contract** with the beneficiary other than an employment contract are eligible personnel costs, if:

(a) the person works under the beneficiary's instructions and, unless otherwise agreed with the beneficiary, on the beneficiary's premises;

(b) the result of the work carried out belongs to the beneficiary, and

(c) the costs are not significantly different from those for personnel performing similar tasks under an employment contract with the beneficiary.

A.3 The **costs of personnel seconded by a third party against payment** are eligible personnel costs, if the conditions in Article 11.1 are met.

[2] For the definition, see Article 2.1(14) of the Rules for Participation Regulation No 1290/2013: '**non-profit legal entity**' means a legal entity which by its legal form is non-profit-making or which has a legal or statutory obligation not to distribute profits to its shareholders or individual members.

A.4 **Costs of owners** of beneficiaries that are small and medium-sized enterprises ('**SME owners**') who are working on the action and who do not receive a salary are eligible personnel costs, if they correspond to the amount per unit set out in Annex 2 multiplied by the number of actual hours worked on the action.

A.5 **Costs of 'beneficiaries that are natural persons'** not receiving a salary are eligible personnel costs, if they correspond to the amount per unit set out in Annex 2 multiplied by the number of actual hours worked on the action.

Calculation

Personnel costs must be calculated by the beneficiaries as follows:

{{hourly rate

multiplied by

the number of actual hours worked on the action},

plus

for non-profit legal entities: additional remuneration to personnel assigned to the action under the conditions set out above (Point A.1)}.

The number of actual hours declared for a person must be identifiable and verifiable (see Article 18).

The total number of hours declared in EU or Euratom grants, for a person for a year, cannot be higher than the annual productive hours used for the calculations of the hourly rate. Therefore, the maximum number of hours that can be declared for the grant is:

{the number of annual productive hours for the year (see below)

minus

total number of hours declared by the beneficiary for that person in that year for other EU or Euratom grants}.

The '**hourly rate**' is one of the following:

(a) for personnel costs declared as **actual costs:** the hourly rate is the amount calculated as follows:

{actual annual personnel costs (excluding additional remuneration) for the person

divided by

number of annual productive hours}.

The beneficiaries must use the annual personnel costs and the number of annual productive hours for each financial year covered by the reporting period. If a financial year is not closed at the end of the reporting period, the beneficiaries must use the hourly rate of the last closed financial year available.

For the 'number of annual productive hours', the beneficiaries may choose one of the following:

(i) 'fixed number of hours': 1 720 hours for persons working full time (or corresponding pro-rata for persons not working full time);

(ii) 'individual annual productive hours': the total number of hours worked by the person in the year for the beneficiary, calculated as follows:

{annual workable hours of the person (according to the employment contract, applicable collective labour agreement or national law)

plus

overtime worked

minus

absences (such as sick leave and special leave)}.

'Annual workable hours' means the period during which the personnel must be working, at the employer's disposal and carrying out his/her activity or duties under the employment contract, applicable collective labour agreement or national working time legislation.

If the contract (or applicable collective labour agreement or national working time legislation) does not allow to determine the annual workable hours, this option cannot be used;

(iii) 'standard annual productive hours': the 'standard number of annual hours' generally applied by the beneficiary for its personnel in accordance with its usual cost accounting practices. This number must be at least 90% of the 'standard annual workable hours'.

If there is no applicable reference for the standard annual workable hours, this option cannot be used.

For all options, the actual time spent on **parental leave** by a person assigned to the action may be deducted from the number of annual productive hours;

(b) for personnel costs declared on the basis of **unit costs**: the hourly rate is one of the following:

(i) for SME owners or beneficiaries that are natural persons: the hourly rate set out in Annex 2 (see Points A.4 and A.5 above), or

(ii) for personnel costs declared on the basis of the beneficiary's usual cost accounting practices: the hourly rate calculated by the beneficiary in accordance with its usual cost accounting practices, if:

- the cost accounting practices used are applied in a consistent manner, based on objective criteria, regardless of the source of funding;

- the hourly rate is calculated using the actual personnel costs recorded in the beneficiary's accounts, excluding any ineligible cost or costs included in other budget categories.

The actual personnel costs may be adjusted by the beneficiary on the basis of budgeted or estimated elements. Those elements must be relevant for calculating

the personnel costs, reasonable and correspond to objective and verifiable information;

and

- the hourly rate is calculated using the number of annual productive hours (see above).

B. Direct costs of subcontracting (including related duties, taxes and charges such as non-deductible value added tax (VAT) paid by the beneficiary) are eligible if the conditions in Article 13.1.1 are met.

C. Direct costs of providing financial support to third parties *not applicable.*

D. Other direct costs

D.1 **Travel costs and related subsistence allowances** (including related duties, taxes and charges such as non-deductible value added tax (VAT) paid by the beneficiary) are eligible if they are in line with the beneficiary's usual practices on travel.

D.2 *The **depreciation costs of equipment, infrastructure or other assets** (new or second-hand) as recorded in the beneficiary's accounts are eligible, if they were purchased in accordance with Article 10.1.1 and written off in accordance with international accounting standards and the beneficiary's usual accounting practices.*

*The **costs of renting or leasing** equipment, infrastructure or other assets (including related duties, taxes and charges such as non-deductible value added tax (VAT) paid by the beneficiary) are also eligible, if they do not exceed the depreciation costs of similar equipment, infrastructure or assets and do not include any financing fees.*

*The costs of equipment, infrastructure or other assets **contributed in-kind against payment** are eligible, if they do not exceed the depreciation costs of similar equipment, infrastructure or assets, do not include any financing fees and if the conditions in Article 11.1 are met.*

The only portion of the costs that will be taken into account is that which corresponds to the duration of the action and rate of actual use for the purposes of the action.

D.3 **Costs of other goods and services** (including related duties, taxes and charges such as non-deductible value added tax (VAT) paid by the beneficiary) are eligible, if they are:

(a) purchased specifically for the action and in accordance with Article 10.1.1 or

(b) contributed in kind against payment and in accordance with Article 11.1.

Such goods and services include, for instance, consumables and supplies, dissemination (including open access), protection of results, certificates on the financial statements (if they are required by the Agreement), certificates on the methodology, translations and publications.

D.4 **Capitalised and operating costs of 'large research infrastructure'**[3] *directly used for the action are eligible, if:*

(a) the value of the large research infrastructure represents at least 75% of the total fixed assets (at historical value in its last closed balance sheet before the date of the signature of the Agreement or as determined on the basis of the rental and leasing costs of the research infrastructure[4]*);*

*(b) the beneficiary's methodology for declaring the costs for large research infrastructure has been positively assessed by the Commission ('**ex-ante assessment**');*

(c) the beneficiary declares as direct eligible costs only the portion which corresponds to the duration of the action and the rate of actual use for the purposes of the action, and

(d) they comply with the conditions as further detailed in the annotations to the H2020 grant agreements.

E. Indirect costs

Indirect costs are eligible if they are declared on the basis of the flat-rate of 25% of the eligible direct costs (see Article 5.2 and Points A to D above), from which are excluded:

(a) costs of subcontracting and

(b) costs of in-kind contributions provided by third parties which are not used on the beneficiary's premises;

(c) *not applicable;*

(d) *not applicable.*

Beneficiaries receiving an operating grant[5] financed by the EU or Euratom budget cannot declare indirect costs for the period covered by the operating grant.

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[3] '**Large research infrastructure**' means research infrastructure of a total value of at least EUR 20 million, for a beneficiary, calculated as the sum of historical asset values of each individual research infrastructure of that beneficiary, as they appear in its last closed balance sheet before the date of the signature of the Agreement or as determined on the basis of the rental and leasing costs of the research infrastructure.

[4] For the definition, see Article 2(6) of Regulation (EU) No 1291/2013 of the European Parliament and of the Council of 11 December 2013 establishing Horizon 2020 - the Framework Programme for Research and Innovation (2014-2020) (OJ L 347, 20.12.2013 p.104)-('**Horizon 2020 Framework Programme Regulation No 1291/2013**'): '**Research infrastructure**' are facilities, resources and services that are used by the research communities to conduct research and foster innovation in their fields. Where relevant, they may be used beyond research, e.g. for education or public services. They include: major scientific equipment (or sets of instruments); knowledge-based resources such as collections, archives or scientific data; e-infrastructures such as data and computing systems and communication networks; and any other infrastructure of a unique nature essential to achieve excellence in research and innovation. Such infrastructures may be 'single-sited', 'virtual' or 'distributed'.

[5] For the definition, see Article 121(1)(b) of Regulation (EU, Euratom) No 966/2012 of the European Parliament and of the Council of 25 October 2012 on the financial rules applicable to the general budget of the Union and repealing Council Regulation (EC, Euratom) No 1605/2002 (OJ L 218, 26.10.2012, p.1) ('**Financial Regulation No 966/2012**'): '**operating grant**' means direct financial contribution, by way of donation, from the budget in order to finance the functioning of a body which pursues an aim of general EU interest or has an objective forming part of and supporting an EU policy.

F. ***Specific cost category(ies)***

Not applicable

6.3 Conditions for costs of linked third parties to be eligible

Costs incurred by linked third parties are eligible if they fulfil — mutatis mutandis — the general and specific conditions for eligibility set out in this Article (Article 6.1 and 6.2) and Article 14.1.1.

6.4 Conditions for in-kind contributions provided by third parties free of charge to be eligible

In-kind contributions provided free of charge are eligible direct costs (for the beneficiary *or linked third party*), if the costs incurred by the third party fulfil — *mutatis mutandis* — the general and specific conditions for eligibility set out in this Article (Article 6.1 and 6.2) and Article 12.1.

6.5 Ineligible costs

'**Ineligible costs**' are:

(a) costs that do not comply with the conditions set out above (Article 6.1 to 6.4), in particular:

(i) costs related to return on capital;

(ii) debt and debt service charges;

(iii) provisions for future losses or debts;

(iv) interest owed;

(v) doubtful debts;

(vi) currency exchange losses;

(vii) bank costs charged by the beneficiary's bank for transfers from the *Commission*;

(viii) excessive or reckless expenditure;

(ix) deductible VAT;

(x) costs incurred during suspension of the implementation of the action (see Article 49);

(b) costs declared under another EU or Euratom grant (including grants awarded by a Member State and financed by the EU or Euratom budget and grants awarded by bodies other than the *Commission* for the purpose of implementing the EU or Euratom budget); in particular, indirect costs if the beneficiary is already receiving an operating grant financed by the EU or Euratom budget in the same period.

6.6 Consequences of declaration of ineligible costs

Declared costs that are ineligible will be rejected (see Article 42).

This may also lead to any of the other measures described in Chapter 6.

CHAPTER 4 RIGHTS AND OBLIGATIONS OF THE PARTIES

SECTION 1 RIGHTS AND OBLIGATIONS RELATED TO IMPLEMENTING THE ACTION

ARTICLE 7 — GENERAL OBLIGATION TO PROPERLY IMPLEMENT THE ACTION

7.1 General obligation to properly implement the action

The beneficiaries must implement the action as described in Annex 1 and in compliance with the provisions of the Agreement and all legal obligations under applicable EU, international and national law.

7.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 8 — RESOURCES TO IMPLEMENT THE ACTION — THIRD PARTIES INVOLVED IN THE ACTION

The beneficiaries must have the appropriate resources to implement the action.

If it is necessary to implement the action, the beneficiaries may:

- purchase goods, works and services (see Article 10);
- use in-kind contributions provided by third parties against payment (see Article 11);
- use in-kind contributions provided by third parties free of charge (see Article 12);
- call upon subcontractors to implement action tasks described in Annex 1 (see Article 13);
- call upon linked third parties to implement action tasks described in Annex 1 (see Article 14).

In these cases, the beneficiaries retain sole responsibility towards the *Commission* and the other beneficiaries for implementing the action.

ARTICLE 9 — IMPLEMENTATION OF ACTION TASKS BY BENEFICIARIES NOT RECEIVING EU FUNDING

Not applicable

ARTICLE 10 — PURCHASE OF GOODS, WORKS OR SERVICES

10.1 Rules for purchasing goods, works or services

10.1.1 If necessary to implement the action, the beneficiaries may purchase goods, works or services.

The beneficiaries must make such purchases ensuring the best value for money or, if appropriate, the lowest price. In doing so, they must avoid any conflict of interests (see Article 35).

The beneficiaries must ensure that the Commission, the European Court of Auditors (ECA) and the European Anti-Fraud Office (OLAF) can exercise their rights under Articles 22 and 23 also towards their contractors.

10.1.2 Beneficiaries that are 'contracting authorities' within the meaning of Directive 2004/18/EC[6] or 'contracting entities' within the meaning of Directive 2004/17/EC[7] must comply with the applicable national law on public procurement.

10.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under Article 10.1.1, the costs related to the contract concerned will be ineligible (see Article 6) and will be rejected (see Article 42).

If a beneficiary breaches any of its obligations under Article 10.1.2, the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 11 — USE OF IN-KIND CONTRIBUTIONS PROVIDED BY THIRD PARTIES AGAINST PAYMENT

11.1 Rules for the use of in-kind contributions against payment

If necessary to implement the action, the beneficiaries may use in-kind contributions provided by third parties against payment.

The beneficiaries may declare costs related to the payment of in-kind contributions as eligible (see Article 6.1 and 6.2), up to the third parties' costs for the seconded persons, contributed equipment, infrastructure or other assets or other contributed goods and services.

The third parties and their contributions must be set out in Annex 1. The *Commission* may however approve in-kind contributions not set out in Annex 1 without amendment (see Article 55), if:

- they are specifically justified in the periodic technical report and
- their use does not entail changes to the Agreement which would call into question the decision awarding the grant or breach the principle of equal treatment of applicants.

[6] Directive 2004/18/EC of the European Parliament and of the Council of 31 March 2004 on the coordination of procedures for the award of public work contracts, public supply contracts and public service contracts (OJ L 134, 30.04.2004, p. 114).

[7] Directive 2004/17/EC of the European Parliament and of the Council of 31 March 2004 coordinating the procurement procedures of entities operating in the water, energy, transport and postal services sectors (OJ L 134, 30.04.2004, p. 1).

The beneficiaries must ensure that the Commission, the European Court of Auditors (ECA) and the European Anti-Fraud Office (OLAF) can exercise their rights under Articles 22 and 23 also towards the third parties.

11.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the costs related to the payment of the in-kind contribution will be ineligible (see Article 6) and will be rejected (see Article 42).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 12 — USE OF IN-KIND CONTRIBUTIONS PROVIDED BY THIRD PARTIES FREE OF CHARGE

12.1 Rules for the use of in-kind contributions free of charge

If necessary to implement the action, the beneficiaries may use in-kind contributions provided by third parties free of charge.

The beneficiaries may declare costs incurred by the third parties for the seconded persons, contributed equipment, infrastructure or other assets or other contributed goods and services as eligible in accordance with Article 6.4.

The third parties and their contributions must be set out in Annex 1. The *Commission* may however approve in-kind contributions not set out in Annex 1 without amendment (see Article 55), if:

- they are specifically justified in the periodic technical report and
- their use does not entail changes to the Agreement which would call into question the decision awarding the grant or breach the principle of equal treatment of applicants.

The beneficiaries must ensure that the Commission, the European Court of Auditors (ECA) and the European Anti-Fraud Office (OLAF) can exercise their rights under Articles 22 and 23 also towards the third parties.

12.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the costs incurred by the third parties related to the in-kind contribution will be ineligible (see Article 6) and will be rejected (see Article 42).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 13 — IMPLEMENTATION OF ACTION TASKS BY SUBCONTRACTORS

13.1 Rules for subcontracting action tasks

13.1.1 If necessary to implement the action, the beneficiaries may award subcontracts covering the implementation of certain action tasks described in Annex 1.

Subcontracting may cover only a limited part of the action.

The beneficiaries must award the subcontracts ensuring the best value for money or, if appropriate, the lowest price. In doing so, they must avoid any conflict of interests (see Article 35).

The tasks to be implemented and the estimated cost for each subcontract must be set out in Annex 1 and the total estimated costs of subcontracting per beneficiary must be set out in Annex 2. The *Commission* may however approve subcontracts not set out in Annex 1 and 2 without amendment (see Article 55), if:

- they are specifically justified in the periodic technical report and

- they do not entail changes to the Agreement which would call into question the decision awarding the grant or breach the principle of equal treatment of applicants.

The beneficiaries must ensure that the Commission, the European Court of Auditors (ECA) and the European Anti-Fraud Office (OLAF) can exercise their rights under Articles 22 and 23 also towards their subcontractors.

13.1.2 The beneficiaries must ensure that their obligations under Articles 35, 36, 38 and 46 also apply to the subcontractors.

Beneficiaries that are ‘contracting authorities’ within the meaning of Directive 2004/18/EC or ‘contracting entities’ within the meaning of Directive 2004/17/EC must comply with the applicable national law on public procurement.

13.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under Article 13.1.1, the costs related to the subcontract concerned will be ineligible (see Article 6) and will be rejected (see Article 42).

If a beneficiary breaches any of its obligations under Article 13.1.2, the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 14 — IMPLEMENTATION OF ACTION TASKS BY LINKED THIRD PARTIES

14.1 Rules for calling upon linked third parties to implement part of the action

*14.1.1 The following **affiliated entities**[9] and **third parties with a legal link to a beneficiary**[10] (‘**linked third parties**’) may implement the action tasks attributed to them in Annex 1:*

- *AGENZIA REGIONALE DI SANITA (ARS), affiliated or linked to CNR-IFC*
- *DEPARTAMENTO DE SALUD GOBIERNO VASCO (BasqueGov), affiliated or linked to BIOEF*

The linked third parties may declare as eligible the costs they incur for implementing the action tasks in accordance with Article 6.3.

The beneficiaries must ensure that the Commission, the European Court of Auditors (ECA) and the European Anti-Fraud Office (OLAF) can exercise their rights under Articles 22 and 23 also towards their linked third parties.

14.1.2 The beneficiaries must ensure that their obligations under Articles 18, 20, 35, 36 and 38 also apply to their linked third parties.

14.2 Consequences of non-compliance

If any obligation under Article 14.1.1 is breached, the costs of the linked third party will be ineligible (see Article 6) and will be rejected (see Article 42).

If any obligation under Article 14.1.2 is breached, the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 15 — FINANCIAL SUPPORT TO THIRD PARTIES

15.1 Rules for providing financial support to third parties

Not applicable

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[9] For the definition, see Article 2.1(2) of the Rules for Participation Regulation No 1290/2013: '**affiliated entity**' means any legal entity that is:
- under the direct or indirect control of a participant, or
- under the same direct or indirect control as the participant, or
- directly or indirectly controlling a participant.

‘Control’ may take any of the following forms:
(a) the direct or indirect holding of more than 50% of the nominal value of the issued share capital in the legal entity concerned, or of a majority of the voting rights of the shareholders or associates of that entity;
(b) the direct or indirect holding, in fact or in law, of decision-making powers in the legal entity concerned.

However the following relationships between legal entities shall not in themselves be deemed to constitute controlling relationships:
(a) the same public investment corporation, institutional investor or venture-capital company has a direct or indirect holding of more than 50% of the nominal value of the issued share capital or a majority of voting rights of the shareholders or associates;
(b) the legal entities concerned are owned or supervised by the same public body.

[10] ‘**Third party with a legal link to a beneficiary**’ is any legal entity which has a legal link to the beneficiary implying collaboration that is not limited to the action.

15.2 Financial support in the form of prizes

Not applicable

15.3 Consequences of non-compliance

Not applicable

ARTICLE 16 — PROVISION OF TRANS-NATIONAL OR VIRTUAL ACCESS TO RESEARCH INFRASTRUCTURE

16.1 Rules for providing trans-national access to research infrastructure

Not applicable

16.2 Rules for providing virtual access to research infrastructure

Not applicable

16.3 Consequences of non-compliance

Not applicable

SECTION 2 RIGHTS AND OBLIGATIONS RELATED TO THE GRANT ADMINISTRATION

ARTICLE 17 — GENERAL OBLIGATION TO INFORM

17.1 General obligation to provide information upon request

The beneficiaries must provide — during implementation of the action or afterwards and in accordance with Article 41.2 — any information requested in order to verify eligibility of the costs, proper implementation of the action and compliance with any other obligation under the Agreement.

17.2 Obligation to keep information up to date and to inform about events and circumstances likely to affect the Agreement

Each beneficiary must keep information stored in the 'Beneficiary Register' (via the electronic exchange system; see Article 52) up to date, in particular, its name, address, legal representatives, legal form and organisation type.

Each beneficiary must immediately inform the coordinator — which must immediately inform the *Commission* and the other beneficiaries — of any of the following:

(a) **events** which are likely to affect significantly or delay the implementation of the action or the EU's financial interests, in particular:

(i) changes in its legal, financial, technical, organisational or ownership situation *or those of its linked third parties and*

(ii) changes in the name, address, legal form, organisation type of its linked third parties;

(b) **circumstances** affecting:

(i) the decision to award the grant or

(ii) compliance with requirements under the Agreement.

17.3 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 18 — KEEPING RECORDS — SUPPORTING DOCUMENTATION

18.1 Obligation to keep records and other supporting documentation

The beneficiaries must — for a period of *five* years after the payment of the balance — keep records and other supporting documentation in order to prove the proper implementation of the action and the costs they declare as eligible.

They must make them available upon request (see Article 17) or in the context of checks, reviews, audits or investigations (see Article 22).

If there are on-going checks, reviews, audits, investigations, litigation or other pursuits of claims under the Agreement (including the extension of findings; see Articles 22), the beneficiaries must keep the records and other supporting documentation until the end of these procedures.

The beneficiaries must keep the original documents. Digital and digitalised documents are considered originals if they are authorised by the applicable national law. The *Commission* may accept non-original documents if it considers that they offer a comparable level of assurance.

18.1.1 Records and other supporting documentation on the scientific and technical implementation

The beneficiaries must keep records and other supporting documentation on scientific and technical implementation of the action in line with the accepted standards in the respective field.

18.1.2 Records and other documentation to support the costs declared

The beneficiaries must keep the records and documentation supporting the costs declared, in particular the following:

(a) for **actual costs**: adequate records and other supporting documentation to prove the costs declared, such as contracts, subcontracts, invoices and accounting records. In addition, the beneficiaries' usual cost accounting practices and internal control procedures must enable direct reconciliation between the amounts declared, the amounts recorded in their accounts and the amounts stated in the supporting documentation;

(b) for **unit costs**: adequate records and other supporting documentation to prove the number of units declared. Beneficiaries do not need to identify the actual eligible costs covered or to keep or provide supporting documentation (such as accounting statements) to prove the amount per unit.

In addition, **for direct personnel costs declared as unit costs calculated in accordance with the beneficiary's usual cost accounting practices**, the beneficiaries must keep adequate records and documentation to prove that the cost accounting practices used comply with the conditions set out in Article 6.2, Point A.

The beneficiaries *and linked third parties* may submit to the Commission, for approval, a certificate (drawn up in accordance with Annex 6) stating that their usual cost accounting practices comply with these conditions ('**certificate on the methodology**'). If the certificate is approved, costs declared in line with this methodology will not be challenged subsequently, unless the beneficiaries have concealed information for the purpose of the approval.

(c) for **flat-rate costs**: adequate records and other supporting documentation to prove the eligibility of the costs to which the flat-rate is applied. The beneficiaries do not need to identify the costs covered or provide supporting documentation (such as accounting statements) to prove the amount declared at a flat-rate.

In addition, for **personnel costs** (declared as actual costs or on the basis of unit costs), the beneficiaries must keep **time records** for the number of hours declared. The time records must be in writing and approved by the persons working on the action and their supervisors, at least monthly. In the absence of reliable time records of the hours worked on the action, the *Commission* may accept alternative evidence supporting the number of hours declared, if it considers that it offers an adequate level of assurance.

As an exception, for **persons working exclusively on the action**, there is no need to keep time records, if the beneficiary signs a **declaration** confirming that the persons concerned have worked exclusively on the action.

For costs declared by linked third parties (see Article 14), it is the beneficiary that must keep the originals of the financial statements and the certificates on the financial statements of the linked third parties.

18.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, costs insufficiently substantiated will be ineligible (see Article 6) and will be rejected (see Article 42), and the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 19 — SUBMISSION OF DELIVERABLES

19.1 Obligation to submit deliverables

The coordinator must submit the '**deliverables**' identified in Annex 1, in accordance with the timing and conditions set out in it.

19.2 Consequences of non-compliance

If the coordinator breaches any of its obligations under this Article, the *Commission* may apply any of the measures described in Chapter 6.

ARTICLE 20 — REPORTING — PAYMENT REQUESTS

20.1 Obligation to submit reports

The coordinator must submit to the *Commission* (see Article 52) the technical and financial reports set out in this Article. These reports include requests for payment and must be drawn up using the forms and templates provided in the electronic exchange system (see Article 52).

20.2 Reporting periods

The action is divided into the following '**reporting periods**':

- RP1: from month 1 to month 18
- *RP2: from month 19 to month 36*
- *RP3: from month 37 to month 54*
- *RP4: from month 55 to month 60*

20.3 Periodic reports — Requests for interim payments

The coordinator must submit a periodic report within 60 days following the end of each reporting period.

The **periodic report** must include the following:

(a) a '**periodic technical report**' containing:

(i) an **explanation of the work carried out** by the beneficiaries;

(ii) an **overview of the progress** towards the objectives of the action, including milestones and deliverables identified in Annex 1.

This report must include explanations justifying the differences between work expected to be carried out in accordance with Annex 1 and that actually carried out.

The report must also detail the exploitation and dissemination of the results and — if required in Annex 1 — an updated '**plan for the exploitation and dissemination of the results**';

(iii) a **summary** for publication by the *Commission*;

(iv) the answers to the '**questionnaire**', covering issues related to the action implementation and the economic and societal impact, notably in the context of the Horizon 2020 key performance indicators and the Horizon 2020 monitoring requirements;

(b) a '**periodic financial report**' containing:

(i) an '**individual financial statement**' (see Annex 4) from each beneficiary *and from each linked third party*, for the reporting period concerned.

The individual financial statement must detail the eligible costs (actual costs, unit costs and flat-rate costs; see Article 6) for each budget category (see Annex 2).

The beneficiaries *and linked third parties* must declare all eligible costs, even if — for actual costs, unit costs and flat-rate costs — they exceed the amounts indicated in the estimated budget (see Annex 2). Amounts which are not declared in the individual financial statement will not be taken into account by the *Commission*.

If an individual financial statement is not submitted for a reporting period, it may be included in the periodic financial report for the next reporting period.

The individual financial statements of the last reporting period must also detail the **receipts of the action** (see Article 5.3.3).

Each beneficiary *and each linked third party* must **certify** that:

- the information provided is full, reliable and true;
- the costs declared are eligible (see Article 6);
- the costs can be substantiated by adequate records and supporting documentation (see Article 18) that will be produced upon request (see Article 17) or in the context of checks, reviews, audits and investigations (see Article 22), and
- for the last reporting period: that all the receipts have been declared (see Article 5.3.3);

(ii) an **explanation of the use of resources** and the information on subcontracting (see Article 13) and in-kind contributions provided by third parties (see Articles 11 and 12) from each beneficiary *and from each linked third party*, for the reporting period concerned;

(iii) *not applicable;*

(iv) a '**periodic summary financial statement**' (see Annex 4), created automatically by the electronic exchange system, consolidating the individual financial statements for the reporting period concerned and including — except for the last reporting period — the **request for interim payment**.

20.4 Final report — Request for payment of the balance

In addition to the periodic report for the last reporting period, the coordinator must submit the final report within 60 days following the end of the last reporting period.

The **final report** must include the following:

(a) a '**final technical report**' with a **summary** for publication containing:

(i) an overview of the results and their exploitation and dissemination;

(ii) the conclusions on the action, and

(iii) the socio-economic impact of the action;

(b) a '**final financial report**' containing:

(i) a '**final summary financial statement**' (see Annex 4), created automatically by the electronic exchange system, consolidating the individual financial statements for all reporting periods and including the **request for payment of the balance** and

(ii) a '**certificate on the financial statements**' (drawn up in accordance with Annex 5) for each beneficiary *and for each linked third party*, if it requests a total contribution of EUR 325 000 or more, as reimbursement of actual costs and unit costs calculated on the basis of its usual cost accounting practices (see Article 5.2 and Article 6.2, Point A).

20.5 Information on cumulative expenditure incurred

Not applicable

20.6 Currency for financial statements and conversion into euro

Financial statements must be drafted in euro.

Beneficiaries *and linked third parties* with accounting established in a currency other than the euro must convert the costs recorded in their accounts into euro, at the average of the daily exchange rates published in the C series of the *Official Journal of the European Union*, calculated over the corresponding reporting period.

If no daily euro exchange rate is published in the *Official Journal of the European Union* for the currency in question, they must be converted at the average of the monthly accounting rates published on the Commission's website, calculated over the corresponding reporting period.

Beneficiaries *and linked third parties* with accounting established in euro must convert costs incurred in another currency into euro according to their usual accounting practices.

20.7 Language of reports

All reports (technical and financial reports, including financial statements) must be submitted in the language of the Agreement.

20.8 Consequences of non-compliance — Suspension of the payment deadline — Termination

If the reports submitted do not comply with this Article, the *Commission* may suspend the payment deadline (see Article 47) and apply any of the other measures described in Chapter 6.

If the coordinator breaches its obligation to submit the reports and if it fails to comply with this obligation within 30 days following a written reminder sent by the *Commission*, the Agreement may be terminated (see Article 50).

ARTICLE 21 — PAYMENTS AND PAYMENT ARRANGEMENTS

21.1 Payments to be made

The following payments will be made to the coordinator:

- one **pre-financing payment**;
- one or more **interim payments**, on the basis of the request(s) for interim payment (see Article 20), and
- one **payment of the balance**, on the basis of the request for payment of the balance (see Article 20).

21.2 Pre-financing payment — Amount — Amount retained for the Guarantee Fund

The aim of the pre-financing is to provide the beneficiaries with a float.

It remains the property of the *EU* until the payment of the balance.

The amount of the pre-financing payment will be EUR **2,939,229.10** (two million nine hundred and thirty nine thousand two hundred and twenty nine EURO and ten eurocents).

The *Commission* will — except if Article 48 applies — make the pre-financing payment to the coordinator within 30 days either from the entry into force of the Agreement (see Article 58) or from 10 days before the starting date of the action (see Article 3), whichever is the latest.

An amount of EUR **367,403.64** (three hundred and sixty seven thousand four hundred and three EURO and sixty four eurocents), corresponding to 5% of the maximum grant amount (see Article 5.1), is retained by the *Commission* from the pre-financing payment and transferred into the '**Guarantee Fund**'.

21.3 Interim payments — Amount — Calculation

Interim payments reimburse the eligible costs incurred for the implementation of the action during the corresponding reporting periods.

The *Commission* will pay to the coordinator the amount due as interim payment within 90 days from receiving the periodic report (see Article 20.3), except if Articles 47 or 48 apply.

Payment is subject to the approval of the periodic report. Its approval does not imply recognition of the compliance, authenticity, completeness or correctness of its content.

The **amount due as interim payment** is calculated by the *Commission* in the following steps:

Step 1 – Application of the reimbursement rates

Step 2 – Limit to 90% of the maximum grant amount

21.3.1 Step 1 — Application of the reimbursement rates

The reimbursement rate(s) (see Article 5.2) are applied to the eligible costs (actual costs, unit costs and flat-rate costs ; see Article 6) declared by the beneficiaries *and the linked third parties* (see Article 20) and approved by the *Commission* (see above) for the concerned reporting period.

21.3.2 Step 2 — Limit to 90% of the maximum grant amount

The total amount of pre-financing and interim payments must not exceed 90% of the maximum grant amount set out in Article 5.1. The maximum amount for the interim payment will be calculated as follows:

{90% of the maximum grant amount (see Article 5.1)

minus

{pre-financing and previous interim payments}}.

21.4 Payment of the balance — Amount — Calculation — Release of the amount retained for the Guarantee Fund

The payment of the balance reimburses the remaining part of the eligible costs incurred by the beneficiaries for the implementation of the action.

If the total amount of earlier payments is greater than the final grant amount (see Article 5.3), the payment of the balance takes the form of a recovery (see Article 44).

If the total amount of earlier payments is lower than the final grant amount, the *Commission* will pay the balance within 90 days from receiving the final report (see Article 20.4), except if Articles 47 or 48 apply.

Payment is subject to the approval of the final report. Its approval does not imply recognition of the compliance, authenticity, completeness or correctness of its content.

The **amount due as the balance** is calculated by the *Commission* by deducting the total amount of pre-financing and interim payments (if any) already made, from the final grant amount determined in accordance with Article 5.3:

{final grant amount (see Article 5.3)

minus

{pre-financing and interim payments (if any) made}}.

At the payment of the balance, the amount retained for the Guarantee Fund (see above) will be released and:

- if the balance is positive: the amount released will be paid in full to the coordinator together with the amount due as the balance;

- if the balance is negative (payment of the balance taking the form of recovery): it will be deducted from the amount released (see Article 44.1.2). If the resulting amount:

    - is positive, it will be paid to the coordinator

- is negative, it will be recovered.

The amount to be paid may however be offset — without the beneficiary's consent — against any other amount owed by the beneficiary to the Commission or an executive agency (under the EU or Euratom budget), up to the maximum EU contribution indicated, for that beneficiary, in the estimated budget (see Annex 2).

21.5 Notification of amounts due

When making payments, the *Commission* will formally notify to the coordinator the amount due, specifying whether it concerns an interim payment or the payment of the balance.

For the payment of the balance, the notification will also specify the final grant amount.

In the case of reduction of the grant or recovery of undue amounts, the notification will be preceded by the contradictory procedure set out in Articles 43 and 44.

21.6 Currency for payments

The *Commission* will make all payments in euro.

21.7 Payments to the coordinator — Distribution to the beneficiaries

Payments will be made to the coordinator.

Payments to the coordinator will discharge the *Commission* from its payment obligation.

The coordinator must distribute the payments between the beneficiaries without unjustified delay.

Pre-financing may however be distributed only:

(a) if the minimum number of beneficiaries set out in the call for proposals has acceded to the Agreement (see Article 56) and

(b) to beneficiaries that have acceded to the Agreement (see Article 56).

21.8 Bank account for payments

All payments will be made to the following bank account:

Name of bank: BARCLAYS BANK PLC
Address of branch: 240, WHITECHAPEL ROAD LONDON, United Kingdom
Full name of the account holder: QUEEN MARY AND WESTFIELD COLLEGE
Full account number (including bank codes):
IBAN code: GB05BARC20570658585966

21.9 Costs of payment transfers

The cost of the payment transfers is borne as follows:

- the *Commission* bears the cost of transfers charged by its bank;

- the beneficiary bears the cost of transfers charged by its bank;

- the party causing a repetition of a transfer bears all costs of the repeated transfer.

21.10 Date of payment

Payments by the *Commission* are considered to have been carried out on the date when they are debited to its account.

21.11 Consequences of non-compliance

21.11.1 If the *Commission* does not pay within the payment deadlines (see above), the beneficiaries are entitled to **late-payment interest** at the rate applied by the European Central Bank (ECB) for its main refinancing operations in euros ('reference rate'), plus three and a half points. The reference rate is the rate in force on the first day of the month in which the payment deadline expires, as published in the C series of the *Official Journal of the European Union*.

If the late-payment interest is lower than or equal to EUR 200, it will be paid to the coordinator only upon request submitted within two months of receiving the late payment.

Late-payment interest is not due if all beneficiaries are EU Member States (including regional and local government authorities or other public bodies acting on behalf of a Member State for the purpose of this Agreement).

Suspension of the payment deadline or payments (see Articles 47 and 48) will not be considered as late payment.

Late-payment interest covers the period running from the day following the due date for payment (see above), up to and including the date of payment.

Late-payment interest is not considered for the purposes of calculating the final grant amount.

21.11.2 If the coordinator breaches any of its obligations under this Article, the grant may be reduced (see Article 43) and the Agreement or the participation of the coordinator may be terminated (see Article 50).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 22 — CHECKS, REVIEWS, AUDITS AND INVESTIGATIONS — EXTENSION OF FINDINGS

22.1 Checks, reviews and audits by the Commission

22.1.1 Right to carry out checks

The Commission will — during the implementation of the action or afterwards — check the proper implementation of the action and compliance with the obligations under the Agreement, including assessing deliverables and reports.

For this purpose the Commission may be assisted by external persons or bodies.

The Commission may also request additional information in accordance with Article 17. The Commission may request beneficiaries to provide such information to it directly.

Information provided must be accurate, precise and complete and in the format requested, including electronic format.

22.1.2 Right to carry out reviews

The Commission may — during the implementation of the action or afterwards — carry out reviews on the proper implementation of the action (including assessment of deliverables and reports), compliance with the obligations under the Agreement and continued scientific or technological relevance of the action.

Reviews may be started **up to two years after the payment of the balance**. They will be formally notified to the coordinator or beneficiary concerned and will be considered to have started on the date of the formal notification.

If the review is carried out on a third party (see Articles 10 to 16), the beneficiary concerned must inform the third party.

The Commission may carry out reviews directly (using its own staff) or indirectly (using external persons or bodies appointed to do so). It will inform the coordinator or beneficiary concerned of the identity of the external persons or bodies. They have the right to object to the appointment on grounds of commercial confidentiality.

The coordinator or beneficiary concerned must provide — within the deadline requested — any information and data in addition to deliverables and reports already submitted (including information on the use of resources). The Commission may request beneficiaries to provide such information to it directly.

The coordinator or beneficiary concerned may be requested to participate in meetings, including with external experts.

For **on-the-spot** reviews, the beneficiaries must allow access to their sites and premises, including to external persons or bodies, and must ensure that information requested is readily available.

Information provided must be accurate, precise and complete and in the format requested, including electronic format.

On the basis of the review findings, a '**review report**' will be drawn up.

The Commission will formally notify the review report to the coordinator or beneficiary concerned, which has 30 days to formally notify observations ('**contradictory review procedure**').

Reviews (including review reports) are in the language of the Agreement.

22.1.3 Right to carry out audits

The Commission may — during the implementation of the action or afterwards — carry out audits on the proper implementation of the action and compliance with the obligations under the Agreement.

Audits may be started **up to two years after the payment of the balance**. They will be formally notified to the coordinator or beneficiary concerned and will be considered to have started on the date of the formal notification.

If the audit is carried out on a third party (see Articles 10 to 16), the beneficiary concerned must inform the third party.

The Commission may carry out audits directly (using its own staff) or indirectly (using external persons or bodies appointed to do so). It will inform the coordinator or beneficiary concerned of the identity of the external persons or bodies. They have the right to object to the appointment on grounds of commercial confidentiality.

The coordinator or beneficiary concerned must provide — within the deadline requested — any information (including complete accounts, individual salary statements or other personal data) to verify compliance with the Agreement. The Commission may request beneficiaries to provide such information to it directly.

For **on-the-spot** audits, the beneficiaries must allow access to their sites and premises, including to external persons or bodies, and must ensure that information requested is readily available.

Information provided must be accurate, precise and complete and in the format requested, including electronic format.

On the basis of the audit findings, a '**draft audit report**' will be drawn up.

The Commission will formally notify the draft audit report to the coordinator or beneficiary concerned, which has 30 days to formally notify observations ('**contradictory audit procedure**'). This period may be extended by the Commission in justified cases.

The '**final audit report**' will take into account observations by the coordinator or beneficiary concerned. The report will be formally notified to it.

Audits (including audit reports) are in the language of the Agreement.

The Commission may also access the beneficiaries' statutory records for the periodical assessment of unit costs or flat-rate amounts.

22.2 Investigations by the European Anti-Fraud Office (OLAF)

Under Regulations No 883/2013[15] and No 2185/96[16] (and in accordance with their provisions and procedures), the European Anti-Fraud Office (OLAF) may — at any moment during implementation of the action or afterwards — carry out investigations, including on-the-spot checks and inspections, to establish whether there has been fraud, corruption or any other illegal activity affecting the financial interests of the EU.

[15] Regulation (EU, Euratom) No 883/2013 of the European Parliament and of the Council of 11 September 2013 concerning investigations conducted by the European Anti-Fraud Office (OLAF) and repealing Regulation (EC) No 1073/1999 of the European Parliament and of the Council and Council Regulation (Euratom) No 1074/1999 (OJ L 248, 18.09.2013, p. 1).

[16] Council Regulation (Euratom, EC) No 2185/1996 of 11 November 1996 concerning on-the-spot checks and inspections carried out by the Commission in order to protect the European Communities' financial interests against fraud and other irregularities (OJ L 292, 15.11.1996, p. 2).

22.3 Checks and audits by the European Court of Auditors (ECA)

Under Article 287 of the Treaty on the Functioning of the European Union (TFEU) and Article 161 of the Financial Regulation No 966/2012[17], the European Court of Auditors (ECA) may — at any moment during implementation of the action or afterwards — carry out audits.

The ECA has the right of access for the purpose of checks and audits.

22.4 Checks, reviews, audits and investigations for international organisations

Not applicable

22.5 Consequences of findings in checks, reviews, audits and investigations — Extension of findings

22.5.1 Findings in this grant

Findings in checks, reviews, audits or investigations carried out in the context of this grant may lead to the rejection of ineligible costs (see Article 42), reduction of the grant (see Article 43), recovery of undue amounts (see Article 44) or to any of the other measures described in Chapter 6.

Rejection of costs or reduction of the grant after the payment of the balance will lead to a revised final grant amount (see Article 5.4).

Findings in checks, reviews, audits or investigations may lead to a request for amendment for the modification of Annex 1 (see Article 55).

Checks, reviews, audits or investigations that find systemic or recurrent errors, irregularities, fraud or breach of obligations may also lead to consequences in other EU or Euratom grants awarded under similar conditions (‘**extension of findings from this grant to other grants**’).

Moreover, findings arising from an OLAF investigation may lead to criminal prosecution under national law.

22.5.2 Findings in other grants

The Commission may extend findings from other grants to this grant (‘**extension of findings from other grants to this grant**’), if:

(a) the beneficiary concerned is found, in other EU or Euratom grants awarded under similar conditions, to have committed systemic or recurrent errors, irregularities, fraud or breach of obligations that have a material impact on this grant and

(b) those findings are formally notified to the beneficiary concerned — together with the list of grants affected by the findings — no later than two years after the payment of the balance of this grant.

[17] Regulation (EU, Euratom) No 966/2012 of the European Parliament and of the Council of 25 October 2012 on the financial rules applicable to the general budget of the Union and repealing Council Regulation (EC, Euratom) No 1605/2002 (OJ L 298, 26.10.2012, p. 1).

The extension of findings may lead to the rejection of costs (see Article 42), reduction of the grant (see Article 43), recovery of undue amounts (see Article 44), suspension of payments (see Article 48), suspension of the action implementation (see Article 49) or termination (see Article 50).

22.5.3 Procedure

The Commission will formally notify the beneficiary concerned the systemic or recurrent errors and its intention to extend these audit findings, together with the list of grants affected.

22.5.3.1 If the findings concern **eligibility of costs**: the formal notification will include:

(a) an invitation to submit observations on the list of grants affected by the findings;

(b) the request to submit **revised financial statements** for all grants affected;

(c) the **correction rate for extrapolation** established by the Commission on the basis of the systemic or recurrent errors, to calculate the amounts to be rejected if the beneficiary concerned:

(i) considers that the submission of revised financial statements is not possible or practicable or

(ii) does not submit revised financial statements.

The beneficiary concerned has 90 days from receiving notification to submit observations, revised financial statements or to propose a duly substantiated **alternative correction method**. This period may be extended by the Commission in justified cases.

The amounts to be rejected will be determined on the basis of the revised financial statements, subject to their approval.

If the Commission does not receive any observations or revised financial statements, does not accept the observations or the proposed alternative correction method or does not approve the revised financial statements, it will formally notify the beneficiary concerned the application of the initially notified correction rate for extrapolation.

If the Commission accepts the alternative correction method proposed by the beneficiary concerned, it will formally notify the application of the accepted alternative correction method.

22.5.3.2 If the findings concern **improper implementation** or a **breach of another obligation**: the formal notification will include:

(a) an invitation to submit observations on the list of grants affected by the findings and

(b) the flat-rate the Commission intends to apply according to the principle of proportionality.

The beneficiary concerned has 90 days from receiving notification to submit observations or to propose a duly substantiated alternative flat-rate.

If the Commission does not receive any observations or does not accept the observations or the proposed alternative flat-rate, it will formally notify the beneficiary concerned the application of the initially notified flat-rate.

If the Commission accepts the alternative flat-rate proposed by the beneficiary concerned, it will formally notify the application of the accepted alternative flat-rate.

22.6 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, any insufficiently substantiated costs will be ineligible (see Article 6) and will be rejected (see Article 42).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 23 — EVALUATION OF THE IMPACT OF THE ACTION

23.1 Right to evaluate the impact of the action

The Commission may carry out interim and final evaluations of the impact of the action measured against the objective of the *EU* programme.

Evaluations may be started during implementation of the action and up to *five* years after the payment of the balance. The evaluation is considered to start on the date of the formal notification to the coordinator or beneficiaries.

The Commission may make these evaluations directly (using its own staff) or indirectly (using external bodies or persons it has authorised to do so).

The coordinator or beneficiaries must provide any information relevant to evaluate the impact of the action, including information in electronic format.

23.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the *Commission* may apply the measures described in Chapter 6.

SECTION 3 RIGHTS AND OBLIGATIONS RELATED TO BACKGROUND AND RESULTS

SUBSECTION 1 GENERAL

ARTICLE 23a — MANAGEMENT OF INTELLECTUAL PROPERTY

23a.1 Obligation to take measures to implement the Commission Recommendation on the management of intellectual property in knowledge transfer activities

Beneficiaries that are universities or other public research organisations must take measures to implement the principles set out in Points 1 and 2 of the Code of Practice annexed to the Commission Recommendation on the management of intellectual property in knowledge transfer activities[18].

This does not change the obligations set out in Subsections 2 and 3 of this Section.

[18] Commission Recommendation C (2008) 1329 of 10.4.2008 on the management of intellectual property in knowledge transfer activities and the Code of Practice for universities and other public research institutions attached to this recommendation.

The beneficiaries must ensure that researchers and third parties involved in the action are aware of them.

23a.2 Consequences of non-compliance

If a beneficiary breaches its obligations under this Article, the *Commission* may apply any of the measures described in Chapter 6.

SUBSECTION 2 RIGHTS AND OBLIGATIONS RELATED TO BACKGROUND

ARTICLE 24 — AGREEMENT ON BACKGROUND

24.1 Agreement on background

The beneficiaries must identify and agree (in writing) on the background for the action ('**agreement on background**').

'**Background**' means any data, know-how or information — whatever its form or nature (tangible or intangible), including any rights such as intellectual property rights — that:

(a) is held by the beneficiaries before they acceded to the Agreement, and

(b) is needed to implement the action or exploit the results.

24.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 25 — ACCESS RIGHTS TO BACKGROUND

25.1 Exercise of access rights — Waiving of access rights — No sub-licensing

To exercise access rights, this must first be requested in writing ('**request for access**').

'**Access rights**' means rights to use results or background under the terms and conditions laid down in this Agreement.

Waivers of access rights are not valid unless in writing.

Unless agreed otherwise, access rights do not include the right to sub-license.

25.2 Access rights for other beneficiaries, for implementing their own tasks under the action

The beneficiaries must give each other access — on a royalty-free basis — to background needed to implement their own tasks under the action, unless the beneficiary that holds the background has — before acceding to the Agreement —:

(a) informed the other beneficiaries that access to its background is subject to legal restrictions or limits, including those imposed by the rights of third parties (including personnel), or

(b) agreed with the other beneficiaries that access would not be on a royalty-free basis.

25.3 Access rights for other beneficiaries, for exploiting their own results

The beneficiaries must give each other access — under fair and reasonable conditions — to background needed for exploiting their own results, unless the beneficiary that holds the background has — before acceding to the Agreement — informed the other beneficiaries that access to its background is subject to legal restrictions or limits, including those imposed by the rights of third parties (including personnel).

'**Fair and reasonable conditions**' means appropriate conditions, including possible financial terms or royalty-free conditions, taking into account the specific circumstances of the request for access, for example the actual or potential value of the results or background to which access is requested and/or the scope, duration or other characteristics of the exploitation envisaged.

Requests for access may be made — unless agreed otherwise — up to one year after the period set out in Article 3.

25.4 Access rights for affiliated entities

Unless otherwise agreed in the consortium agreement, access to background must also be given — under fair and reasonable conditions (see above; Article 25.3) and unless it is subject to legal restrictions or limits, including those imposed by the rights of third parties (including personnel) — to affiliated entities[19] established in an EU Member State or '**associated country**'[20], if this is needed to exploit the results generated by the beneficiaries to which they are affiliated.

Unless agreed otherwise (see above; Article 25.1), the affiliated entity concerned must make the request directly to the beneficiary that holds the background.

Requests for access may be made — unless agreed otherwise — up to one year after the period set out in Article 3.

25.5 Access rights for third parties

Not applicable

25.6 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

[19] For the definition, see 'affiliated entity' footnote (Article 14.1).

[20] For the definition, see Article 2.1(3) of the Rules for Participation Regulation No 1290/2013: '**associated country**' means a third country which is party to an international agreement with the Union, as identified in *Article 7 of Horizon 2020 Framework Programme Regulation No 1291/2013. Article 7 sets out the conditions for association of non-EU countries to Horizon 2020.*

SUBSECTION 3 RIGHTS AND OBLIGATIONS RELATED TO RESULTS

ARTICLE 26 — OWNERSHIP OF RESULTS

26.1 Ownership by the beneficiary that generates the results

Results are owned by the beneficiary that generates them.

'**Results**' means any (tangible or intangible) output of the action such as data, knowledge or information — whatever its form or nature, whether it can be protected or not — that is generated in the action, as well as any rights attached to it, including intellectual property rights.

26.2 Joint ownership by several beneficiaries

Two or more beneficiaries own results jointly if:

(a) they have jointly generated them and

(b) it is not possible to:

(i) establish the respective contribution of each beneficiary, or

(ii) separate them for the purpose of applying for, obtaining or maintaining their protection (see Article 27).

The joint owners must agree (in writing) on the allocation and terms of exercise of their joint ownership ('**joint ownership agreement**'), to ensure compliance with their obligations under this Agreement.

Unless otherwise agreed in the joint ownership agreement, each joint owner may grant non-exclusive licences to third parties to exploit jointly-owned results (without any right to sub-license), if the other joint owners are given:

(a) at least 45 days advance notice and

(b) fair and reasonable compensation.

Once the results have been generated, joint owners may agree (in writing) to apply another regime than joint ownership (such as, for instance, transfer to a single owner (see Article 30) with access rights for the others).

26.3 Rights of third parties (including personnel)

If third parties (including personnel) may claim rights to the results, the beneficiary concerned must ensure that it complies with its obligations under the Agreement.

If a third party generates results, the beneficiary concerned must obtain all necessary rights (transfer, licences or other) from the third party, in order to be able to respect its obligations as if those results were generated by the beneficiary itself.

If obtaining the rights is impossible, the beneficiary must refrain from using the third party to generate the results.

26.4 *EU* ownership, to protect results

26.4.1 *The EU* may — with the consent of the beneficiary concerned — assume ownership of results to protect them, if a beneficiary intends — up to four years after the period set out in Article 3 — to disseminate its results without protecting them, except in any of the following cases:

(a) the lack of protection is because protecting the results is not possible, reasonable or justified (given the circumstances);

(b) the lack of protection is because there is a lack of potential for commercial or industrial exploitation, or

(c) the beneficiary intends to transfer the results to another beneficiary or third party established in an EU Member State or associated country, which will protect them.

Before the results are disseminated and unless any of the cases above under Points (a), (b) or (c) applies, the beneficiary must formally notify the *Commission* and at the same time inform it of any reasons for refusing consent. The beneficiary may refuse consent only if it can show that its legitimate interests would suffer significant harm.

If the *Commission* decides to assume ownership, it will formally notify the beneficiary concerned within 45 days of receiving notification.

No dissemination relating to these results may before the end of this period or, if the *Commission* takes a positive decision, until it has taken the necessary steps to protect the results.

26.4.2 *The EU* may — with the consent of the beneficiary concerned — assume ownership of results to protect them, if a beneficiary intends — up to four years after the period set out in Article 3 — to stop protecting them or not to seek an extension of protection, except in any of the following cases:

(a) the protection is stopped because of a lack of potential for commercial or industrial exploitation;

(b) an extension would not be justified given the circumstances.

A beneficiary that intends to stop protecting results or not seek an extension must — unless any of the cases above under Points (a) or (b) applies — formally notify the *Commission* at least 60 days before the protection lapses or its extension is no longer possible and at the same time inform it of any reasons for refusing consent. The beneficiary may refuse consent only if it can show that its legitimate interests would suffer significant harm.

If the *Commission* decides to assume ownership, it will formally notify the beneficiary concerned within 45 days of receiving notification.

26.5 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such breaches may also lead to the any of the other measures described in Chapter 6.

ARTICLE 27 — PROTECTION OF RESULTS — VISIBILITY OF EU FUNDING

27.1 Obligation to protect the results

Each beneficiary must examine the possibility of protecting its results and must adequately protect them — for an appropriate period and with appropriate territorial coverage — if:

(a) the results can reasonably be expected to be commercially or industrially exploited and

(b) protecting them is possible, reasonable and justified (given the circumstances).

When deciding on protection, the beneficiary must consider its own legitimate interests and the legitimate interests (especially commercial) of the other beneficiaries.

27.2 *EU* ownership, to protect the results

If a beneficiary intends not to protect its results, to stop protecting them or not seek an extension of protection, *the EU* may — under certain conditions (see Article 26.4) — assume ownership to ensure their (continued) protection.

27.3 Information on EU funding

Applications for protection of results (including patent applications) filed by or on behalf of a beneficiary must — unless the *Commission* requests or agrees otherwise or unless it is impossible — include the following:

> *"The project leading to this application has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 733001" .*

27.4 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such a breach may also lead to any of the other measures described in Chapter 6.

ARTICLE 28 — EXPLOITATION OF RESULTS

28.1 Obligation to exploit the results

Each beneficiary must — up to four years after the period set out in Article 3 — take measures aiming to ensure '**exploitation**' of its results (either directly or indirectly, in particular through transfer or licensing; see Article 30) by:

(a) using them in further research activities (outside the action);

(b) developing, creating or marketing a product or process;

(c) creating and providing a service, or

(d) using them in standardisation activities.

This does not change the security obligations in Article 37, which still apply.

28.2 Results that could contribute to European or international standards — Information on EU funding

If results are incorporated in a standard, the beneficiary concerned must — unless the *Commission* requests or agrees otherwise or unless it is impossible — ask the standardisation body to include the following statement in (information related to) the standard:

> *"Results incorporated in this standard received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 733001" .*

28.3 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced in accordance with Article 43.

Such a breach may also lead to any of the other measures described in Chapter 6.

ARTICLE 29 — DISSEMINATION OF RESULTS — OPEN ACCESS — VISIBILITY OF EU FUNDING

29.1 Obligation to disseminate results

Unless it goes against their legitimate interests, each beneficiary must — as soon as possible — '**disseminate**' its results by disclosing them to the public by appropriate means (other than those resulting from protecting or exploiting the results), including in scientific publications (in any medium).

This does not change the obligation to protect results in Article 27, the confidentiality obligations in Article 36, the security obligations in Article 37 or the obligations to protect personal data in Article 39, all of which still apply.

A beneficiary that intends to disseminate its results must give advance notice to the other beneficiaries of — unless agreed otherwise — at least 45 days, together with sufficient information on the results it will disseminate.

Any other beneficiary may object within — unless agreed otherwise — 30 days of receiving notification, if it can show that its legitimate interests in relation to the results or background would be significantly harmed. In such cases, the dissemination may not take place unless appropriate steps are taken to safeguard these legitimate interests.

If a beneficiary intends not to protect its results, it may — under certain conditions (see Article 26.4.1) — need to formally notify the *Commission* before dissemination takes place.

29.2 Open access to scientific publications

Each beneficiary must ensure open access (free of charge online access for any user) to all peer-reviewed scientific publications relating to its results.

In particular, it must:

(a) as soon as possible and at the latest on publication, deposit a machine-readable electronic copy of the published version or final peer-reviewed manuscript accepted for publication in a repository for scientific publications;

Moreover, the beneficiary must aim to deposit at the same time the research data needed to validate the results presented in the deposited scientific publications.

(b) ensure open access to the deposited publication — via the repository — at the latest:

(i) on publication, if an electronic version is available for free via the publisher, or

(ii) within six months of publication (twelve months for publications in the social sciences and humanities) in any other case.

(c) ensure open access — via the repository — to the bibliographic metadata that identify the deposited publication.

The bibliographic metadata must be in a standard format and must include all of the following:

- the terms *"European Union (EU)" and "Horizon 2020"*;
- the name of the action, acronym and grant number;
- the publication date, and length of embargo period if applicable, and
- a persistent identifier.

29.3 Open access to research data

Not applicable

29.4 Information on EU funding — Obligation and right to use the EU emblem

Unless the *Commission* requests or agrees otherwise or unless it is impossible, any dissemination of results (in any form, including electronic) must:

(a) display the EU emblem and

(b) include the following text:

"This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 733001" .

When displayed together with another logo, the EU emblem must have appropriate prominence.

For the purposes of their obligations under this Article, the beneficiaries may use the EU emblem without first obtaining approval from the *Commission*.

This does not however give them the right to exclusive use.

Moreover, they may not appropriate the EU emblem or any similar trademark or logo, either by registration or by any other means.

29.5 Disclaimer excluding *Commission* responsibility

Any dissemination of results must indicate that it reflects only the author's view and that the *Commission* is not responsible for any use that may be made of the information it contains.

29.6 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such a breach may also lead to any of the other measures described in Chapter 6.

ARTICLE 30 — TRANSFER AND LICENSING OF RESULTS

30.1 Transfer of ownership

Each beneficiary may transfer ownership of its results.

It must however ensure that its obligations under Articles 26.2, 26.4, 27, 28, 29, 30 and 31 also apply to the new owner and that this owner has the obligation to pass them on in any subsequent transfer.

This does not change the security obligations in Article 37, which still apply.

Unless agreed otherwise (in writing) for specifically-identified third parties or unless impossible under applicable EU and national laws on mergers and acquisitions, a beneficiary that intends to transfer ownership of results must give at least 45 days advance notice (or less if agreed in writing) to the other beneficiaries that still have (or still may request) access rights to the results. This notification must include sufficient information on the new owner to enable any beneficiary concerned to assess the effects on its access rights.

Unless agreed otherwise (in writing) for specifically-identified third parties, any other beneficiary may object within 30 days of receiving notification (or less if agreed in writing), if it can show that the transfer would adversely affect its access rights. In this case, the transfer may not take place until agreement has been reached between the beneficiaries concerned.

30.2 Granting licenses

Each beneficiary may grant licences to its results (or otherwise give the right to exploit them), if:

(a) this does not impede the rights under Article 31 and

(b) *not applicable.*

In addition to Points (a) and (b), exclusive licences for results may be granted only if all the other beneficiaries concerned have waived their access rights (see Article 31.1).

This does not change the dissemination obligations in Article 29 or security obligations in Article 37, which still apply.

30.3 *Commission* right to object to transfers or licensing

Not applicable

30.4 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such a breach may also lead to any of the other measures described in Chapter 6.

ARTICLE 31 — ACCESS RIGHTS TO RESULTS

31.1 Exercise of access rights — Waiving of access rights — No sub-licensing

The conditions set out in Article 25.1 apply.

The obligations set out in this Article do not change the security obligations in Article 37, which still apply.

31.2 Access rights for other beneficiaries, for implementing their own tasks under the action

The beneficiaries must give each other access — on a royalty-free basis — to results needed for implementing their own tasks under the action.

31.3 Access rights for other beneficiaries, for exploiting their own results

The beneficiaries must give each other — under fair and reasonable conditions (see Article 25.3) — access to results needed for exploiting their own results.

Requests for access may be made — unless agreed otherwise — up to one year after the period set out in Article 3.

31.4 Access rights of affiliated entities

Unless agreed otherwise in the consortium agreement, access to results must also be given — under fair and reasonable conditions (Article 25.3) — to affiliated entities established in an EU Member State or associated country, if this is needed for those entities to exploit the results generated by the beneficiaries to which they are affiliated.

Unless agreed otherwise (see above; Article 31.1), the affiliated entity concerned must make any such request directly to the beneficiary that owns the results.

Requests for access may be made — unless agreed otherwise — up to one year after the period set out in Article 3.

31.5 Access rights for the EU institutions, bodies, offices or agencies and EU Member States

The beneficiaries must give access to their results — on a royalty-free basis — to EU institutions, bodies, offices or agencies, for developing, implementing or monitoring EU policies or programmes.

Such access rights are limited to non-commercial and non-competitive use.

This does not change the right to use any material, document or information received from the beneficiaries for communication and publicising activities (see Article 38.2).

31.6 Access rights for third parties

Not applicable

31.7 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

SECTION 4 OTHER RIGHTS AND OBLIGATIONS

ARTICLE 32 — RECRUITMENT AND WORKING CONDITIONS FOR RESEARCHERS

32.1 Obligation to take measures to implement the European Charter for Researchers and Code of Conduct for the Recruitment of Researchers

The beneficiaries must take all measures to implement the principles set out in the Commission Recommendation on the European Charter for Researchers and the Code of Conduct for the Recruitment of Researchers[22], in particular regarding:

- working conditions;
- transparent recruitment processes based on merit, and
- career development.

The beneficiaries must ensure that researchers and third parties involved in the action are aware of them.

32.2 Consequences of non-compliance

If a beneficiary breaches its obligations under this Article, the *Commission* may apply any of the measures described in Chapter 6.

ARTICLE 33 — GENDER EQUALITY

33.1 Obligation to aim for gender equality

The beneficiaries must take all measures to promote equal opportunities between men and women in the implementation of the action. They must aim, to the extent possible, for a gender balance at all levels of personnel assigned to the action, including at supervisory and managerial level.

33.2 Consequences of non-compliance

If a beneficiary breaches its obligations under this Article, the *Commission* may apply any of the measures described in Chapter 6.

[22] Commission Recommendation 2005/251/EC of 11 March 2005 on the European Charter for Researchers and on a Code of Conduct for the Recruitment of Researchers (OJ L 75, 22.3.2005, p. 67).

ARTICLE 34 — ETHICS

34.1 Obligation to comply with ethical principles

The beneficiaries must carry out the action in compliance with:

(a) ethical principles (including the highest standards of research integrity — as set out, for instance, in the European Code of Conduct for Research Integrity[23] — and including, in particular, avoiding fabrication, falsification, plagiarism or other research misconduct) and

(b) applicable international, EU and national law.

Funding will not be granted for activities carried out outside the EU if they are prohibited in all Member States.

The beneficiaries must ensure that the activities under the action have an exclusive focus on civil applications.

The beneficiaries must ensure that the activities under the action do not:

(a) aim at human cloning for reproductive purposes;

(b) intend to modify the genetic heritage of human beings which could make such changes heritable (with the exception of research relating to cancer treatment of the gonads, which may be financed), or

(c) intend to create human embryos solely for the purpose of research or for the purpose of stem cell procurement, including by means of somatic cell nuclear transfer.

34.2 Activities raising ethical issues

Activities raising ethical issues must comply with the '**ethics requirements**' set out in Annex 1.

Before the beginning of an activity raising an ethical issue, the coordinator must submit (see Article 52) to the *Commission* copy of:

(a) any ethics committee opinion required under national law and

(b) any notification or authorisation for activities raising ethical issues required under national law.

If these documents are not in English, the coordinator must also submit an English summary of the submitted opinions, notifications and authorisations (containing, if available, the conclusions of the committee or authority concerned).

If these documents are specifically requested for the action, the request must contain an explicit reference to the action title. The coordinator must submit a declaration by each beneficiary concerned that all the submitted documents cover the action tasks.

[23] The European Code of Conduct for Research Integrity of ALLEA (All European Academies) and ESF (European Science Foundation) of March 2011.
http://www.esf.org/fileadmin/Public_documents/Publications/Code_Conduct_ResearchIntegrity.pdf

34.3 Activities involving human embryos or human embryonic stem cells

Activities involving research on human embryos or human embryonic stem cells may be carried out only if:

- they are set out in Annex 1 or
- the coordinator has obtained explicit approval (in writing) from the *Commission* (see Article 52).

34.4 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43) and the Agreement or participation of the beneficiary may be terminated (see Article 50).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 35 — CONFLICT OF INTERESTS

35.1 Obligation to avoid a conflict of interests

The beneficiaries must take all measures to prevent any situation where the impartial and objective implementation of the action is compromised for reasons involving economic interest, political or national affinity, family or emotional ties or any other shared interest (‘**conflict of interests**’).

They must formally notify to the *Commission* without delay any situation constituting or likely to lead to a conflict of interests and immediately take all the necessary steps to rectify this situation.

The *Commission* may verify that the measures taken are appropriate and may require additional measures to be taken by a specified deadline.

35.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43) and the Agreement or participation of the beneficiary may be terminated (see Article 50).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 36 — CONFIDENTIALITY

36.1 General obligation to maintain confidentiality

During implementation of the action and for four years after the period set out in Article 3, the parties must keep confidential any data, documents or other material (in any form) that is identified as confidential at the time it is disclosed (‘**confidential information**’).

If a beneficiary requests, the *Commission* may agree to keep such information confidential for an additional period beyond the initial four years.

If information has been identified as confidential only orally, it will be considered to be confidential only if this is confirmed in writing within 15 days of the oral disclosure.

Unless otherwise agreed between the parties, they may use confidential information only to implement the Agreement.

The beneficiaries may disclose confidential information to their personnel or third parties involved in the action only if they:

(a) need to know to implement the Agreement and

(b) are bound by an obligation of confidentiality.

This does not change the security obligations in Article 37, which still apply.

The *Commission* may disclose confidential information to its staff, other EU institutions and bodies or third parties, if:

(a) this is necessary to implement the Agreement or safeguard the EU's financial interests and

(b) the recipients of the information are bound by an obligation of confidentiality.

Under the conditions set out in Article 4 of the Rules for Participation Regulation No 1290/2013[24], the Commission must moreover make available information on the results to other EU institutions, bodies, offices or agencies as well as Member States or associated countries.

The confidentiality obligations no longer apply if:

(a) the disclosing party agrees to release the other party;

(b) the information was already known by the recipient or is given to him without obligation of confidentiality by a third party that was not bound by any obligation of confidentiality;

(c) the recipient proves that the information was developed without the use of confidential information;

(d) the information becomes generally and publicly available, without breaching any confidentiality obligation, or

(e) the disclosure of the information is required by EU or national law.

36.2 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

[24] Regulation (EU) No 1290/2013 of the European Parliament and of the Council of 11 December 2013 laying down the rules for participation and dissemination in "Horizon 2020 - the Framework Programme for Research and Innovation (2014-2020)" (OJ L 347, 20.12.2013 p.81).

ARTICLE 37 — SECURITY-RELATED OBLIGATIONS

37.1 Results with a security recommendation

Not applicable

37.2 Classified results

Not applicable

37.3 Activities involving dual-use goods or dangerous materials and substances

Not applicable

37.4 Consequences of non-compliance

Not applicable

ARTICLE 38 — PROMOTING THE ACTION — VISIBILITY OF EU FUNDING

38.1 Communication activities by beneficiaries

38.1.1 Obligation to promote the action and its results

The beneficiaries must promote the action and its results, by providing targeted information to multiple audiences (including the media and the public) in a strategic and effective manner.

This does not change the dissemination obligations in Article 29, the confidentiality obligations in Article 36 or the security obligations in Article 37, all of which still apply.

Before engaging in a communication activity expected to have a major media impact, the beneficiaries must inform the *Commission* (see Article 52).

38.1.2 Information on EU funding — Obligation and right to use the EU emblem

Unless the *Commission* requests or agrees otherwise or unless it is impossible, any communication activity related to the action (including in electronic form, via social media, etc.) and any infrastructure, equipment and major results funded by the grant must:

(a) display the EU emblem and

(b) include the following text:

> For communication activities: *"This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 733001"* .
>
> For infrastructure, equipment and major results: *"This [infrastructure][equipment][insert type of result] is part of a project that has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 733001"* .

When displayed together with another logo, the EU emblem must have appropriate prominence.

For the purposes of their obligations under this Article, the beneficiaries may use the EU emblem without first obtaining approval from the *Commission*.

This does not, however, give them the right to exclusive use.

Moreover, they may not appropriate the EU emblem or any similar trademark or logo, either by registration or by any other means.

38.1.3 Disclaimer excluding *Commission* responsibility

Any communication activity related to the action must indicate that it reflects only the author's view and that the *Commission* is not responsible for any use that may be made of the information it contains.

38.2 Communication activities by the *Commission*

38.2.1 Right to use beneficiaries' materials, documents or information

The *Commission* may use, for its communication and publicising activities, information relating to the action, documents notably summaries for publication and public deliverables as well as any other material, such as pictures or audio-visual material that it receives from any beneficiary (including in electronic form).

This does not change the confidentiality obligations in Article 36 and the security obligations in Article 37, all of which still apply.

However, if the *Commission's* use of these materials, documents or information would risk compromising legitimate interests, the beneficiary concerned may request the *Commission* not to use it (see Article 52).

The right to use a beneficiary's materials, documents and information includes:

(a) **use for its own purposes** (in particular, making them available to persons working for the *Commission* or any other EU institution, body, office or agency or body or institutions in EU Member States; and copying or reproducing them in whole or in part, in unlimited numbers);

(b) **distribution to the public** (in particular, publication as hard copies and in electronic or digital format, publication on the internet, as a downloadable or non-downloadable file, broadcasting by any channel, public display or presentation, communicating through press information services, or inclusion in widely accessible databases or indexes);

(c) **editing or redrafting** for communication and publicising activities (including shortening, summarising, inserting other elements (such as meta-data, legends, other graphic, visual, audio or text elements), extracting parts (e.g. audio or video files), dividing into parts, use in a compilation);

(d) **translation**;

(e) giving **access in response to individual requests** under Regulation No 1049/2001[25], without the right to reproduce or exploit;

[25] Regulation (EC) No 1049/2001 of the European Parliament and of the Council of 30 May 2001 regarding public access to European Parliament, Council and Commission documents, OJ L 145, 31.5.2001, p. 43.

(f) **storage** in paper, electronic or other form;

(g) **archiving**, in line with applicable document-management rules, and

(h) the right to authorise **third parties** to act on its behalf or sub-license the modes of use set out in Points (b),(c),(d) and (f) to third parties if needed for the communication and publicising activities of the *Commission*.

If the right of use is subject to rights of a third party (including personnel of the beneficiary), the beneficiary must ensure that it complies with its obligations under this Agreement (in particular, by obtaining the necessary approval from the third parties concerned).

Where applicable (and if provided by the beneficiaries), the *Commission* will insert the following information:

> "© – [year] – [name of the copyright owner]. All rights reserved. Licensed to the *European Union (EU)* under conditions."

38.3 Consequences of non-compliance

If a beneficiary breaches any of its obligations under this Article, the grant may be reduced (see Article 43).

Such breaches may also lead to any of the other measures described in Chapter 6.

ARTICLE 39 — PROCESSING OF PERSONAL DATA

39.1 Processing of personal data by the Commission

Any personal data under the Agreement will be processed by the Commission under Regulation No 45/2001[26] and according to the 'notifications of the processing operations' to the Data Protection Officer (DPO) of the Commission (publicly accessible in the DPO register).

Such data will be processed by the '**data controller**' of the Commission for the purposes of implementing, managing and monitoring the Agreement or protecting the financial interests of the EU or Euratom (including checks, reviews, audits and investigations; see Article 22).

The persons whose personal data are processed have the right to access and correct their own personal data. For this purpose, they must send any queries about the processing of their personal data to the data controller, via the contact point indicated in the 'service specific privacy statement(s) (SSPS)' that are published on the Commission websites.

They also have the right to have recourse at any time to the European Data Protection Supervisor (EDPS).

[26] Regulation (EC) No 45/2001 of the European Parliament and of the Council of 18 December 2000 on the protection of individuals with regard to the processing of personal data by the Community institutions and bodies and on the free movement of such data (OJ L 8, 12.01.2001, p. 1).

39.2 Processing of personal data by the beneficiaries

The beneficiaries must process personal data under the Agreement in compliance with applicable EU and national law on data protection (including authorisations or notification requirements).

The beneficiaries may grant their personnel access only to data that is strictly necessary for implementing, managing and monitoring the Agreement.

The beneficiaries must inform the personnel whose personal data are collected and processed by the Commission. For this purpose, they must provide them with the service specific privacy statement (SSPS) (see above), before transmitting their data to the Commission.

39.3 Consequences of non-compliance

If a beneficiary breaches any of its obligations under Article 39.2, the *Commission* may apply any of the measures described in Chapter 6.

ARTICLE 40 — ASSIGNMENTS OF CLAIMS FOR PAYMENT AGAINST THE *COMMISSION*

The beneficiaries may not assign any of their claims for payment against the *Commission* to any third party, except if approved by the *Commission* on the basis of a reasoned, written request by the coordinator (on behalf of the beneficiary concerned).

If the *Commission* has not accepted the assignment or the terms of it are not observed, the assignment will have no effect on it.

In no circumstances will an assignment release the beneficiaries from their obligations towards the *Commission*.

CHAPTER 5 DIVISION OF BENEFICIARIES' ROLES AND RESPONSIBILITIES

ARTICLE 41 — DIVISION OF BENEFICIARIES' ROLES AND RESPONSIBILITIES — RELATIONSHIP WITH COMPLEMENTARY BENEFICIARIES — RELATIONSHIP WITH PARTNERS OF A JOINT ACTION

41.1 Roles and responsibilities towards the *Commission*

The beneficiaries have full responsibility for implementing the action and complying with the Agreement.

The beneficiaries are jointly and severally liable for the **technical implementation** of the action as described in Annex 1. If a beneficiary fails to implement its part of the action, the other beneficiaries become responsible for implementing this part (without being entitled to any additional EU funding for doing so), unless the *Commission* expressly relieves them of this obligation.

The **financial responsibility** of each beneficiary is governed by Articles 44, 45 and 46.

41.2 Internal division of roles and responsibilities

The internal roles and responsibilities of the beneficiaries are divided as follows:

(a) Each **beneficiary** must:

(i) keep information stored in the 'Beneficiary Register' (via the electronic exchange system) up to date (see Article 17);

(ii) inform the coordinator immediately of any events or circumstances likely to affect significantly or delay the implementation of the action (see Article 17);

(iii) submit to the coordinator in good time:

- individual financial statements for itself *and its linked third parties* and, if required, certificates on the financial statements (see Article 20);

- the data needed to draw up the technical reports (see Article 20);

- ethics committee opinions and notifications or authorisations for activities raising ethical issues (see Article 34);

- any other documents or information required by the Commission under the Agreement, unless the Agreement requires the beneficiary to submit this information directly to the Commission.

(b) The **coordinator** must:

(i) monitor that the action is implemented properly (see Article 7);

(ii) act as the intermediary for all communications between the beneficiaries and the *Commission* (in particular, providing the *Commission* with the information described in Article 17), unless the Agreement specifies otherwise;

(iii) request and review any documents or information required by the *Commission* and verify their completeness and correctness before passing them on to the *Commission*;

(iv) submit the deliverables and reports to the *Commission* (see Articles 19 and 20);

(v) ensure that all payments are made to the other beneficiaries without unjustified delay (see Article 21);

(vi) inform the *Commission* of the amounts paid to each beneficiary, when required under the Agreement (see Articles 44 and 50) or requested by the *Commission*.

The coordinator may not delegate the above-mentioned tasks to any other beneficiary or subcontract them to any third party.

41.3 Internal arrangements between beneficiaries — Consortium agreement

*The beneficiaries must have internal arrangements regarding their operation and co-ordination to ensure that the action is implemented properly. These internal arrangements must be set out in a written '**consortium agreement**' between the beneficiaries, which may cover:*

- *internal organisation of the consortium;*
- *management of access to the electronic exchange system;*
- *distribution of EU funding;*
- *additional rules on rights and obligations related to background and results (including whether access rights remain or not, if a beneficiary is in breach of its obligations) (see Section 3 of Chapter 4);*
- *settlement of internal disputes;*
- *liability, indemnification and confidentiality arrangements between the beneficiaries.*

The consortium agreement must not contain any provision contrary to the Agreement.

41.4 Relationship with complementary beneficiaries — Collaboration agreement

Not applicable

41.5 Relationship with partners of a joint action — Coordination agreement

Not applicable

CHAPTER 6 REJECTION OF COSTS — REDUCTION OF THE GRANT — RECOVERY — PENALTIES — DAMAGES — SUSPENSION — TERMINATION — FORCE MAJEURE

SECTION 1 REJECTION OF COSTS — REDUCTION OF THE GRANT — RECOVERY — PENALTIES

ARTICLE 42 — REJECTION OF INELIGIBLE COSTS

42.1 Conditions

42.1.1 The *Commission* will — at the time of an **interim payment**, **at the payment of the balance** or **afterwards** — reject any costs which are ineligible (see Article 6), in particular following checks, reviews, audits or investigations (see Article 22).

42.1.2 The rejection may also be based on the **extension of findings from other grants to this grant**, under the conditions set out in Article 22.5.2.

42.2 Ineligible costs to be rejected — Calculation — Procedure

Ineligible costs will be rejected in full.

If the *Commission* rejects costs **without reduction of the grant** (see Article 43) or **recovery of undue amounts** (see Article 44), it will formally notify the coordinator or beneficiary concerned the rejection of costs, the amounts and the reasons why (if applicable, together with the notification of amounts due; see Article 21.5). The coordinator or beneficiary concerned may — within 30 days of receiving notification — formally notify the *Commission* of its disagreement and the reasons why.

If the *Commission* rejects costs **with reduction of the grant** or **recovery of undue amounts**, it will formally notify the rejection in the '**pre-information letter**' on reduction or recovery set out in Articles 43 and 44.

42.3 Effects

If the *Commission* rejects costs at the time of an **interim payment** or **the payment of the balance**, it will deduct them from the total eligible costs declared, for the action, in the periodic or final summary financial statement (see Articles 20.3 and 20.4). It will then calculate the interim payment or payment of the balance as set out in Articles 21.3 or 21.4.

If the *Commission* — **after an interim payment but before the payment of the balance** — rejects costs declared in a periodic summary financial statement, it will deduct them from the total eligible costs declared, for the action, in the next periodic summary financial statement or in the final summary financial statement. It will then calculate the interim payment or payment of the balance as set out in Articles 21.3 or 21.4.

If the *Commission* rejects costs **after the payment of the balance**, it will deduct the amount rejected from the total eligible costs declared, by the beneficiary, in the final summary financial statement. It will then calculate the revised final grant amount as set out in Article 5.4.

ARTICLE 43 — REDUCTION OF THE GRANT

43.1 Conditions

43.1.1 The *Commission* may — **at the payment of the balance** or **afterwards** — reduce the maximum grant amount (see Article 5.1), if the action has not been implemented properly as described in Annex 1 or another obligation under the Agreement has been breached.

43.1.2 The *Commission* may also reduce the maximum grant amount on the basis of the **extension of findings from other grants to this grant**, under the conditions set out in Article 22.5.2.

43.2 Amount to be reduced — Calculation — Procedure

The amount of the reduction will be proportionate to the improper implementation of the action or to the seriousness of the breach.

Before reduction of the grant, the *Commission* will formally notify a '**pre-information letter**' to the coordinator or beneficiary concerned:

- informing it of its intention to reduce the grant, the amount it intends to reduce and the reasons why and

- inviting it to submit observations within 30 days of receiving notification

If the *Commission* does not receive any observations or decides to pursue reduction despite the observations it has received, it will formally notify **confirmation** of the reduction (if applicable, together with the notification of amounts due; see Article 21).

43.3 Effects

If the *Commission* reduces the grant at the time of **the payment of the balance**, it will calculate the reduced grant amount for the action and then determine the amount due as payment of the balance (see Articles 5.3.4 and 21.4).

If the *Commission* reduces the grant **after the payment of the balance**, it will calculate the revised final grant amount for the beneficiary concerned (see Article 5.4). If the revised final grant amount for the beneficiary concerned is lower than its share of the final grant amount, the *Commission* will recover the difference (see Article 44).

ARTICLE 44 — RECOVERY OF UNDUE AMOUNTS

44.1 Amount to be recovered — Calculation — Procedure

The *Commission* will — after **termination of the participation of a beneficiary, at the payment of the balance** or **afterwards** — claim back any amount that was paid but is not due under the Agreement.

Each beneficiary's financial responsibility in case of recovery is limited to its own debt *(including undue amounts paid by the Commission for costs declared by its linked third parties)*, except for the amount retained for the Guarantee Fund (see Article 21.4).

44.1.1 Recovery after termination of a beneficiary's participation

If recovery takes place after termination of a beneficiary's participation (including the coordinator), the *Commission* will claim back the undue amount from the beneficiary concerned, by formally notifying it a debit note (see Article 50.2 and 50.3). This note will specify the amount to be recovered, the terms and the date for payment.

If payment is not made by the date specified in the debit note, the Commission will **recover** the amount:

(a) by '**offsetting**' it — without the beneficiary's consent — against any amounts owed to the beneficiary concerned by the Commission or an executive agency (from the EU or Euratom budget).

In exceptional circumstances, to safeguard the EU's financial interests, the *Commission* may offset before the payment date specified in the debit note;

(b) *not applicable;*

(c) by **taking legal action** (see Article 57) or by **adopting an enforceable decision** under Article 299 of the Treaty on the Functioning of the EU (TFEU) and Article 79(2) of the Financial regulation No 966/2012.

If payment is not made by the date specified in the debit note, the amount to be recovered (see above) will be increased by **late-payment interest** at the rate set out in Article 21.11, from the day following the payment date in the debit note, up to and including the date the Commission receives full payment of the amount.

Partial payments will be first credited against expenses, charges and late-payment interest and then against the principal.

Bank charges incurred in the recovery process will be borne by the beneficiary, unless Directive 2007/64/EC[27] applies.

44.1.2 Recovery at payment of the balance

If the payment of the balance takes the form of a recovery (see Article 21.4), the *Commission* will formally notify a '**pre-information letter**' to the coordinator:

- informing it of its intention to recover, the amount due as the balance and the reasons why;
- specifying that it intends to deduct the amount to be recovered from the amount retained for the Guarantee Fund;
- requesting the coordinator to submit a report on the distribution of payments to the beneficiaries within 30 days of receiving notification, and
- inviting the coordinator to submit observations within 30 days of receiving notification.

If no observations are submitted or the *Commission* decides to pursue recovery despite the observations it has received, it will **confirm recovery** (together with the notification of amounts due; see Article 21.5) and:

- pay the difference between the amount to be recovered and the amount retained for the Guarantee Fund, **if the difference is positive** or
- formally notify to the coordinator a **debit note** for the difference between the amount to be recovered and the amount retained for the Guarantee Fund, **if the difference is negative**. This note will also specify the terms and the date for payment.

If the coordinator does not repay the *Commission* by the date in the debit note and has not submitted the report on the distribution of payments: the Commission will **recover** the amount set out in the debit note from the coordinator (see below).

If the coordinator does not repay the *Commission* by the date in the debit note, but has submitted the report on the distribution of payments: the *Commission* will:

(a) identify the beneficiaries for which the amount calculated as follows is negative:

{{{{beneficiary's costs declared in the final summary financial statement and approved by the *Commission* multiplied by the reimbursement rate set out in Article 5.2 for the beneficiary concerned

[27] Directive 2007/64/EC of the European Parliament and of the Council of 13 November 2007 on payment services in the internal market amending Directives 97/7/EC, 2002/65/EC, 2005/60/EC and 2006/48/EC and repealing Directive 97/5/EC (OJ L 319, 05.12.2007, p. 1).

plus

its linked third parties' costs declared in the final summary financial statement and approved by the Commission multiplied by the reimbursement rate set out in Article 5.2 for each linked third party concerned}

divided by

the EU contribution for the action calculated according to Article 5.3.1}

multiplied by

the final grant amount (see Article 5.3)},

minus

{pre-financing and interim payments received by the beneficiary}}.

(b) formally notify to each beneficiary identified according to point (a) a **debit note** specifying the terms and date for payment. The amount of the debit note is calculated as follows:

{{amount calculated according to point (a) for the beneficiary concerned

divided by

the sum of the amounts calculated according to point (a) for all the beneficiaries identified according to point (a)}

multiplied by

the amount set out in the debit note formally notified to the coordinator}.

If payment is not made by the date specified in the debit note, the *Commission* will **recover** the amount:

(a) by '**offsetting**' it — without the beneficiary's consent — against any amounts owed to the beneficiary concerned by the Commission or an executive agency (from the EU or Euratom budget).

In exceptional circumstances, to safeguard the EU's financial interests, the *Commission* may offset before the payment date specified in the debit note;

(b) by **drawing on the Guarantee Fund**. The Commission will formally notify the beneficiary concerned the debit note on behalf of the Guarantee Fund and recover the amount:

(i) *not applicable;*

(ii) by **taking legal action** (see Article 57) or by **adopting an enforceable decision** under Article 299 of the Treaty on the Functioning of the EU (TFEU) and Article 79(2) of the Financial Regulation No 966/2012.

If payment is not made by the date in the debit note, the amount to be recovered (see above) will be increased by **late-payment interest** at the rate set out in Article 21.11, from the day following the payment date in the debit note, up to and including the date the Commission receives full payment of the amount.

Partial payments will be first credited against expenses, charges and late-payment interest and then against the principal.

Bank charges incurred in the recovery process will be borne by the beneficiary, unless Directive 2007/64/EC applies.

44.1.3 Recovery of amounts after payment of the balance

If, for a beneficiary, the revised final grant amount (see Article 5.4) is lower than its share of the final grant amount, it must repay the difference to the *Commission*.

The beneficiary's share of the final grant amount is calculated as follows:

{{{beneficiary's costs declared in the final summary financial statement and approved by the *Commission* multiplied by the reimbursement rate set out in Article 5.2 for the beneficiary concerned

plus

its linked third parties' costs declared in the final summary financial statement and approved by the Commission multiplied by the reimbursement rate set out in Article 5.2 for each linked third party concerned}

divided by

the EU contribution for the action calculated according to Article 5.3.1}

multiplied by

the final grant amount (see Article 5.3)}.

If the coordinator has not distributed amounts received (see Article 21.7), the *Commission* will also recover these amounts.

The *Commission* will formally notify a **pre-information letter** to the beneficiary concerned:

- informing it of its intention to recover, the due amount and the reasons why and
- inviting it to submit observations within 30 days of receiving notification.

If no observations are submitted or the *Commission* decides to pursue recovery despite the observations it has received, it will **confirm** the amount to be recovered and formally notify to the beneficiary concerned a **debit note**. This note will also specify the terms and the date for payment.

If payment is not made by the date specified in the debit note, the *Commission* will **recover** the amount:

(a) by '**offsetting**' it — without the beneficiary's consent — against any amounts owed to the beneficiary concerned by the Commission or an executive agency (from the EU or Euratom budget).

In exceptional circumstances, to safeguard the EU's financial interests, the *Commission* may offset before the payment date specified in the debit note;

(b) by **drawing on the Guarantee Fund**. The Commission will formally notify the beneficiary concerned the debit note on behalf of the Guarantee Fund and recover the amount:

(i) *not applicable;*

(ii) by **taking legal action** (see Article 57) or by **adopting an enforceable decision** under Article 299 of the Treaty on the Functioning of the EU (TFEU) and Article 79(2) of the Financial Regulation No 966/2012.

If payment is not made by the date in the debit note, the amount to be recovered (see above) will be increased by **late-payment interest** at the rate set out in Article 21.11, from the day following the date for payment in the debit note, up to and including the date the Commission receives full payment of the amount.

Partial payments will be first credited against expenses, charges and late-payment interest and then against the principal.

Bank charges incurred in the recovery process will be borne by the beneficiary, unless Directive 2007/64/EC applies.

ARTICLE 45 — ADMINISTRATIVE AND FINANCIAL PENALTIES

45.1 Conditions

Under Articles 109 and 131(4) of the Financial Regulation No 966/2012, the *Commission* may impose **administrative** and **financial penalties** if a beneficiary:

(a) has committed substantial errors, irregularities or fraud or is in serious breach of its obligations under the Agreement or

(b) has made false declarations about information required under the Agreement or for the submission of the proposal (or has not supplied such information).

Each beneficiary is responsible for paying the financial penalties imposed on it.

Under Article 109(3) of the Financial Regulation No 966/2012, the Commission may — under certain conditions and limits — publish decisions imposing administrative or financial penalties.

45.2 Duration — Amount of penalty — Calculation

Administrative penalties exclude the beneficiary from all contracts and grants financed from the EU or Euratom budget for a maximum of five years from the date the infringement is established by the *Commission*.

If the beneficiary commits another infringement within five years of the date the first infringement is established, the *Commission* may extend the exclusion period up to 10 years.

Financial penalties will be between 2% and 10% of the maximum EU contribution indicated, for the beneficiary concerned, in the estimated budget (see Annex 2).

If the beneficiary commits another infringement within five years of the date the first infringement is established, the *Commission* may increase the rate of financial penalties to between 4% and 20%.

45.3 Procedure

Before applying a penalty, the *Commission* will formally notify the beneficiary concerned:

- informing it of its intention to impose a penalty, its duration or amount and the reasons why and

- inviting it to submit observations within 30 days.

If the *Commission* does not receive any observations or decides to impose the penalty despite of observations it has received, it will formally notify **confirmation** of the penalty to the beneficiary concerned and — in case of financial penalties — deduct the penalty from the payment of the balance or formally notify a **debit note**, specifying the amount to be recovered, the terms and the date for payment.

If payment is not made by the date specified in the debit note, the Commission may **recover** the amount:

(a) by '**offsetting**' it — without the beneficiary's consent — against any amounts owed to the beneficiary concerned by the Commission or an executive agency (from the EU or Euratom budget).

In exceptional circumstances, to safeguard the EU's financial interests, the *Commission* may offset before the payment date specified in the debit note;

(b) by **taking legal action** (see Article 57) or by **adopting an enforceable decision** under Article 299 of the Treaty on the Functioning of the EU (TFEU) and Article 79(2) of the Financial Regulation No 966/2012.

If payment is not made by the date in the debit note, the amount to be recovered (see above) will be increased by **late-payment interest** at the rate set out in Article 21.11, from the day following the payment date in the debit note, up to and including the date the Commission receives full payment of the amount.

Partial payments will be first credited against expenses, charges and late-payment interest and then against the principal.

Bank charges incurred in the recovery process will be borne by the beneficiary, unless Directive 2007/64/EC applies.

SECTION 2 LIABILITY FOR DAMAGES

ARTICLE 46 — LIABILITY FOR DAMAGES

46.1 Liability of the *Commission*

The *Commission* cannot be held liable for any damage caused to the beneficiaries or to third parties as a consequence of implementing the Agreement, including for gross negligence.

The *Commission* cannot be held liable for any damage caused by any of the beneficiaries or third parties involved in the action, as a consequence of implementing the Agreement.

46.2 Liability of the beneficiaries

46.2.1 Conditions

Except in case of force majeure (see Article 51), the beneficiaries must compensate the *Commission* for any damage it sustains as a result of the implementation of the action or because the action was not implemented in full compliance with the Agreement.

Each beneficiary is responsible for paying the damages claimed from it.

46.2.2 Amount of damages - Calculation

The amount the *Commission* can claim from a beneficiary will correspond to the damage caused by that beneficiary.

46.2.3 Procedure

Before claiming damages, the *Commission* will formally notify the beneficiary concerned:

- informing it of its intention to claim damages, the amount and the reasons why and
- inviting it to submit observations within 30 days.

If the *Commission* does not receive any observations or decides to claim damages despite the observations it has received, it will formally notify **confirmation** of the claim for damages and a **debit note**, specifying the amount to be recovered, the terms and the date for payment.

If payment is not made by the date specified in the debit note, the Commission may **recover** the amount:

(a) by '**offsetting**' it — without the beneficiary's consent — against any amounts owed to the beneficiary concerned by the Commission or an executive agency (from the EU or Euratom budget).

In exceptional circumstances, to safeguard the EU's financial interests, the *Commission* may offset before the payment date specified in the debit note;

(b) by **taking legal action** (see Article 57) or by **adopting an enforceable decision** under Article 299 of the Treaty on the Functioning of the EU (TFEU) and Article 79(2) of the Financial Regulation No 966/2012.

If payment is not made by the date in the debit note, the amount to be recovered (see above) will be increased by **late-payment interest** at the rate set out in Article 21.11, from the day following the

payment date in the debit note, up to and including the date the Commission receives full payment of the amount.

Partial payments will be first credited against expenses, charges and late-payment interest and then against the principal.

Bank charges incurred in the recovery process will be borne by the beneficiary, unless Directive 2007/64/EC applies.

SECTION 3 SUSPENSION AND TERMINATION

ARTICLE 47 — SUSPENSION OF PAYMENT DEADLINE

47.1 Conditions

The *Commission* may — at any moment — suspend the payment deadline (see Article 21.2 to 21.4) if a request for payment (see Article 20) cannot be approved because:

(a) it does not comply with the provisions of the Agreement (see Article 20);

(b) the technical reports or financial reports have not been submitted or are not complete or additional information is needed, or

(c) there is doubt about the eligibility of the costs declared in the financial statements and additional checks, reviews, audits or investigations are necessary.

47.2 Procedure

The *Commission* will formally notify the coordinator of the suspension and the reasons why.

The suspension will **take effect** the day notification is sent by the *Commission* (see Article 52).

If the conditions for suspending the payment deadline are no longer met, the suspension will be **lifted** — and the remaining period will resume.

If the suspension exceeds two months, the coordinator may request the *Commission* if the suspension will continue.

If the payment deadline has been suspended due to the non-compliance of the technical or financial reports (see Article 20) and the revised report or statement is not submitted or was submitted but is also rejected, the *Commission* may also terminate the Agreement or the participation of the beneficiary (see Article 50.3.1(l)).

ARTICLE 48 — SUSPENSION OF PAYMENTS

48.1 Conditions

The *Commission* may — at any moment — suspend, in whole or in part, the pre-financing payment and interim payments for one or more beneficiaries or the payment of the balance for all beneficiaries, if a beneficiary:

(a) has committed or is suspected of having committed substantial errors, irregularities, fraud or serious breach of obligations in the award procedure or under this Agreement or

(b) has committed — in other EU or Euratom grants awarded to it under similar conditions — systemic or recurrent errors, irregularities, fraud or serious breach of obligations that have a material impact on this grant (**extension of findings from other grants to this grant**; see Article 22.5.2).

48.2 Procedure

Before suspending payments, the *Commission* will formally notify the coordinator:

- informing it of its intention to suspend payments and the reasons why and

- inviting it to submit observations within 30 days of receiving notification.

If the *Commission* does not receive observations or decides to pursue the procedure despite the observations it has received, it will formally notify **confirmation** of the suspension. Otherwise, it will formally notify that the suspension procedure is not continued.

The suspension will **take effect** the day the confirmation notification is sent by the *Commission*.

If the conditions for resuming payments are met, the suspension will be **lifted**. The *Commission* will formally notify the coordinator.

During the suspension, the periodic report(s) (see Article 20.3) must not contain any individual financial statements from the beneficiary concerned *and its linked third parties*. When the *Commission* resumes payments, the coordinator may include them in the next periodic report.

The beneficiaries may suspend implementation of the action (see Article 49.1) or terminate the Agreement or the participation of the beneficiary concerned (see Article 50.1 and 50.2).

ARTICLE 49 — SUSPENSION OF THE ACTION IMPLEMENTATION

49.1 Suspension of the action implementation, by the beneficiaries

49.1.1 Conditions

The beneficiaries may suspend implementation of the action or any part of it, if exceptional circumstances — in particular *force majeure* (see Article 51) — make implementation impossible or excessively difficult.

49.1.2 Procedure

The coordinator must immediately formally notify to the *Commission* the suspension (see Article 52), stating:

- the reasons why and

- the expected date of resumption.

The suspension will **take effect** the day this notification is received by the *Commission*.

Once circumstances allow for implementation to resume, the coordinator must immediately formally notify the *Commission* and request an **amendment** of the Agreement to set the date on which the action will be resumed, extend the duration of the action and make other changes necessary to adapt the action to the new situation (see Article 55) — unless the Agreement or the participation of a beneficiary has been terminated (see Article 50).

The suspension will be **lifted** with effect from the resumption date set out in the amendment. This date may be before the date on which the amendment enters into force.

Costs incurred during suspension of the action implementation are not eligible (see Article 6).

49.2 Suspension of the action implementation, by the *Commission*

49.2.1 Conditions

The *Commission* may suspend implementation of the action or any part of it:

(a) if a beneficiary has committed or is suspected of having committed substantial errors, irregularities, fraud or serious breach of obligations in the award procedure or under this Agreement;

(b) if a beneficiary has committed — in other EU or Euratom grants awarded to it under similar conditions — systemic or recurrent errors, irregularities, fraud or serious breach of obligations that have a material impact on this grant (**extension of findings from other grants to this grant**; see Article 22.5.2), or

(c) if the action is suspected of having lost its scientific or technological relevance.

49.2.2 Procedure

Before suspending implementation of the action, the *Commission* will formally notify the coordinator:

- informing it of its intention to suspend the implementation and the reasons why and

- inviting it to submit observations within 30 days of receiving notification.

If the *Commission* does not receive observations or decides to pursue the procedure despite the observations it has received, it will formally notify **confirmation** of the suspension. Otherwise, it will formally notify that the procedure is not continued.

The suspension will **take effect** five days after confirmation notification is received by the coordinator (or on a later date specified in the notification).

It will be **lifted** if the conditions for resuming implementation of the action are met.

The coordinator will be formally notified of the lifting and the Agreement will be **amended** to set the date on which the action will be resumed, extend the duration of the action and make other changes necessary to adapt the action to the new situation (see Article 55) — unless the Agreement has already been terminated (see Article 50).

The suspension will be lifted with effect from the resumption date set out in the amendment. This date may be before the date on which the amendment enters into force.

Costs incurred during suspension are not eligible (see Article 6).

The beneficiaries may not claim damages due to suspension by the *Commission* (see Article 46).

Suspension of the action implementation does not affect the *Commission's* right to terminate the Agreement or participation of a beneficiary (see Article 50), reduce the grant or recover amounts unduly paid (see Articles 43 and 44).

ARTICLE 50 — TERMINATION OF THE AGREEMENT OR OF THE PARTICIPATION OF ONE OR MORE BENEFICIARIES

50.1 Termination of the Agreement by the beneficiaries

50.1.1 Conditions and procedure

The beneficiaries may terminate the Agreement.

The coordinator must formally notify termination to the *Commission* (see Article 52), stating:

- the reasons why and
- the date the termination will take effect. This date must be after the notification.

If no reasons are given or if the *Commission* considers the reasons do not justify termination, the Agreement will be considered to have been '**terminated improperly**'.

The termination will **take effect** on the day specified in the notification.

50.1.2 Effects

The coordinator must — within 60 days from when termination takes effect — submit:

(i) a periodic report (for the open reporting period until termination; see Article 20.3) and

(ii) the final report (see Article 20.4).

If the *Commission* does not receive the reports within the deadline (see above), only costs which are included in an approved periodic report will be taken into account.

The *Commission* will **calculate** the final grant amount (see Article 5.3) and the balance (see Article 21.4) on the basis of the reports submitted. Only costs incurred until termination are eligible (see Article 6). Costs relating to contracts due for execution only after termination are not eligible.

Improper termination may lead to a reduction of the grant (see Article 43).

After termination, the beneficiaries' obligations (in particular Articles 20, 22, 23, Section 3 of Chapter 4, 36, 37, 38 and 40) continue to apply.

50.2 Termination of the participation of one or more beneficiaries, by the beneficiaries

50.2.1 Conditions and procedure

The participation of one or more beneficiaries may be terminated by the coordinator, on request of the beneficiary concerned or on behalf of the other beneficiaries.

The coordinator must formally notify termination to the *Commission* (see Article 52) and inform the beneficiary concerned.

If the coordinator's participation is terminated without its agreement, the formal notification must be done by another beneficiary (acting on behalf of the other beneficiaries).

The notification must include:

- the reasons why;
- the opinion of the beneficiary concerned (or proof that this opinion has been requested in writing);
- the date the termination takes effect. This date must be after the notification, and
- a request for amendment (see Article 55), with a proposal for reallocation of the tasks and the estimated budget of the beneficiary concerned (see Annexes 1 and 2) and, if necessary, the addition of one or more new beneficiaries (see Article 56). If termination takes effect after the period set out in Article 3, no request for amendment must be included unless the beneficiary concerned is the coordinator. In this case, the request for amendment must propose a new coordinator.

If this information is not given or if the *Commission* considers that the reasons do not justify termination, the participation will be considered to have been **terminated improperly**.

The termination will **take effect** on the day specified in the notification.

50.2.2 Effects

The coordinator must — within 30 days from when termination takes effect — submit:

(i) a report on the distribution of payments to the beneficiary concerned and

(ii) if termination takes effect during the period set out in Article 3, a '**termination report**' from the beneficiary concerned, for the open reporting period until termination, containing an overview of the progress of the work, an overview of the use of resources, the individual financial statement and, if applicable, the certificate on the financial statement (see Articles 20.3 and 20.4).

The information in the termination report must also be included in the periodic report for the next reporting period (see Article 20.3).

If the request for amendment is rejected by the *Commission*, (because it calls into question the decision awarding the grant or breaches the principle of equal treatment of applicants), the Agreement may be terminated according to Article 50.3.1(c).

If the request for amendment is accepted by the *Commission*, the Agreement is **amended** to introduce the necessary changes (see Article 55).

The *Commission* will **calculate** — on the basis of the periodic reports, the termination report and the report on the distribution of payments — if the (pre-financing and interim) payments received by the beneficiary concerned exceed the beneficiary's EU contribution (calculated by applying the reimbursement rate(s) to the eligible costs declared by the beneficiary *and its linked third parties* and approved by the *Commission*). Only costs incurred by the beneficiary concerned until termination takes effect are eligible (see Article 6). Costs relating to contracts due for execution only after termination are not eligible.

- If the payments received **exceed the amounts due**:

  - if termination takes effect during the period set out in Article 3 and the request for amendment is accepted, the beneficiary concerned must repay to the coordinator the amount unduly received. The *Commission* will formally notify the amount unduly received and request the beneficiary concerned to repay it to the coordinator within 30 days of receiving notification. If it does not repay the coordinator, the *Commission* will draw upon the Guarantee Fund to pay the coordinator and then notify a **debit note** on behalf of the Guarantee Fund to the beneficiary concerned (see Article 44);

  - in all other cases (in particular if termination takes effect after the period set out in Article 3), the *Commission* will formally notify a **debit note** to the beneficiary concerned. If payment is not made by the date in the debit note, the Guarantee Fund will pay to the *Commission* the amount due and the *Commission* will notify a debit note on behalf of the Guarantee Fund to the beneficiary concerned (see Article 44);

  - if the beneficiary concerned is the former coordinator, it must repay the new coordinator according to the procedure above, unless:

    - termination is after an interim payment and

    - the former coordinator has not distributed amounts received as pre-financing or interim payments (see Article 21.7).

    In this case, the *Commission* will formally notify a **debit note** to the former coordinator. If payment is not made by the date in the debit note, the Guarantee Fund will pay to the *Commission* the amount due. The *Commission* will then pay the new coordinator and notify a debit note on behalf of the Guarantee Fund to the former coordinator (see Article 44).

- If the payments received **do not exceed the amounts due**: amounts owed to the beneficiary concerned will be included in the next interim or final payment.

If the *Commission* does not receive the termination report within the deadline (see above), only costs included in an approved periodic report will be taken into account.

If the *Commission* does not receive the report on the distribution of payments within the deadline (see above), it will consider that:

- the coordinator did not distribute any payment to the beneficiary concerned and that

- the beneficiary concerned must not repay any amount to the coordinator.

Improper termination may lead to a reduction of the grant (see Article 43) or termination of the Agreement (see Article 50).

After termination, the concerned beneficiary's obligations (in particular Articles 20, 22, 23, Section 3 of Chapter 4, 36, 37, 38 and 40) continue to apply.

50.3 Termination of the Agreement or the participation of one or more beneficiaries, by the *Commission*

50.3.1 Conditions

The *Commission* may terminate the Agreement or the participation of one or more beneficiaries, if:

(a) one or more beneficiaries do not accede to the Agreement (see Article 56);

(b) a change to their legal, financial, technical, organisational or ownership situation *(or those of its linked third parties)* is likely to substantially affect or delay the implementation of the action or calls into question the decision to award the grant;

(c) following termination of participation for one or more beneficiaries (see above), the necessary changes to the Agreement would call into question the decision awarding the grant or breach the principle of equal treatment of applicants (see Article 55);

(d) implementation of the action is prevented by force majeure (see Article 51) or suspended by the coordinator (see Article 49.1) and either:

(i) resumption is impossible, or

(ii) the necessary changes to the Agreement would call into question the decision awarding the grant or breach the principle of equal treatment of applicants;

(e) a beneficiary is declared bankrupt, being wound up, having its affairs administered by the courts, has entered into an arrangement with creditors, has suspended business activities, or is subject to any other similar proceedings or procedures under national law;

(f) a beneficiary (or a natural person who has the power to represent or take decisions on its behalf) has been found guilty of professional misconduct, proven by any means;

(g) a beneficiary does not comply with the applicable national law on taxes and social security;

(h) the action has lost scientific or technological relevance;

(i) *not applicable;*

(j) *not applicable;*

(k) a beneficiary (or a natural person who has the power to represent or take decisions on its behalf) has committed fraud, corruption, or is involved in a criminal organisation, money laundering or any other illegal activity affecting the EU's financial interests;

(l) a beneficiary (or a natural person who has the power to represent or take decisions on its behalf) has — in the award procedure or under the Agreement — committed:

(i) substantial errors, irregularities, fraud or

(ii) serious breach of obligations, including improper implementation of the action, submission of false information, failure to provide required information, breach of ethical principles;

(m) a beneficiary has committed — in other EU or Euratom grants awarded to it under similar conditions — systemic or recurrent errors, irregularities, fraud or serious breach of obligations that have a material impact on this grant (‘**extension of findings from other grants to this grant**’).

50.3.2 Procedure

Before terminating the Agreement or participation of one or more beneficiaries, the *Commission* will formally notify the coordinator:

- informing it of its intention to terminate and the reasons why and

- inviting it, within 30 days of receiving notification, to submit observations and — in case of Point (l.ii) above — to inform the *Commission* of the measures to ensure compliance with the obligations under the Agreement.

If the *Commission* does not receive observations or decides to pursue the procedure despite the observations it has received, it will formally notify to the coordinator **confirmation** of the termination and the date it will take effect. Otherwise, it will formally notify that the procedure is not continued.

The termination will **take effect**:

- for terminations under Points (b), (c), (e), (g), (h), (j), and (l.ii) above: on the day specified in the notification of the confirmation (see above);

- for terminations under Points (a), (d), (f), (i), (k), (l.i) and (m) above: on the day after the notification of the confirmation is received by the coordinator.

50.3.3 Effects

(a) for **termination of the Agreement**:

The coordinator must — within 60 days from when termination takes effect — submit:

(i) a periodic report (for the last open reporting period until termination; see Article 20.3) and

(ii) a final report (see Article 20.4).

If the Agreement is terminated for breach of the obligation to submit the reports (see Articles 20.8 and 50.3.1(l)), the coordinator may not submit any reports after termination.

If the *Commission* does not receive the reports within the deadline (see above), only costs which are included in an approved periodic report will be taken into account.

The *Commission* will **calculate** the final grant amount (see Article 5.3) and the balance (see Article 21.4) on the basis of the reports submitted. Only costs incurred until termination takes effect are eligible (see Article 6). Costs relating to contracts due for execution only after termination are not eligible.

This does not affect the *Commission's* right to reduce the grant (see Article 43) or to impose administrative and financial penalties (Article 45).

The beneficiaries may not claim damages due to termination by the *Commission* (see Article 46).

After termination, the beneficiaries' obligations (in particular Articles 20, 22, 23, Section 3 of Chapter 4, 36, 37, 38 and 40) continue to apply.

(b) for **termination of the participation of one or more beneficiaries**:

The coordinator must — within 60 days from when termination takes effect — submit:

(i) a report on the distribution of payments to the beneficiary concerned;

(ii) a request for amendment (see Article 55), with a proposal for reallocation of the tasks and estimated budget of the beneficiary concerned (see Annexes 1 and 2) and, if necessary, the addition of one or more new beneficiaries (see Article 56). If termination is notified after the period set out in Article 3, no request for amendment must be submitted unless the beneficiary concerned is the coordinator. In this case the request for amendment must propose a new coordinator, and

(iii) if termination takes effect during the period set out in Article 3, a **termination report** from the beneficiary concerned, for the open reporting period until termination, containing an overview of the progress of the work, an overview of the use of resources, the individual financial statement and, if applicable, the certificate on the financial statement (see Article 20).

The information in the termination report must also be included in the periodic report for the next reporting period (see Article 20.3).

If the request for amendment is rejected by the *Commission* (because it calls into question the decision awarding the grant or breaches the principle of equal treatment of applicants), the Agreement may be terminated according to Article 50.3.1(c).

If the request for amendment is accepted by the *Commission*, the Agreement is **amended** to introduce the necessary changes (see Article 55).

The *Commission* will **calculate** — on the basis of the periodic reports, the termination report and the report on the distribution of payments — if the (pre-financing and interim) payments

received by the beneficiary concerned exceed the beneficiary's EU contribution (calculated by applying the reimbursement rate(s) to the eligible costs declared by the beneficiary *and its linked third parties* and approved by the *Commission*). Only costs incurred by the beneficiary concerned until termination takes effect are eligible (see Article 6). Costs relating to contracts due for execution only after termination are not eligible.

- If the payments received **exceed the amounts due**:

  - if termination takes effect during the period set out in Article 3 and the request for amendment is accepted, the beneficiary concerned must repay to the coordinator the amount unduly received. The *Commission* will formally notify the amount unduly received and request the beneficiary concerned to repay it to the coordinator within 30 days of receiving notification. If it does not repay the coordinator, the *Commission* will draw upon the Guarantee Fund to pay the coordinator and then notify a debit note on behalf of the Guarantee Fund to the beneficiary concerned (see Article 44);

  - in all other cases, in particular if termination takes effect after the period set out in Article 3, the *Commission* will formally notify a **debit note** to the beneficiary concerned. If payment is not made by the date in the debit note, the Guarantee Fund will pay to the *Commission* the amount due and the *Commission* will notify a debit note on behalf of the Guarantee Fund to the beneficiary concerned (see Article 44);

  - if the beneficiary concerned is the former coordinator, it must repay the new coordinator the amount unduly received, unless:

    - termination takes effect after an interim payment and

    - the former coordinator has not distributed amounts received as pre-financing or interim payments (see Article 21.7)

    In this case, the *Commission* will formally notify a **debit note** to the former coordinator. If payment is not made by the date in the debit note, the Guarantee Fund will pay to the *Commission* the amount due. The *Commission* will then pay the new coordinator and notify a debit note on behalf of the Guarantee Fund to the former coordinator (see Article 44).

- If the payments received **do not exceed the amounts due**: amounts owed to the beneficiary concerned will be included in the next interim or final payment.

If the *Commission* does not receive the termination report within the deadline (see above), only costs included in an approved periodic report will be taken into account.

If the *Commission* does not receive the report on the distribution of payments within the deadline (see above), it will consider that:

- the coordinator did not distribute any payment to the beneficiary concerned, and that

- the beneficiary concerned must not repay any amount to the coordinator.

After termination, the concerned beneficiary's obligations (in particular Articles 20, 22, 23, Section 3 of Chapter 4, 36, 37, 38 and 40) continue to apply.

SECTION 4 FORCE MAJEURE

ARTICLE 51 — FORCE MAJEURE

'Force majeure' means any situation or event that:

- prevents either party from fulfilling their obligations under the Agreement,
- was unforeseeable, exceptional situation and beyond the parties' control,
- was not due to error or negligence on their part (or on the part of third parties involved in the action), and
- proves to be inevitable in spite of exercising all due diligence.

The following cannot be invoked as force majeure:

- any default of a service, defect in equipment or material or delays in making them available, unless they stem directly from a relevant case of force majeure,
- labour disputes or strikes, or
- financial difficulties.

Any situation constituting force majeure must be formally notified to the other party without delay, stating the nature, likely duration and foreseeable effects.

The parties must immediately take all the necessary steps to limit any damage due to force majeure and do their best to resume implementation of the action as soon as possible.

The party prevented by force majeure from fulfilling its obligations under the Agreement cannot be considered in breach of them.

CHAPTER 7 FINAL PROVISIONS

ARTICLE 52 — COMMUNICATION BETWEEN THE PARTIES

52.1 Form and means of communication

Communication under the Agreement (information, requests, submissions, 'formal notifications', etc.) must:

- be made in writing and
- bear the number of the Agreement.

Until the payment of the balance: all communication must be made through the electronic exchange system and using the forms and templates provided there.

After the payment of the balance: formal notifications must be made by registered post with proof of delivery ('formal notification on paper').

Communications in the electronic exchange system must be made by persons authorised according to the 'Terms and Conditions of Use of the electronic exchange system'. For naming the authorised persons, each beneficiary must have designated — before the signature of this Agreement — a 'Legal Entity Appointed Representative (LEAR)'. The role and tasks of the LEAR are stipulated in his/her appointment letter (see Terms and Conditions of Use of the electronic exchange system).

If the electronic exchange system is temporarily unavailable, instructions will be given on the Commission websites.

52.2 Date of communication

Communications are considered to have been made when they are sent by the sending party (i.e. on the date and time they are sent through the electronic exchange system).

Formal notifications through the **electronic** exchange system are considered to have been made when they are received by the receiving party (i.e. on the date and time of acceptance by the receiving party, as indicated by the time stamp). A formal notification that has not been accepted within 10 days after sending is considered to have been accepted.

Formal notifications **on paper** sent by **registered post** with proof of delivery (only after the payment of the balance) are considered to have been made on either:

- the delivery date registered by the postal service or
- the deadline for collection at the post office.

If the electronic exchange system is temporarily unavailable, the sending party cannot be considered in breach of its obligation to send a communication within a specified deadline.

52.3 Addresses for communication

The **electronic** exchange system must be accessed via the following URL:

https://ec.europa.eu/research/participants/portal/desktop/en/projects/

The *Commission* will formally notify the coordinator and beneficiaries in advance any changes to this URL.

Formal notifications on paper (only after the payment of the balance) addressed **to the *Commission*** must be sent to the following address:

European Commission
DIRECTORATE-GENERAL FOR RESEARCH & INNOVATION
Non-communicable diseases and the challenge of healthy ageing
Directorate HEALTH
B-1049 Brussels Belgium

Formal notifications on paper (only after the payment of the balance) addressed **to the beneficiaries** must be sent to their legal address as specified in the 'Beneficiary Register'.

ARTICLE 53 — INTERPRETATION OF THE AGREEMENT

53.1 Precedence of the Terms and Conditions over the Annexes

The provisions in the Terms and Conditions of the Agreement take precedence over its Annexes.

Annex 2 takes precedence over Annex 1.

53.2 Privileges and immunities

Not applicable

ARTICLE 54 — CALCULATION OF PERIODS, DATES AND DEADLINES

In accordance with Regulation No 1182/71[28], periods expressed in days, months or years are calculated from the moment the triggering event occurs.

The day during which that event occurs is not considered as falling within the period.

ARTICLE 55 — AMENDMENTS TO THE AGREEMENT

55.1 Conditions

The Agreement may be amended, unless the amendment entails changes to the Agreement which would call into question the decision awarding the grant or breach the principle of equal treatment of applicants.

Amendments may be requested by any of the parties.

55.2 Procedure

The party requesting an amendment must submit a request for amendment signed in the electronic exchange system (see Article 52).

The coordinator submits and receives requests for amendment on behalf of the beneficiaries (see Annex 3).

If a change of coordinator is requested without its agreement, the submission must be done by another beneficiary (acting on behalf of the other beneficiaries).

The request for amendment must include:

- the reasons why;
- the appropriate supporting documents;

[28] Regulation (EEC, Euratom) No 1182/71 of the Council of 3 June 1971 determining the rules applicable to periods, dates and time-limits (OJ L 124, 8.6.1971, p. 1).

- for a change of coordinator without its agreement: the opinion of the coordinator (or proof that this opinion has been requested in writing).

The *Commission* may request additional information.

If the party receiving the request agrees, it must sign the amendment in the electronic exchange system within 45 days of receiving notification (or any additional information the *Commission* has requested). If it does not agree, it must formally notify its disagreement within the same deadline. The deadline may be extended, if necessary for the assessment of the request. If no notification is received within the deadline, the request is considered to have been rejected

An amendment **enters into force** on the day of the signature of the receiving party.

An amendment **takes effect** on the date agreed by the parties or, in the absence of such an agreement, on the date on which the amendment enters into force.

ARTICLE 56 — ACCESSION TO THE AGREEMENT

56.1 Accession of the beneficiaries mentioned in the Preamble

The other beneficiaries must accede to the Agreement by signing the Accession Form (see Annex 3) in the electronic exchange system (see Article 52) within 30 days after its entry into force (see Article 58).

They will assume the rights and obligations under the Agreement with effect from the date of its entry into force (see Article 58).

If a beneficiary does not accede to the Agreement within the above deadline, the coordinator must — within 30 days — request an amendment to make any changes necessary to ensure proper implementation of the action. This does not affect the *Commission's* right to terminate the Agreement (see Article 50).

56.2 Addition of new beneficiaries

In justified cases, the beneficiaries may request the addition of a new beneficiary.

For this purpose, the coordinator must submit a request for amendment in accordance with Article 55. It must include an Accession Form (see Annex 3) signed by the new beneficiary in the electronic exchange system (see Article 52).

New beneficiaries must assume the rights and obligations under the Agreement with effect from the date of their accession specified in the Accession Form (see Annex 3).

ARTICLE 57 — APPLICABLE LAW AND SETTLEMENT OF DISPUTES

57.1 Applicable law

The Agreement is governed by the applicable EU law, supplemented if necessary by the law of Belgium.

57.2 Dispute settlement

If a dispute concerning the interpretation, application or validity of the Agreement cannot be settled amicably, the General Court — or, on appeal, the Court of Justice of the European Union — has sole jurisdiction. Such actions must be brought under Article 272 of the Treaty on the Functioning of the EU (TFEU).

As an exception, if such a dispute is between the Commission and INTERNATIONAL CHARITABLE FUND OMNI-NET FOR CHILDREN, the competent Belgian courts have sole jurisdiction.

If a dispute concerns administrative or financial penalties, offsetting or an enforceable decision under Article 299 TFEU (see Articles 44, 45 and 46), the beneficiaries must bring action before the General Court — or, on appeal, the Court of Justice of the European Union — under Article 263 TFEU.

ARTICLE 58 — ENTRY INTO FORCE OF THE AGREEMENT

The Agreement will enter into force on the day of signature by the *Commission* or the coordinator, depending on which is later.

SIGNATURES

For the coordinator

For the *Commission*

EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR RESEARCH & INNOVATION
Non-communicable diseases and the challenge of healthy ageing

ANNEX 1 (part A)

Research and Innovation action

NUMBER — 733001 — EUROlinkCAT

Table of Contents

1.1. The project summary

Project Number [1]	733001	Project Acronym [2]	EUROlinkCAT

One form per project

General information	
Project title [3]	EUROlinkCAT: Establishing a linked European Cohort of Children with Congenital Anomalies
Starting date [4]	01/01/2017
Duration in months [5]	60
Call (part) identifier [6]	H2020-SC1-2016-RTD
Topic	SC1-PM-04-2016 Networking and optimising the use of population and patient cohorts at EU level
Fixed EC Keywords	Patient stratification, Health determinants, Cohort studies
Free keywords	congenital anomaly birth defect children linkage EUROCAT Education Mortality Morbidity e-forum social media Hospital discharge data Prescription Length of stay in hospital Parent empowerment

Abstract [7]

Over 130,000 children born in Europe every year will have a congenital anomaly (CA; birth defect). These CAs, which are often rare diseases, are a major cause of infant mortality, childhood morbidity and long-term disability. EUROCAT is an established European network of population-based registries for the epidemiologic surveillance of CAs. EUROlinkCAT will use the EUROCAT infrastructure to support 21 EUROCAT registries in 13 European countries to link their CA data to mortality, hospital discharge, prescription and educational databases. Each registry will send standard aggregate tables and analysis results to a Central Results Repository (CRR) thus respecting data security issues surrounding sensitive data. The CRR will contain standardised summary data and analyses on an estimated 200,000 children with a CA born from 1995 to 2014 up to age 10, enabling hypotheses on their health and education to be investigated at an EU level. This enhanced information will allow optimisation of personalised care and treatment decisions for children with rare CAs.

Registries will be supported in using social media platforms to connect with families who live with CAs in their regions. A novel sustainable e-forum, “ConnectEpeople”, will link these families with local, national and international registries and information resources. ConnectEpeople will involve these families in setting research priorities and ensuring a meaningful dissemination of results.

Findings will provide evidence to inform national treatment guidelines, such as concerning screening programs, to optimise diagnosis, prevention and treatment for these children and reduce health inequalities in Europe. An economic evaluation of the hospitalisation costs associated with CA will be provided

The CRR and associated documentation, including linkage and standardisation procedures and “ConnectEpeople” forum will be available post-EUROlinkCAT thus facilitating future local and EU level analyses.

1.2. List of Beneficiaries

Project Number [1]	733001	Project Acronym [2]	EUROlinkCAT

List of Beneficiaries

No	Name	Short name	Country	Project entry month[8]	Project exit month
1	QUEEN MARY UNIVERSITY OF LONDON	QMUL	United Kingdom	1	60
2	UNIVERSITY OF ULSTER	UU	United Kingdom	1	60
3	REGION SYDDANMARK	RSD	Denmark	1	60
4	UNIVERSITY OF NEWCASTLE UPON TYNE	UNEW	United Kingdom	1	60
5	UNIVERSITA DEGLI STUDI DI FERRARA	UNIFE	Italy	1	60
6	KLINIKA ZA DJECJE BOLESTI ZAGREB	KDB	Croatia	1	60
7	CONSIGLIO NAZIONALE DELLE RICERCHE	CNR-IFC	Italy	1	60
8	ACADEMISCH ZIEKENHUIS GRONINGEN	UMCG	Netherlands	1	60
9	PUBLIC HEALTH WALES NATIONAL HEALTH SERVICE TRUST	PHW NHS	United Kingdom	1	60
10	INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE	INSERM	France	1	60
11	FUNDACION PARA EL FOMENTO DE LA INVESTIGACION SANITARIA Y BIOMEDICA DELA COMUNITAT VALENCIANA	FISABIO	Spain	1	60
12	UNIWERSYTET MEDYCZNY IM KAROLA MARCINKOWSKIEGO W POZNANIU	PUMS	Poland	1	60
13	TERVEYDEN JA HYVINVOINNIN LAITOS	THL	Finland	1	60
14	INTERNATIONAL CHARITABLE FUND OMNI-NET FOR CHILDREN	OMNI NET	Ukraine	1	60
15	OTTO-VON-GUERICKE-UNIVERSITAET MAGDEBURG	OVGU	Germany	1	60
16	INSTITUTO NACIONAL DE SAUDE DR. RICARDO JORGE	INSA	Portugal	1	60
17	CENTRE HOSPITALIER UNIVERSITAIRE DE LA REUNION	CHURéunion	France	1	60
18	PROVINCIAAL INSTITUUT VOOR HYGIENE	PIH	Belgium	1	60
19	ASOCIACION INSTITUTO BIODONOSTIA	BIOEF	Spain	1	60
20	BIOMEDICAL COMPUTING LIMITED	BIOMED	United Kingdom	1	60
21	REDBURN SOLUTIONS LIMITED	Redburn	United Kingdom	1	60

1.2. List of Beneficiaries

No	Name	Short name	Country	Project entry month[8]	Project exit month
22	SWANSEA UNIVERSITY	SU	United Kingdom	1	60

1.3. Workplan Tables - Detailed implementation

1.3.1. WT1 List of work packages

WP Number[9]	WP Title	Lead beneficiary[10]	Person-months[11]	Start month[12]	End month[13]
WP1	Coordination and management of EUROlinkCAT	1 - QMUL	113.85	1	60
WP2	Building EUROlinkCAT Central Results Repository	2 - UU	330.95	1	60
WP3	Mortality associated with Congenital Anomalies	4 - UNEW	36.00	4	60
WP4	Morbidity associated with Congenital Anomalies	3 - RSD	65.00	4	60
WP5	Educational achievements and needs of children with Congenital Anomalies	4 - UNEW	44.00	1	60
WP6	Accuracy of anomaly coding in health care databases	3 - RSD	38.00	4	60
WP7	ConnectEpeople	2 - UU	148.22	1	60
WP8	Dissemination and Evaluation	5 - UNIFE	52.35	1	60
WP9	Ethics requirements	1 - QMUL	N/A	1	60
		Total	828.37		

1.3.2. WT2 list of deliverables

Deliverable Number[14]	Deliverable Title	WP number[9]	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
D1.1	Initial Website Online	WP1	1 - QMUL	Websites, patents filling, etc.	Public	6
D2.1	Build Website	WP2	20 - BIOMED	Websites, patents filling, etc.	Public	3
D2.2	Provide linked aggregate data to WP3,WP4,WP5,WP6	WP2	2 - UU	Other	Confidential, only for members of the consortium (including the Commission Services)	39
D2.3	Interactive website tables	WP2	2 - UU	Report	Public	42
D2.4	Manual describing data held in the Central Results Registry	WP2	2 - UU	Report	Public	50
D3.1	Report on survival and risk factors for survival for children born with a congenital anomaly	WP3	4 - UNEW	Report	Public	39
D3.2	Report on geographical variations in Europe on survival of children born with a congenital anomaly	WP3	7 - CNR-IFC	Report	Public	42
D4.1	Report on Hospitalisations and surgery across Europe for the first 5 years of life	WP4	3 - RSD	Report	Public	42
D4.2	Report on Infections and use of antibiotics during the first 5 years of life	WP4	2 - UU	Report	Public	51
D4.3	Report on prenatal diagnosis and morbidity	WP4	3 - RSD	Report	Public	54
D5.1	Report on Education achievements and needs of children born with a congenital anomaly and geographical variation in Europe	WP5	4 - UNEW	Report	Public	54
D5.2	Report on predictions of the numbers of	WP5	4 - UNEW	Report	Public	57

Deliverable Number[14]	Deliverable Title	WP number[9]	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
	children with education needs					
D6.1	Report on the evaluation of specific congenital anomaly coding in health care databases including a computer algorithm to improve these codes	WP6	8 - UMCG	Report	Public	54
D7.1	Formation of e stakeholder forum “ConnectEpeople”	WP7	2 - UU	Report	Public	14
D7.2	Report evaluating E-Systems for linking researchers, professionals and consumers across Europe	WP7	2 - UU	Report	Public	58
D8.1	Information Leaflet	WP8	5 - UNIFE	Report	Public	3
D8.2	Consultation meeting	WP8	6 - KDB	Websites, patents filling, etc.	Public	14
D8.3	Report to EU institutions hosting health care databases with guidelines for improving the quality of the congenital anomaly coding	WP8	3 - RSD	Websites, patents filling, etc.	Public	57
D8.4	Dissemination conference	WP8	12 - PUMS	Websites, patents filling, etc.	Public	58
D9.1	H - Requirement No. 1	WP9	1 - QMUL	Ethics	Confidential, only for members of the consortium (including the Commission Services)	24
D9.2	NEC - Requirement No. 2	WP9	1 - QMUL	Ethics	Confidential, only for members of the consortium (including the Commission Services)	1
D9.3	POPD - Requirement No. 3	WP9	1 - QMUL	Ethics	Confidential, only for members of the consortium (including the	6

Deliverable Number[14]	Deliverable Title	WP number[9]	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
					Commission Services)	

1.3.3. WT3 Work package descriptions

Work package number [9]	WP1	**Lead beneficiary** [10]	1 - QMUL
Work package title	Coordination and management of EUROlinkCAT		
Start month	1	**End month**	60

Objectives

To successfully manage and monitor the EUROlinkCAT project by providing guidance and support to ensure strong collaboration between all work packages and providing secure financial management.

Description of work and role of partners

WP1 - Coordination and management of EUROlinkCAT [Months: 1-60]
QMUL, UU, RSD, UNEW, UNIFE, KDB, CNR-IFC, UMCG, PUMS, BIOMED
This work package (WP) will be led by QMUL (Joan Morris). The person months given for this WP includes 60 person months of Project Manager, 16 person months of Joan Morris's time and 6 person months of administrative support in QMUL in addition to all members of the steering group having time for their management and scientific responsibilities (2.7 months)

The specific tasks are to:
1. Provide Scientific management
a. QMUL will monitor scientific progress of all WPs to ensure milestones and deliverables are on time. If there are any delays QMUL will investigate the reasons and consult with the management team as to the best way to resolve such issues and provide additional support. UU and RSD will support QMUL in these tasks as members of the management team
2. Provide financial management
a. QMUL will perform financial management, negotiate with the EU, inform partners of EU rules and deadlines, oversee progress of spending according to the budget, and manage the subcontractor contracts.
3. Collate final and period reports for the Commission
a. The final and periodic reports will be collated from all WP leaders by QMUL, and along with financial reports and audit certificates will be submitted to the Commission.
4. Co-ordinate dissemination of progress and results
a. QMUL will be responsible for uploading the content to the website for this project (WP2 will build the website and WP8 will provide dissemination material for the website)
b. QMUL will be responsible for the co-ordination of dissemination across WPs.
5. Organise meetings
a. QMUL will be responsible for meeting organisation of all meetings apart from the consultation meeting in Croatia (month 14) and the dissemination workshop in Poland (month 58).
b. A meeting will be held annually of all participants (including all scientific staff involved) and subcontractors. This meeting will be held in the same location directly before or after the 5 annual EUROCAT Registry Leaders Meetings (RLM). The consortium steering committee will meet during the 7 above mentioned meetings and will have 3 additional meetings (10 meetings over the 5 years). The coding and standardisation committee will meet 7 times (5 during above mentioned meetings and two additional meetings) to ensure standardisation of linked data variables and all analysis across participating registries and WPs. The Ethics and Data Protection Board will be invited to 1 meeting annually. If any unforeseen issues arise QMUL will organise a teleconference to discuss them.
6. Provide archiving
a. QMUL will provide a fully indexed archive for at least six years beyond the end of the last project deliverable. Archiving will follow the guidelines of the Queen Mary University of London Research Governance Steering Committee, reviewed by the Consortium Steering Group. The archive will include all protocols, ethical approvals, meeting minutes, draft and final reports, comments by all stakeholders and responses to those comments.
7. Support the consortium steering group.
a. QMUL will be responsible for the provision of meeting agendas, meeting minutes, actions and meeting organisation.
8. Support the Ethics and Data Protection Board (EDPB).
a. QMUL will be responsible for compiling and retaining a complete portfolio of copies of Informed Consent Forms and Information Sheets that cover all aspects of the research by all of the partners of the Consortium throughout the lifetime of the project

b. QMUL will be responsible for providing the EDPB with an annual report, ensuring they have been fully informed of any ethical issues and organising one meeting annually.

Participation per Partner

Partner number and short name	WP1 effort
1 - QMUL	88.25
2 - UU	5.65
3 - RSD	2.80
4 - UNEW	2.70
5 - UNIFE	2.70
6 - KDB	2.70
7 - CNR-IFC	2.70
8 - UMCG	2.70
12 - PUMS	2.70
20 - BIOMED	0.95
Total	113.85

List of deliverables

Deliverable Number[14]	Deliverable Title	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
D1.1	Initial Website Online	1 - QMUL	Websites, patents filling, etc.	Public	6

Description of deliverables

1. Uploading content to the Website (QMUL) (Month 6)

D1.1 : Initial Website Online [6]

Uploading the content to the website, with the first version ready by month 6

Schedule of relevant Milestones

Milestone number[18]	Milestone title	Lead beneficiary	Due Date (in months)	Means of verification
MS1	General consortium meetings during the Registry Leaders Meeting	1 - QMUL	6	General consortium meetings during the Registry Leaders Meeting – including minutes uploaded to membership-only section of website (QMUL) (6,18,30,42,54)
MS2	Steering Group meetings	1 - QMUL	6	Steering Group meetings – including minutes uploaded

Schedule of relevant Milestones

Milestone number[18]	Milestone title	Lead beneficiary	Due Date (in months)	Means of verification
				to membership-only section of website (QMUL) (6,12,18,24,30,36,42,48,54)

Work package number [9]	WP2	Lead beneficiary [10]	2 - UU
Work package title	Building EUROlinkCAT Central Results Repository		
Start month	1	End month	60

Objectives

To develop standard operating procedures to enable each participating registry to create a linked standardised dataset so that aggregate data and any analytical results can be collectively pooled for a pan-European analysis.
To build a Central Results Repository to collate standardised output tables and individual registry analysis results to enable a pan-European analysis of mortality, morbidity and educational achievements and needs of children with congenital anomalies across Europe

Description of work and role of partners

WP2 - Building EUROlinkCAT Central Results Repository [Months: 1-60]
UU, QMUL, RSD, UNEW, UNIFE, KDB, CNR-IFC, UMCG, PHW NHS, INSERM, FISABIO, THL, OMNI NET, OVGU, INSA, CHURéunion, PIH, BIOEF, BIOMED, SU
This WP will be led by UU (Maria Loane) and BIOMEDical Computing Ltd (James Densem). Statistical expertise and advice will be provided by QMUL (Joan Morris).

The functions of this WP are (i) to enable each participating registry to create a linked standardised dataset using the coding protocols, algorithms and Data Quality Indicators (DQIs) developed in this WP (ii) to create the EUROlinkCAT Central Results Repository to collate linked standardised aggregated tables and analysis results (ii) to transfer the pooled tables to the relevant task leaders involved in WP3, 4, 5 and 6 and (iv) to create the EUROlinkCAT website including interactive data tables

This WP includes all registries contributing linked aggregate data for use in specific WPs as the registries are responsible for providing the information on their local databases, for obtaining local governance approval to participate in the linkage studies, for linking the relevant local databases and for generating the output tables for analysis. The leaders of WP 3-6 are also involved as they provide the study protocols specifying the study design, study variables, analysis plan, and the outline structure of the tables to collectively pool the results from each registry for analysis. Each participating registry will send standard aggregate tables and analysis results to be included in the Central Results Repository. Linked individual case data will be retained locally. Each task/ component task lists the participants involved.

1. Ascertain individual registry capacity to link existing administrative/ clinical/ educational/ prescription data to their congenital anomaly data in the EUROCAT Data Management Program (EDMP) (lead partner UU). For each registry:
• Catalogue and document the datasets available for linkage, including regional or national coverage, years included and the availability of children without anomalies (controls) [All registries, UU]
• Produce meta-data/ data dictionary to describe these datasets. This includes a description of the dataset and variable names, variable descriptions/ definitions, coding instructions/ values (in English) [UU, BIOMED]
• Conduct an initial scoping exercise to assess the quality of the data to be linked (Quality Assurance) i.e. for study inclusion/ exclusion criteria purposes and for creating derived variables we need to ascertain if the variables are mostly complete or incomplete. [All registries, UU]
• Upload all the above documentation to the membership-only section of the website as individual WP leaders using linked data need this information for developing study protocols [UU]
• Develop a detailed data management plan conforming to all EU and national legislation.
• Oversee local registry ethics / research governance permission for conducting linkage studies [UU]
• Apply for ethical permission at Ulster University to hold the EUROlinkCATCentral Results Repository [UU]
2. Standardise linked data across participating registries (lead partners UU, BIOMED).
• Create a common data model (independent from study protocol/ study design). This task ensures that all variables/ proxy variables are standardised across all registries [UU, BIOMED, QMUL]
• Develop rules for each registry to generate derived study variables from the existing data [UU, BIOMED, QMUL]
• Develop rules for each registry to implement different study designs for example according to whether children without anomalies are available as controls [UU, BIOMED, QMUL]
• Agree the common model with registries to ensure correct interpretation of local variables [UU, all registries]
3. Create the linked datasets needed for the protocols of WP3-6 (lead partners UU, QMUL).

• Create registry-specific syntax scripts to derive study variables, to implement study designs, and to run the pre-defined analysis for each WP study. These will be replicated by another individual for quality assurance [UU, BIOMED, QMUL]
• Registry data providers run the registry-specific syntax scripts using STATA, SPSS, or equivalent program to generate the required output aggregated tables and analytical results for WP3-6 analysis [All registries]
• Each registry/ data provider produces a data linkage report for quality assessment. This includes verification and validation of the derived variables/ data transformations, the methodology used to link cases in the different datasets, and matching success [All registries, UU]
• Develop a set of DQIs for the Central Results Repository to assess data quality i.e. to compare registries against the EUROCAT average [UU, QMUL]
• Upload all the above documentation to the membership-only section of the website for internal documentation [UU]
4. Develop the EUROlinkCAT Central Results Repository and associated website (lead partners BIOMED, UU)
• Build the website and install a CMS on the website [BIOMED]
• Develop a Central Results Repository for holding the registry aggregate output tables and analysis results (such as Odds Ratios and adjusted Odds Ratios) to be used in European meta-analysis [BIOMED]
• Implement DQIs in the Central Results Repository for comparison of registries to the EUROlinkCAT average [BIOMED]
• Create interactive web tables hosting aggregate tables: detailed information will be available on a membership-only section of the website, whilst more aggregated data will be available on the public section of the website [BIOMED, QMUL]
• Provide text for website relating to Central Results Repository [BIOMED, UU, QMUL]
• Provide appropriate standard operating procedures documenting the Central Results Repository resource i.e. definitions, processes, activities, data security and data archiving [UU]
• Provide linked aggregate data (tables or analysis results) to other WPs to assess mortality, morbidity and educational outcomes of children with congenital anomalies [UU]
• Co-ordinate external data requests [UU, QMUL]

Participation per Partner

Partner number and short name	WP2 effort
1 - QMUL	72.85
2 - UU	60.55
3 - RSD	16.55
4 - UNEW	5.55
5 - UNIFE	18.00
6 - KDB	15.50
7 - CNR-IFC	12.55
8 - UMCG	13.05
9 - PHW NHS	0.55
10 - INSERM	3.50
11 - FISABIO	15.50
13 - THL	18.00
14 - OMNI NET	12.50
15 - OVGU	3.75
16 - INSA	8.00
17 - CHURéunion	12.00
18 - PIH	3.25
19 - BIOEF	10.50

Partner number and short name	WP2 effort
20 - BIOMED	12.35
22 - SU	16.45
Total	330.95

List of deliverables

Deliverable Number[14]	Deliverable Title	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
D2.1	Build Website	20 - BIOMED	Websites, patents filling, etc.	Public	3
D2.2	Provide linked aggregate data to WP3,WP4,WP5,WP6	2 - UU	Other	Confidential, only for members of the consortium (including the Commission Services)	39
D2.3	Interactive website tables	2 - UU	Report	Public	42
D2.4	Manual describing data held in the Central Results Registry	2 - UU	Report	Public	50

Description of deliverables

1. Build the website and install a CMS on the website (BIOMED) (Task 4, Month 3)
2. Provide linked aggregate data (tables and analysis results) to WP3,4,5 and 6. (UU) (Task 3, Month 39)
3. Develop Interactive website tables. (BIOMED, UU) (Month 42)
4. Produce Manual describing the data held in the Central Results Repository, including the syntax scripts used to output the tables. (BIOMED, UU, QMUL) (Task4, Uploaded to website Month 50).

D2.1 : Build Website [3]

Build the website and install a CMS on the website

D2.2 : Provide linked aggregate data to WP3,WP4,WP5,WP6 [39]

Provide linked aggregate data to WP3,WP4,WP5,WP6

D2.3 : Interactive website tables [42]

Interactive website tables

D2.4 : Manual describing data held in the Central Results Registry [50]

Manual describing data held in the Central Results Registry

Schedule of relevant Milestones

Milestone number[18]	Milestone title	Lead beneficiary	Due Date (in months)	Means of verification
MS3	Produce a fully documented Report of the local data sources / content of data available for each registry	2 - UU	12	Produce a fully documented Report of the local data sources / content of data available for each registry

Schedule of relevant Milestones

Milestone number[18]	Milestone title	Lead beneficiary	Due Date (in months)	Means of verification
	(includes variable names, variable descriptions, definitions, coding instructions/ values).			(includes variable names, variable descriptions, definitions, coding instructions/ values). (UU) (Task 1, Uploaded to website Month 12)
MS4	Confirm the agreed variables standardised across Europe (i.e. the common model)	2 - UU	15	Confirm the agreed variables standardised across Europe (i.e. the common model). Relates to task 2. (UU) (Month 15).
MS5	Create registry-specific syntax scripts to derive study variables, to implement study designs, and to run the pre-defined analysis for WP3	2 - UU	22	Create registry-specific syntax scripts to derive study variables, to implement study designs, and to run the pre-defined analysis for WP3
MS6	Create registry-specific syntax scripts to derive study variables, to implement study designs, and to run the pre-defined analysis for WP4	2 - UU	34	Create registry-specific syntax scripts to derive study variables, to implement study designs, and to run the pre-defined analysis for WP4
MS7	Create registry-specific syntax scripts to derive study variables, to implement study designs, and to run the pre-defined analysis for WP6	2 - UU	34	Create registry-specific syntax scripts to derive study variables, to implement study designs, and to run the pre-defined analysis for WP6
MS8	Create registry-specific syntax scripts to derive study variables, to implement study designs, and to run the pre-defined analysis for WP5	2 - UU	37	Create registry-specific syntax scripts to derive study variables, to implement study designs, and to run the pre-defined analysis for WP5
MS9	Produce Data Quality Report describing data quality, specificity of coding, prevalence of exposure, and presence of missing data for each participating registry compared to the average.	2 - UU	48	Produce Data Quality Report describing data quality, specificity of coding, prevalence of exposure, and presence of missing data for each participating registry compared to the average.

Work package number [9]	WP3	**Lead beneficiary** [10]	4 - UNEW
Work package title	Mortality associated with Congenital Anomalies		
Start month	4	**End month**	60

Objectives

To expand the knowledge on the survival of children born with congenital anomalies for the first 10 years of life and to evaluate prenatal diagnosis and other risk factors for survival in Europe.

Description of work and role of partners

WP3 - Mortality associated with Congenital Anomalies [Months: 4-60]
UNEW, QMUL, RSD, UNIFE, KDB, CNR-IFC, UMCG, PHW NHS, INSERM, FISABIO, THL, OMNI NET, OVGU, CHURéunion, PIH, BIOEF, SU
This WP will be led by UNEW (Judith Rankin) and CNR-IFC (Anna Pierini).
The specific tasks are to:
1. Evaluate the survival of babies with specific congenital anomalies and by selected EUROCAT congenital anomaly subgroups across Europe (UNEW)
2. Investigate whether survival of infants and children is associated with occurrence of a prenatal diagnosis (UNEW)
3. Investigate whether there are geographic variations in survival across Europe for specific congenital anomaly subgroups (CNR-IFC)
4. Investigate the association of risk factors (gender, birth weight, gestation length, maternal age, parity, socio-economic status, non-European origin of the parents) and survival (UNEW)
For each task the lead partners (UNEW, CNR-IFC) will be responsible for completing literature reviews on the topic, designing study protocols, organising subgroup meetings, receiving data from WP2 Central Results Repository, analysing data and writing final reports/scientific papers. Each partner/registry is responsible for performing local analyses and aggregating the data, sending the results to the Central Results Repository, and taking part in discussion of results and commenting on drafts of each paper.
Analysis will focus on some EUROCAT subgroups of specific congenital anomalies (for example spina bifida, Tetralogy of Fallot, oro-facial clefts, esophageal atresia, small intestinal atresia/stenosis, anorectal atresia, bladder extrophy, diaphragmatic hernia, omphalocele, gastroschisis and certain syndromes).

Participation per Partner

Partner number and short name	WP3 effort
1 - QMUL	1.00
3 - RSD	1.00
4 - UNEW	11.00
5 - UNIFE	1.00
6 - KDB	1.00
7 - CNR-IFC	11.00
8 - UMCG	1.00
9 - PHW NHS	0.50
10 - INSERM	1.00
11 - FISABIO	1.00
13 - THL	1.00
14 - OMNI NET	1.00

Partner number and short name	WP3 effort
15 - OVGU	1.00
17 - CHURéunion	1.00
18 - PIH	1.00
19 - BIOEF	1.00
22 - SU	0.50
Total	36.00

List of deliverables

Deliverable Number[14]	Deliverable Title	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
D3.1	Report on survival and risk factors for survival for children born with a congenital anomaly	4 - UNEW	Report	Public	39
D3.2	Report on geographical variations in Europe on survival of children born with a congenital anomaly	7 - CNR-IFC	Report	Public	42

Description of deliverables

1. Report : Survival and risk factors for survival for children born with a congenital anomaly (UNEW) (Month 39)
2. Report : Geographical variations in Europe on survival of children born with a congenital anomaly (CNR-IFC) (Month 42)

D3.1 : Report on survival and risk factors for survival for children born with a congenital anomaly [39]

Report on survival and risk factors for survival for children born with a congenital anomaly

D3.2 : Report on geographical variations in Europe on survival of children born with a congenital anomaly [42]

Report on geographical variations in Europe on survival of children born with a congenital anomaly

Schedule of relevant Milestones

Milestone number[18]	Milestone title	Lead beneficiary	Due Date (in months)	Means of verification
MS5	Create registry-specific syntax scripts to derive study variables, to implement study designs, and to run the pre-defined analysis for WP3	2 - UU	22	Create registry-specific syntax scripts to derive study variables, to implement study designs, and to run the pre-defined analysis for WP3
MS10	Study protocol for ethical approval, available on membership-only section of website	4 - UNEW	8	Study protocol for ethical approval, available on membership-only section of website

Schedule of relevant Milestones

Milestone number[18]	Milestone title	Lead beneficiary	Due Date (in months)	Means of verification
MS11	2. Protocol for analysis plan prepared for Survival and risk factors for survival for children born with a congenital anomaly, available on membership-only section of website	4 - UNEW	12	2. Protocol for analysis plan prepared for Survival and risk factors for survival for children born with a congenital anomaly, available on membership-only section of website
MS12	Protocol for analysis plan prepared for Geographical variations in Europe on survival of children with a congenital anomaly, available on membership-only section of website	5 - UNIFE	15	Protocol for analysis plan prepared for Geographical variations in Europe on survival of children with a congenital anomaly, available on membership-only section of website

Work package number [9]	WP4	**Lead beneficiary** [10]	3 - RSD
Work package title	Morbidity associated with Congenital Anomalies		
Start month	4	**End month**	60

Objectives

To expand the knowledge on the health and clinical course of children with congenital anomalies up to the first 10 years of life and to evaluate different treatment guidlines in prenatal, neonatal and childhood care in Europe to optimise diagnosis, treatment and health for these children.

Description of work and role of partners

WP4 - Morbidity associated with Congenital Anomalies [Months: 4-60]
RSD, QMUL, UU, UNEW, UNIFE, KDB, CNR-IFC, UMCG, PHW NHS, FISABIO, THL, OMNI NET, INSA, CHURéunion, BIOEF, SU
This WP will be led by RSD (Ester Garne) and UU (Maria Loane).
The morbidity of children with specific congenital anomalies will be measured by the number of days spent in hospital, occurrence of surgery, days in intensive care units, outpatient contacts and prescriptions of medicine for infections and respiratory illness. The specific tasks are to:
1. Evaluate the long term morbidity of children with specific congenital anomalies (RSD)
2. Evaluate if morbidity is lower if the congenital anomalies were diagnosed prenatally for selected anomalies (spina bifida, transposition, diaphragmatic hernia, gastroschisis and others) (FIN)
3. Evaluate the morbidity of children with specific congenital anomalies with respect to prescription of medications for infections and respiratory illness (UU)
4. Evaluate geographic variations in morbidity across Europe for children with congenital anomalies and investigating risk factors and possible explanations for observed health inequalities (UU)
5. Evaluate the costs of hospitalisation across Europe during the first 5 years of life for children born with a congenital anomaly (QMUL,UU)
For each task the lead partner (RSD, UU, FIN, QMUL) will be responsible for completing literature reviews on the topic, designing study protocols, organising subgroup meetings, receiving data from WP2 Central Results Repository, analysing data and writing final reports/scientific papers.
Each partner/registry is responsible for performing local analyses and aggregating the data, sending the results to the Central Results Repository, and taking part in discussion of results and commenting on drafts of each paper.
Analysis will be done for standard EUROCAT subgroups of specific congenital anomalies (for example spina bifida, Tetralogy of Fallot, esophageal atresia, club foot and many others).

Participation per Partner

Partner number and short name	WP4 effort
1 - QMUL	8.00
2 - UU	24.00
3 - RSD	11.00
4 - UNEW	1.00
5 - UNIFE	1.00
6 - KDB	1.00
7 - CNR-IFC	1.00
8 - UMCG	1.00
9 - PHW NHS	0.50
11 - FISABIO	1.00

Partner number and short name	WP4 effort
13 - THL	11.00
14 - OMNI NET	1.00
16 - INSA	1.00
17 - CHURéunion	1.00
19 - BIOEF	1.00
22 - SU	0.50
Total	65.00

List of deliverables

Deliverable Number[14]	Deliverable Title	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
D4.1	Report on Hospitalisations and surgery across Europe for the first 5 years of life	3 - RSD	Report	Public	42
D4.2	Report on Infections and use of antibiotics during the first 5 years of life	2 - UU	Report	Public	51
D4.3	Report on prenatal diagnosis and morbidity	3 - RSD	Report	Public	54

Description of deliverables

1. Report: Hospitalisations/number of days in hospitals and operations across Europe for the first 5 years of life for children born with a congenital anomaly. Relates to task 1. (RSD) (Month 45)
2. Report: Infections and respiratory illness defined as use of medications during the first 5 years of life for children born with a congenital anomaly. Relates to task 2. (UU) (Month 51).
3. Report: Is there a relationship between prenatal diagnosis and lower morbidity if the congenital anomaly is diagnosed prenatally? Relates to task 3. (FIN) (Month54).

D4.1 : Report on Hospitalisations and surgery across Europe for the first 5 years of life [42]

Report on Hospitalisations and surgery across Europe for the first 5 years of life

D4.2 : Report on Infections and use of antibiotics during the first 5 years of life [51]

Report on Infections and use of antibiotics during the first 5 years of life

D4.3 : Report on prenatal diagnosis and morbidity [54]

Report on prenatal diagnosis and morbidity

Schedule of relevant Milestones

Milestone number[18]	Milestone title	Lead beneficiary	Due Date (in months)	Means of verification
MS6	Create registry-specific syntax scripts to derive study variables, to implement study	2 - UU	34	Create registry-specific syntax scripts to derive study variables, to implement study

Schedule of relevant Milestones

Milestone number[18]	Milestone title	Lead beneficiary	Due Date (in months)	Means of verification
	designs, and to run the pre-defined analysis for WP4			designs, and to run the pre-defined analysis for WP4
MS10	Study protocol for ethical approval, available on membership-only section of website	4 - UNEW	8	Study protocol for ethical approval, available on membership-only section of website
MS13	Protocol for analysis plan prepared for Hospitalisations/ number of days in hospitals and operations across Europe for the first 5 years of life for children born with a congenital anomaly., available on membership-only section of website	3 - RSD	12	Protocol for analysis plan prepared for Hospitalisations/ number of days in hospitals and operations across Europe for the first 5 years of life for children born with a congenital anomaly., available on membership-only section of website
MS14	Protocol for analysis plan prepared for Infections and respiratory illness defined as use of medications during the first 5 years of life for children born with a congenital anomaly, available on membership-only section of website	2 - UU	15	Protocol for analysis plan prepared for Infections and respiratory illness defined as use of medications during the first 5 years of life for children born with a congenital anomaly, available on membership-only section of website
MS15	Protocol for analysis plan prepared Is there a relationship between prenatal diagnosis and lower morbidity if the congenital anomaly is diagnosed prenatally?, available on membership-only section of website	3 - RSD	15	Protocol for analysis plan prepared Is there a relationship between prenatal diagnosis and lower morbidity if the congenital anomaly is diagnosed prenatally?, available on membership-only section of website
MS16	Protocol for analysis plan prepared Geographic variations in Europe for morbidity for children born with a congenital anomaly, available on membership-only section of website	2 - UU	18	Protocol for analysis plan prepared Geographic variations in Europe for morbidity for children born with a congenital anomaly, available on membership-only section of website
MS17	Protocol for analysis plan prepared for The costs of hospitalisation across Europe during the first 5 years of life for children born with a congenital anomaly, available on membership-only section of website	1 - QMUL	21	Protocol for analysis plan prepared for The costs of hospitalisation across Europe during the first 5 years of life for children born with a congenital anomaly, available on membership-only section of website

Work package number [9]	WP5	**Lead beneficiary** [10]	4 - UNEW
Work package title	Educational achievements and needs of children with Congenital Anomalies		
Start month	1	**End month**	60

Objectives

To expand the knowledge on the educational achievements and needs of children with specific congenital anomalies and to provide predictions of their future needs.

Description of work and role of partners

WP5 - Educational achievements and needs of children with Congenital Anomalies [Months: 1-60]
UNEW, QMUL, RSD, UNIFE, PHW NHS, THL, SU
This WP will be led by UNEW (Judith Rankin) and UNIFE (Amanda Neville).
The specific tasks are to:
1. Identify the data available on education across countries of Europe and address issues in combining it. (UNIFE)
2. Determine the educational achievements and needs of children born with a congenital anomaly by congenital anomaly subgroup (UNEW)
3. Evaluate if educational achievements and needs are associated with clinical (the use of anaesthesia, surgery, days spent in hospital) and sociodemographic factors (gender, maternal age, socioeconomic status) (UNEW)
4. To undertake statistical modelling of data to provide predictions of the number of children with congenital anomalies across Europe under 11 with congenital anomalies who will have specific educational needs (UNEW)
For each task the lead partner (UNEW) will be responsible for completing literature reviews on the topic, designing study protocols, organising subgroup meetings, receiving data from WP2 Central Results Repository, analysing data, discussing the results with colleagues from the School of Environment, Education and Development at the University of Manchester (http://www.seed.manchester.ac.uk/subjects/education/research/sean/send/), and writing final reports/ scientific papers (9 months)
Each partner/registry is responsible for performing local analyses and aggregating the data, sending the results to the Central Results Repository, and taking part in discussion of results and commenting on drafts of each paper.
Analysis will be done for standard EUROCAT subgroups of specific congenital anomalies (examples spina bifida, Tetralogy of Fallot, esophageal atresia, Downs syndrome).

Participation per Partner

Partner number and short name	WP5 effort
1 - QMUL	1.00
3 - RSD	1.00
4 - UNEW	30.00
5 - UNIFE	10.00
9 - PHW NHS	0.50
13 - THL	1.00
22 - SU	0.50
Total	44.00

List of deliverables

Deliverable Number[14]	Deliverable Title	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
D5.1	Report on Education achievements and needs of children born with a congenital anomaly and geographical variation in Europe	4 - UNEW	Report	Public	54
D5.2	Report on predictions of the numbers of children with education needs	4 - UNEW	Report	Public	57

Description of deliverables

1. Report: Education achievements and needs of children born with a congenital anomaly and geographical variation in Europe (UNEW) (Month 54)
2. Report: The predictions of the number of children with congenital anomalies across Europe under 11 who will have specific educational needs. (UNEW) (Month 57)

D5.1 : Report on Education achievements and needs of children born with a congenital anomaly and geographical variation in Europe [54]

Report on Education achievements and needs of children born with a congenital anomaly and geographical variation in Europe

D5.2 : Report on predictions of the numbers of children with education needs [57]

Report on predictions of the numbers of children with education needs

Schedule of relevant Milestones

Milestone number[18]	Milestone title	Lead beneficiary	Due Date (in months)	Means of verification
MS8	Create registry-specific syntax scripts to derive study variables, to implement study designs, and to run the pre-defined analysis for WP5	2 - UU	37	Create registry-specific syntax scripts to derive study variables, to implement study designs, and to run the pre-defined analysis for WP5
MS10	Study protocol for ethical approval, available on membership-only section of website	4 - UNEW	8	Study protocol for ethical approval, available on membership-only section of website
MS18	Protocol for analysis plan prepared for Education achievements and needs of children born with a congenital anomaly and geographical variation in Europe, available on membership-only section of website	4 - UNEW	26	Protocol for analysis plan prepared for Education achievements and needs of children born with a congenital anomaly and geographical variation in Europe, available on membership-only section of website

Schedule of relevant Milestones

Milestone number[18]	Milestone title	Lead beneficiary	Due Date (in months)	Means of verification
MS19	Protocol for analysis plan prepared for How do clinical and sociodemographic factors impact on educational achievements and needs for children born with a congenital anomaly?, available on membership-only section of website	4 - UNEW	23	Protocol for analysis plan prepared for How do clinical and sociodemographic factors impact on educational achievements and needs for children born with a congenital anomaly?, available on membership-only section of website
MS20	Protocol for analysis plan prepared for the predictions of the number of children with congenital anomalies across Europe under 11 who will have specific educational needs, available on membership-only section of website	4 - UNEW	26	Protocol for analysis plan prepared for the predictions of the number of children with congenital anomalies across Europe under 11 who will have specific educational needs, available on membership-only section of website

Work package number [9]	WP6	**Lead beneficiary** [10]	3 - RSD
Work package title	Accuracy of anomaly coding in health care databases		
Start month	4	**End month**	60

Objectives

To evaluate the accuracy and the quality of the ICD coding of congenital anomalies in health care databases compared to EUROCAT data
To develop algorithms for use of health care data in the surveillance of congenital anomalies to improve the quality of the data
To evaluate the accuracy and the quality of data on terminations of pregnancy for fetal anomalies from health care databases and provide advice on coding to improve it

Description of work and role of partners

WP6 - Accuracy of anomaly coding in health care databases [Months: 4-60]
RSD, QMUL, UNEW, UNIFE, KDB, CNR-IFC, UMCG, PHW NHS, FISABIO, THL, BIOEF, SU
This WP will be led by RSD (Ester Garne) and UMCG (Hermien de Walle).
Once EUROCAT cases have been linked (WP2) comparison of the congenital anomaly coding in hospital discharge databases can be evaluated using EUROCAT as the gold standard. The level of under-ascertainment of cases in EUROCAT may also be estimated. Similarly the civil registration of terminations of pregnancy for fetal anomalies of all EUROCAT cases in mortality databases can be evaluated. Differences in prevalence of specific anomalies in the two systems can be evaluated. The potential or the problems in using health care databases for surveillance of trends and clusters of congenital anomalies can be accurately assessed. The specific tasks are to:
1. Evaluate the accuracy of coding of all specific EUROCAT congenital anomaly subgroups in hospital discharge databases (UMCG)
2. Evaluate the accuracy of coding of registration status and anomaly coding of terminations of pregnancy with fetal anomalies in different datasets (RSD).
3. Develop algorithms to improve use of routine databases – for example in hospital discharge data use surgical codes for club foot, coding of specific oral clefts and examine ASD coding with focus on over-reporting in the neonatal period (UNIFE)

Participation per Partner

Partner number and short name	WP6 effort
1 - QMUL	1.00
3 - RSD	10.00
4 - UNEW	1.00
5 - UNIFE	10.00
6 - KDB	1.00
7 - CNR-IFC	1.00
8 - UMCG	10.00
9 - PHW NHS	0.50
11 - FISABIO	1.00
13 - THL	1.00
19 - BIOEF	1.00
22 - SU	0.50

Partner number and short name	WP6 effort
Total	38.00

List of deliverables

Deliverable Number[14]	Deliverable Title	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
D6.1	Report on the evaluation of specific congenital anomaly coding in health care databases including a computer algorithm to improve these codes	8 - UMCG	Report	Public	54

Description of deliverables

1. Report on the evaluation of specific congenital anomaly coding in health care databases (UMCG) including a computer algorithm to improve these codes (UNIFE) (Month 54)

D6.1 : Report on the evaluation of specific congenital anomaly coding in health care databases including a computer algorithm to improve these codes [54]

Report on the evaluation of specific congenital anomaly coding in health care databases including a computer algorithm to improve these codes

Schedule of relevant Milestones

Milestone number[18]	Milestone title	Lead beneficiary	Due Date (in months)	Means of verification
MS7	Create registry-specific syntax scripts to derive study variables, to implement study designs, and to run the pre-defined analysis for WP6	2 - UU	34	Create registry-specific syntax scripts to derive study variables, to implement study designs, and to run the pre-defined analysis for WP6
MS10	Study protocol for ethical approval, available on membership-only section of website	4 - UNEW	8	Study protocol for ethical approval, available on membership-only section of website
MS21	Protocol for analysis plan prepared for evaluation of specific congenital anomaly coding in health care databases, available on membership-only section of website	8 - UMCG	35	Protocol for analysis plan prepared for evaluation of specific congenital anomaly coding in health care databases, available on membership-only section of website
MS22	Protocol for analysis plan prepared for coding (registration status and anomaly coding) of terminations of pregnancy for fetal anomalies in mortality	3 - RSD	35	Protocol for analysis plan prepared for coding (registration status and anomaly coding) of terminations of pregnancy for fetal anomalies in mortality

Schedule of relevant Milestones

Milestone number[18]	Milestone title	Lead beneficiary	Due Date (in months)	Means of verification
	and health care databases, available on membership-only section of website			and health care databases, available on membership-only section of website
MS23	Protocol for analysis plan prepared for algorithm for using congenital anomaly data from hospital discharge databases, available on membership-only section of website	5 - UNIFE	35	Protocol for analysis plan prepared for algorithm for using congenital anomaly data from hospital discharge databases, available on membership-only section of website

Work package number [9]	WP7	Lead beneficiary [10]	2 - UU
Work package title	ConnectEpeople		
Start month	1	End month	60

Objectives

To connect researchers with families who live with congenital anomalies (CA) across Europe to involve them in setting research priorities and ensuring that research results are disseminated in a meaningful way.
To establish a sustainable e-forum, "ConnectEpeople", for providing regional, national and international support to families with congenital anomalies through maintaining the links between the EUROCAT congenital anomaly registries and the families.

Description of work and role of partners

WP7 - ConnectEpeople [Months: 1-60]
UU, QMUL, RSD, UNEW, UNIFE, KDB, CNR-IFC, UMCG, FISABIO, PUMS, OVGU, INSA, CHURéunion, Redburn
This WP will be led by UU (Marlene Sinclair) and PUMS (Anna Latos-Bielenska). Redburn Solutions Ltd will provide the IT support and expertise required to establish the e-forum "ConnectEpeople"
ConnectEpeople is about registries contacting parents and carers of children with congenital anomalies in their regions and creating a network linking them with local, national and international registries and evidence-based information resources.
This WP will scope the current networks available within the EU registries and their links to parent groups and evidence based resources. It will then survey parent groups to identify their specific information needs related to one of four congenital anomalies: Down syndrome (a visible anomaly with many health issues including intellectual disability), Severe congenital heart defects (non-visible anomalies with very high mortality requiring multiple surgeries), Spina bifida (a visible anomaly which can be physically disabling and intellectually disabling with potential to require surgery) and Cleft lip with cleft palate (a visible anomaly with associated speech problems requiring multiple surgeries). An e-forum will be created to link parents with professionals and researchers. This forum will connect the micro network of parent groups at individual registry level first then with each other at a meso level and at the macro level with the full EUROlinkCAT researchers thus creating a new line of communication to directly connect the researchers and the parents. The resulting e-forum will work together with researchers to interpret data emerging form the various WPs on morbidity, mortality and education; using m-technologies. The data will be translated into meaningful messages that are relevant, accessible and easily understood using info graphics, wordles and videos where appropriate.
The specific tasks are :
1. Each registry will identify at least one parent support group concerned with each of the four congenital anomalies chosen and work with them face to face or by twitter, Facebook, email, skype, webinar, live chat or blogging to identify all of the current communication networks they use to obtain information about their children's conditions. The availability and quality of the data in relation to morbidity, mortality, and education will be reviewed. Each local registry and parent group network will be linked to create a virtual stakeholder forum "ConnectEpeople", where a summary of this network scoping exercise will be presented.
2. Each registry will communicate to the families what information is being collected plus what specific hypothesis are planned to be investigated in EUROlinkCAT. This information will be produced in English and the Registry Leaders will be responsible for communicating it to their network in their native language. The parents views on additional hypothesis will be sought firstly within each local registry and parent group network and then on "ConnectEpeople" forum. A face to face consultation meeting involving registry leaders and any connecting parents using webinar and skype will finalise the decisions about the research priorities.
3. In years 3 and 4 two sets of key findings (one each year) from the WPs will be placed on the "ConnectEpeople" forum and Registry Leaders will be responsible for communicating these to their network in their native language and consulting with them about the interpretation and dissemination of these key messages. Live face to face meetings involving registries and connecting parents using webinar and skype will occur. A graphic designer will develop suitable images that will facilitate interpretation of complex data on morbidity and mortality issues for the web.
4. In year 5 the effectiveness of the e-communication system will be assessed using a mixed method approach. Google analytics will be used to demonstrate the number of visitors to the "ConnectEpeople" forum and their online activity. Registry Leaders will be responsible for asking people to complete a survey to explore perceptions of impact resulting

from “ConnectEpeople”, to explore new networks and developments that have occurred during the study and to evaluate what worked well and what improvements could be introduced.
The long term outcome anticipated from this WP is an E-connected European Consumer-led Stakeholder Group that operates post project delivery and contributes to the continued work of EUROlinkCAT and EUROCAT.

Participation per Partner

Partner number and short name	WP7 effort
1 - QMUL	13.00
2 - UU	66.00
3 - RSD	15.00
4 - UNEW	4.00
5 - UNIFE	5.00
6 - KDB	5.00
7 - CNR-IFC	4.00
8 - UMCG	5.00
11 - FISABIO	5.00
12 - PUMS	5.00
15 - OVGU	5.00
16 - INSA	5.00
17 - CHURéunion	5.00
21 - Redburn	6.22
Total	148.22

List of deliverables

Deliverable Number[14]	Deliverable Title	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
D7.1	Formation of e stakeholder forum “ConnectEpeople”	2 - UU	Report	Public	14
D7.2	Report evaluating E-Systems for linking researchers, professionals and consumers across Europe	2 - UU	Report	Public	58

Description of deliverables

1. Formation of e stakeholder forum “ConnectEpeople” (Month 14)(UU)
2. Report evaluating E-Systems for linking researchers, professionals and consumers across Europe (Month 58)(UU)

D7.1 : Formation of e stakeholder forum “ConnectEpeople” [14]

Formation of e stakeholder forum “ConnectEpeople”

D7.2 : Report evaluating E-Systems for linking researchers, professionals and consumers across Europe [58]

Report evaluating E-Systems for linking researchers, professionals and consumers across Europe

Schedule of relevant Milestones

Milestone number[18]	Milestone title	Lead beneficiary	Due Date (in months)	Means of verification
MS24	Summary of scoping exercise on communication networks used by parent support groups	2 - UU	12	Summary of scoping exercise on communication networks used by parent support groups
MS25	Synopsis of families' research priorities so WP leaders can incorporate into study protocols if possible	2 - UU	12	Synopsis of families' research priorities so WP leaders can incorporate into study protocols if possible
MS26	Upload graphics representing mortality and morbidity results to membership-only section of website, and then live website after they have been published in papers	2 - UU	48	Upload graphics representing mortality and morbidity results to membership-only section of website, and then live website after they have been published in papers

Work package number [9]	WP8	Lead beneficiary [10]	5 - UNIFE
Work package title	Dissemination and Evaluation		
Start month	1	End month	60

Objectives

To disseminate a comprehensive and consistent set of ideas arising from the results from the EUROlinkCAT project in order to maximise their impact
To evaluate the EUROlinkCAT project

Description of work and role of partners

WP8 - Dissemination and Evaluation [Months: 1-60]
UNIFE, QMUL, UU, RSD, UNEW, KDB, CNR-IFC, UMCG, PHW NHS, INSERM, FISABIO, PUMS, THL, OMNI NET, OVGU, INSA, CHURéunion, PIH, BIOEF, BIOMED
This WP will be led by UNIFE (Amanda Neville), PUMS (Anna Latos-Bielenska) and KDB (Ingeborg Barisic)
The focus of this WP is to target utilisable information in appropriate ways to the different stake holders in this project, from Public health policy units and professionals to individuals and care givers recognising that a wide range of dissemination methods are needed given the wide range of stakeholders that will be interested in EUROlinkCAT. Results from WP7 will inform the additional dissemination of information using new technologies, such as face book, to individual members of society. The specific tasks are :
Initial dissemination
1. Create an email list of potential stake holders to include parent support groups, special interest groups in addition to existing European networks such as ICORD and EUcerd and Public Health Bodies. (KDB) (month 2)
2. Design promotional material for the website including an information leaflet and distribute to potential stakeholders. A strategy for dissemination suitable for different countries (languages) will be agreed. (UNIFE) (month 3)
3. Organise a consultation and training meeting of Registry Leaders in Croatia and any connecting parents using webinar and skype to finalise the decisions about research priorities. Specific areas of research that stake holders are interested in and communication pathways and methods other than publishing scientific papers for dissemination will be considered. (KDB) (month 9)
Continued Dissemination
4. Update website, information leaflet and other promotional material, ensuring that early results (such as Data quality indicators) are visible and comprehensible.
5. Continue to investigate and liaise with other European
6. Poland does not have established national electronic healthcare databases. A meeting with relevant Polish experts will be convened to discuss results from WP2 and WP6 to inform best practices for creating electronic databases.
Dissemination and Evaluation at end of project
7. Organise a dissemination conference in Poland to agree a set of recommendations to improve the mortality, morbidity and education of children in Europe with congenital anomalies. Recommendations about establishing devolved databases including issues around informed consent, ethics approval, data security, patients' rights to their own data and data release will be presented. One session of the workshop will be specifically devoted to the establishment and continued development of the EUROlinkCAT cohort of devolved databases and their strength over using unlinked routine health care data. The Workshop will be the occasion for a co-ordinated press release in the European countries. An evaluation of the project by the stake holders will be included. (PUMS)
8. Use the results from WP7 to inform the additional dissemination of information using new technologies, such as face book, to individual members of society in different countries.
9. Ensure lay summaries are available for all major results.
10. Disseminate the project's findings with Public Health Institutes across Europe about children with Congenital Anomalies and the associations with mortality, morbidity and education and how variations across Europe influence policy making

Participation per Partner

Partner number and short name	WP8 effort
1 - QMUL	14.05
2 - UU	0.60
3 - RSD	9.60
4 - UNEW	0.30
5 - UNIFE	7.30
6 - KDB	5.80
7 - CNR-IFC	1.80
8 - UMCG	0.30
9 - PHW NHS	0.30
10 - INSERM	0.30
11 - FISABIO	0.30
12 - PUMS	9.30
13 - THL	0.30
14 - OMNI NET	0.30
15 - OVGU	0.30
16 - INSA	0.30
17 - CHURéunion	0.30
18 - PIH	0.30
19 - BIOEF	0.30
20 - BIOMED	0.30
Total	52.35

List of deliverables

Deliverable Number[14]	Deliverable Title	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
D8.1	Information Leaflet	5 - UNIFE	Report	Public	3
D8.2	Consultation meeting	6 - KDB	Websites, patents filling, etc.	Public	14
D8.3	Report to EU institutions hosting health care databases with guidelines for improving the quality of the congenital anomaly coding	3 - RSD	Websites, patents filling, etc.	Public	57
D8.4	Dissemination conference	12 - PUMS	Websites, patents filling, etc.	Public	58

Description of deliverables

1. Produce initial information leaflet to promote EUROlinkCAT project (UNIFE) (month 3)
2. Initial EUROlinkCAT consultation meeting (KDB) (month 14)
3. Report to EU institutions hosting health care databases with guidelines for improving the quality of the congenital anomaly coding – together with WP6 (RSD) (month 57)
4. Final EUROlinkCAT dissemination conference (PUMS) (month 58)

D8.1 : Information Leaflet [3]

Produce initial information leaflet to promote EUROlinkCAT project.

D8.2 : Consultation meeting [14]

Consultation meeting

D8.3 : Report to EU institutions hosting health care databases with guidelines for improving the quality of the congenital anomaly coding [57]

Report to EU institutions hosting health care databases with guidelines for improving the quality of the congenital anomaly coding

D8.4 : Dissemination conference [58]

Dissemination conference

Schedule of relevant Milestones

Milestone number[18]	**Milestone title**	**Lead beneficiary**	**Due Date (in months)**	**Means of verification**
MS27	Evaluate frequency of visits to EUROlinkCAT webpages using Google analytics	5 - UNIFE	58	Evaluate frequency of visits to EUROlinkCAT webpages using Google analytics
MS28	Ensure Lay Summaries are on the website within 3 months of acceptance of each paper	5 - UNIFE	60	Ensure Lay Summaries are on the website within 3 months of acceptance of each paper

Work package number [9]	WP9	Lead beneficiary [10]	1 - QMUL
Work package title	Ethics requirements		
Start month	1	End month	60

Objectives

The objective is to ensure compliance with the 'ethics requirements' set out in this work package.

Description of work and role of partners

WP9 - Ethics requirements [Months: 1-60]
QMUL
This work package sets out the 'ethics requirements' that the project must comply with.

List of deliverables

Deliverable Number[14]	Deliverable Title	Lead beneficiary	Type[15]	Dissemination level[16]	Due Date (in months)[17]
D9.1	H - Requirement No. 1	1 - QMUL	Ethics	Confidential, only for members of the consortium (including the Commission Services)	24
D9.2	NEC - Requirement No. 2	1 - QMUL	Ethics	Confidential, only for members of the consortium (including the Commission Services)	1
D9.3	POPD - Requirement No. 3	1 - QMUL	Ethics	Confidential, only for members of the consortium (including the Commission Services)	6

Description of deliverables

The 'ethics requirements' that the project must comply with are included as deliverables in this work package.

D9.1 : H - Requirement No. 1 [24]

Detailed information must be provided on the informed consent procedures that will be implemented for the participation of humans in the context of reuse of their personal data and potentially biological samples. More specifically, the applicants must clarify how consent/assent will be ensured as children are clearly involved. Current project related templates of the informed consent forms and information sheet must be submitted, and procedure implemented to gain re-reconsent detailed (annoucements with dedicated contacts in a set of medias, etc...). In short, the procedure to be adopted to gain permission for such secondary use should be described. Potentially vulnerable patients/individuals will be involved in the research. Therefore, the procedures that will be used to assess the decision-making capacity of these participants must be provided in order to ensure that only those able to give consent will be involved in the research. Details on incidental findings policy must be provided. A complete portfolio of copies of all ethical approvals that cover all aspects of the research by all of the partners of the Consortium throughout the lifetime of the project must be compiled and retained by the Consotium and must be available to the Commission if requested and for Ethics Checks or Audits. Copies of current ethics approvals for the research with humans must be submitted. A complete portfolio of copies of Informed Consent Forms and Information Sheets that

cover all aspects of the research by all of the partners of the Consortium throughout the lifetime of the project must be compiled and retained by the Consortium and must be available to the Commission if requested and for Ethics Checks or Audits. Copies of opinion or confirmation by the competent Institutional Data Protection Officer and/ or authorization or notification by the National Data Protection Authority must be submitted (which ever applies according to the Data Protection Directive (EC Directive 95/46, currently under revision, and the national law).

D9.2 : NEC - Requirement No. 2 [1]

The applicant must confirm that the ethical standards and guidelines of Horizon2020 will be rigorously applied, regardless of the country in which the research is carried out. In this respect, and Ukraine not being in the EU adequacy list, the applicant must provide details on the material which will be imported to/exported from EU and provide the adequate authorisations.

D9.3 : POPD - Requirement No. 3 [6]

The applicants must devise a data management plan including detailed information on the procedures that will be implemented for data collection, storage, protection, retention and destruction and confirmation that they comply with national and EU legislation, as well as copies of current opinion or confirmation by the competent Institutional Data Protection Officer and/or authorization or notification by the National Data Protection Authority (which ever applies according to the Data Protection Directive (EC Directive 95/46, still applcable till May the 24th 2018 and the national law). During the lifetime of this project (on 25/05/2018) the EU General Data Protection Regulation (Regulation (EU) 2016/679), revising Directive 95/46/EC on Data Protection and Privacy, will come into force. The applicant needs to take this into account to ensure continuous compliance. Information on data structure and Templates of the informed consent forms and information sheet must also be included. Likewise, the situation of the british partner as regard to EU law might change during the course of the project. The applicants must take steps to ensure the sustainability and compliance with European rules of the processes used by the UK partner.

Schedule of relevant Milestones

Milestone number[18]	Milestone title	Lead beneficiary	Due Date (in months)	Means of verification

1.3.4. WT4 List of milestones

Milestone number[18]	Milestone title	WP number[9]	Lead beneficiary	Due Date (in months)[17]	Means of verification
MS1	General consortium meetings during the Registry Leaders Meeting	WP1	1 - QMUL	6	General consortium meetings during the Registry Leaders Meeting – including minutes uploaded to membership-only section of website (QMUL) (6,18,30,42,54)
MS2	Steering Group meetings	WP1	1 - QMUL	6	Steering Group meetings – including minutes uploaded to membership-only section of website (QMUL) (6,12,18,24,30,36,42,48,54)
MS3	Produce a fully documented Report of the local data sources / content of data available for each registry (includes variable names, variable descriptions, definitions, coding instructions/ values).	WP2	2 - UU	12	Produce a fully documented Report of the local data sources / content of data available for each registry (includes variable names, variable descriptions, definitions, coding instructions/ values). (UU) (Task 1, Uploaded to website Month 12)
MS4	Confirm the agreed variables standardised across Europe (i.e. the common model)	WP2	2 - UU	15	Confirm the agreed variables standardised across Europe (i.e. the common model). Relates to task 2. (UU) (Month 15).
MS5	Create registry-specific syntax scripts to derive study variables, to implement study designs, and to run the pre-defined analysis for WP3	WP2, WP3	2 - UU	22	Create registry-specific syntax scripts to derive study variables, to implement study designs, and to run the pre-defined analysis for WP3
MS6	Create registry-specific syntax scripts to derive study variables, to implement study designs, and to run the pre-defined analysis for WP4	WP2, WP4	2 - UU	34	Create registry-specific syntax scripts to derive study variables, to implement study designs, and to run the pre-defined analysis for WP4
MS7	Create registry-specific syntax scripts to derive study variables, to implement study designs, and to run the pre-defined analysis for WP6	WP2, WP6	2 - UU	34	Create registry-specific syntax scripts to derive study variables, to implement study designs, and to run the pre-defined analysis for WP6

Milestone number[18]	Milestone title	WP number[9]	Lead beneficiary	Due Date (in months)[17]	Means of verification
MS8	Create registry-specific syntax scripts to derive study variables, to implement study designs, and to run the pre-defined analysis for WP5	WP2, WP5	2 - UU	37	Create registry-specific syntax scripts to derive study variables, to implement study designs, and to run the pre-defined analysis for WP5
MS9	Produce Data Quality Report describing data quality, specificity of coding, prevalence of exposure, and presence of missing data for each participating registry compared to the average.	WP2	2 - UU	48	Produce Data Quality Report describing data quality, specificity of coding, prevalence of exposure, and presence of missing data for each participating registry compared to the average.
MS10	Study protocol for ethical approval, available on membership-only section of website	WP3, WP4, WP5, WP6	4 - UNEW	8	Study protocol for ethical approval, available on membership-only section of website
MS11	2. Protocol for analysis plan prepared for Survival and risk factors for survival for children born with a congenital anomaly, available on membership-only section of website	WP3	4 - UNEW	12	2. Protocol for analysis plan prepared for Survival and risk factors for survival for children born with a congenital anomaly, available on membership-only section of website
MS12	Protocol for analysis plan prepared for Geographical variations in Europe on survival of children with a congenital anomaly, available on membership-only section of website	WP3	5 - UNIFE	15	Protocol for analysis plan prepared for Geographical variations in Europe on survival of children with a congenital anomaly, available on membership-only section of website
MS13	Protocol for analysis plan prepared for Hospitalisations/ number of days in hospitals and operations across Europe for the first 5 years of life for children born with a congenital anomaly., available	WP4	3 - RSD	12	Protocol for analysis plan prepared for Hospitalisations/ number of days in hospitals and operations across Europe for the first 5 years of life for children born with a congenital anomaly., available on membership-only section of website

Milestone number[18]	Milestone title	WP number[9]	Lead beneficiary	Due Date (in months)[17]	Means of verification
	on membership-only section of website				
MS14	Protocol for analysis plan prepared for Infections and respiratory illness defined as use of medications during the first 5 years of life for children born with a congenital anomaly, available on membership-only section of website	WP4	2 - UU	15	Protocol for analysis plan prepared for Infections and respiratory illness defined as use of medications during the first 5 years of life for children born with a congenital anomaly, available on membership-only section of website
MS15	Protocol for analysis plan prepared Is there a relationship between prenatal diagnosis and lower morbidity if the congenital anomaly is diagnosed prenatally?, available on membership-only section of website	WP4	3 - RSD	15	Protocol for analysis plan prepared Is there a relationship between prenatal diagnosis and lower morbidity if the congenital anomaly is diagnosed prenatally?, available on membership-only section of website
MS16	Protocol for analysis plan prepared Geographic variations in Europe for morbidity for children born with a congenital anomaly, available on membership-only section of website	WP4	2 - UU	18	Protocol for analysis plan prepared Geographic variations in Europe for morbidity for children born with a congenital anomaly, available on membership-only section of website
MS17	Protocol for analysis plan prepared for The costs of hospitalisation across Europe during the first 5 years of life for children born with a congenital anomaly, available on membership-only section of website	WP4	1 - QMUL	21	Protocol for analysis plan prepared for The costs of hospitalisation across Europe during the first 5 years of life for children born with a congenital anomaly, available on membership-only section of website
MS18	Protocol for analysis plan prepared for Education achievements and needs of children born with a congenital anomaly and geographical variation	WP5	4 - UNEW	26	Protocol for analysis plan prepared for Education achievements and needs of children born with a congenital anomaly and geographical variation in Europe, available on

Milestone number[18]	Milestone title	WP number[9]	Lead beneficiary	Due Date (in months)[17]	Means of verification
	in Europe, available on membership-only section of website				membership-only section of website
MS19	Protocol for analysis plan prepared for How do clinical and sociodemographic factors impact on educational achievements and needs for children born with a congenital anomaly?, available on membership-only section of website	WP5	4 - UNEW	23	Protocol for analysis plan prepared for How do clinical and sociodemographic factors impact on educational achievements and needs for children born with a congenital anomaly?, available on membership-only section of website
MS20	Protocol for analysis plan prepared for the predictions of the number of children with congenital anomalies across Europe under 11 who will have specific educational needs, available on membership-only section of website	WP5	4 - UNEW	26	Protocol for analysis plan prepared for the predictions of the number of children with congenital anomalies across Europe under 11 who will have specific educational needs, available on membership-only section of website
MS21	Protocol for analysis plan prepared for evaluation of specific congenital anomaly coding in health care databases, available on membership-only section of website	WP6	8 - UMCG	35	Protocol for analysis plan prepared for evaluation of specific congenital anomaly coding in health care databases, available on membership-only section of website
MS22	Protocol for analysis plan prepared for coding (registration status and anomaly coding) of terminations of pregnancy for fetal anomalies in mortality and health care databases, available on membership-only section of website	WP6	3 - RSD	35	Protocol for analysis plan prepared for coding (registration status and anomaly coding) of terminations of pregnancy for fetal anomalies in mortality and health care databases, available on membership-only section of website
MS23	Protocol for analysis plan prepared for algorithm for using congenital anomaly data from	WP6	5 - UNIFE	35	Protocol for analysis plan prepared for algorithm for using congenital anomaly data from hospital discharge databases, available on

Milestone number[18]	Milestone title	WP number[9]	Lead beneficiary	Due Date (in months)[17]	Means of verification
	hospital discharge databases, available on membership-only section of website				membership-only section of website
MS24	Summary of scoping exercise on communication networks used by parent support groups	WP7	2 - UU	12	Summary of scoping exercise on communication networks used by parent support groups
MS25	Synopsis of families' research priorities so WP leaders can incorporate into study protocols if possible	WP7	2 - UU	12	Synopsis of families' research priorities so WP leaders can incorporate into study protocols if possible
MS26	Upload graphics representing mortality and morbidity results to membership-only section of website, and then live website after they have been published in papers	WP7	2 - UU	48	Upload graphics representing mortality and morbidity results to membership-only section of website, and then live website after they have been published in papers
MS27	Evaluate frequency of visits to EUROlinkCAT webpages using Google analytics	WP8	5 - UNIFE	58	Evaluate frequency of visits to EUROlinkCAT webpages using Google analytics
MS28	Ensure Lay Summaries are on the website within 3 months of acceptance of each paper	WP8	5 - UNIFE	60	Ensure Lay Summaries are on the website within 3 months of acceptance of each paper

1.3.5. WT5 Critical Implementation risks and mitigation actions

Risk number	Description of risk	WP Number	Proposed risk-mitigation measures
1	Non-availability of the data from a registry either due to i. Refusal of ethics permission in a register ii. Refusal of permissions to link to a specific dataset iii. Difficulties in linking iv. Lack of funding for a registry Likelihood of occurring in more than one registry : low	WP2, WP3, WP4, WP5, WP6, WP7	For each work package there are several registries that can contribute so the withdrawal of one or two is not critical to the overall delivery of the project. For the first year of the project approaches to other replacement registries will be made. For instance Norway is likely to be able to contribute at a later stage, but cannot commit their resources at present. Difficulties in linking are unlikely as all the planned linkages have been performed already by at least one register Registry funding is not guaranteed, but all the participant registries have had secure funding for over 10 years and therefore we believe are likely to continue to be funded. This project will use data already collected and therefore if the registry is no longer funded the data already collected may still be available for use. The project is not dependent on future data collection by the registries.
2	Delays in obtaining data from a registry either due to i. Delays in ethics permission ii. Delays in performing the linkage Likelihood of occurring in more than one registry : low	WP2, WP3, WP4, WP5, WP6, WP7	Up to 24 months has been allowed for such permissions and linkage to occur. Although no progress can be made in the linkage for a specific registry until the correct permissions are in place, the work in standardising all the variable definitions can occur. Considerable work can also be completed on coding and ensuring consistency with available data whilst waiting for the final registries to have their data available. Even preliminary analysis can be performed. If severe delays are occurring in only one or two registries the Steering Committee will decide, by consensus, if the final analysis will exclude data from a specific registry in order to meet the deliverable and milestone due dates. Such a decision will need to be followed by an amendment to the action.
3	Withdrawal of partners from the project due to unforeseen circumstances. Liklihood of occurrence: low	WP1, WP2, WP3, WP4, WP5, WP6, WP7, WP8	No one partner is essential to the project. All work packages have a leader and a deputy leader to ensure continuity if the leader is no longer available.
4	Major delays in WP2 producing the Central Results Repository Likelihood of occurring : low	WP2	WP2 is led by UU with a deputy leader BioMedical Computing. There is also a contribution from a research fellow in QMUL confirming all the syntax scripts. This could be done by other statisticians in different work packages (it does not have to be done by just 1 person) and the research fellow could then spend more time working for WP2. BioMedical Computing would also be able to increase their contribution. If there are severe delays QMUL (Professor Morris) would be able to contribute more.

Risk number	Description of risk	WP Number	Proposed risk-mitigation measures
5	Non participation in the e-forum “ConnectEpeople” by families with children with anomalies within the first 36 months	WP7	This would indicate that the e-forum was not providing what the families wished to be provided with. UU would need to develop a strategy for Individual registries to approach families to investigate this in more detail and hopefully the design of the e-forum could be adapted. The revised objective would be to have an established e-forum by completion of the project.
6	Poor Quality of the Linked Data Likelihood of occurring in one or more registries in one or more linked data sets : medium	WP2, WP3, WP4, WP5, WP6, WP7, WP8	All linked data sources will be examined for data quality using specifically developed data quality indicators. Those data sets of too poor a quality will not be included in subsequent analysis. For all work packages the main analyses will involve the variables in the data that will be most robust to poor completion (for example date of death rather than cause of death will be analysed). If there is insufficient data of a reasonable quality available to perform the analysis this is an important result and the researchers will aim to produce a detailed set of recommendations to improve the data for future use.
7	The EDPB identifies a serious ethics issue concerning one or more registries : Likelihood of occurring : low	WP2, WP3, WP4, WP5, WP6	The Project Management Team will consult with the registry and the EDPB in order to rectify this issue. If the EDPB recommends that the data from this registry cannot be used this will be followed and an amendment to the action will be submitted.

1.3.6. WT6 Summary of project effort in person-months

	WP1	WP2	WP3	WP4	WP5	WP6	WP7	WP8	WP9	Total Person/Months per Participant
1 - QMUL	88.25	72.85	1	8	1	1	13	14.05		199.15
2 - UU	5.65	60.55	0	24	0	0	66	0.60		156.80
3 - RSD	2.80	16.55	1	11	1	10	15	9.60		66.95
4 - UNEW	2.70	5.55	11	1	30	1	4	0.30		55.55
5 - UNIFE	2.70	18	1	1	10	10	5	7.30		55
6 - KDB	2.70	15.50	1	1	0	1	5	5.80		32
7 - CNR-IFC	2.70	12.55	11	1	0	1	4	1.80		34.05
· ARS	0	0	0	0	0	0	0	0	0	0
8 - UMCG	2.70	13.05	1	1	0	10	5	0.30		33.05
9 - PHW NHS	0	0.55	0.50	0.50	0.50	0.50	0	0.30		2.85
10 - INSERM	0	3.50	1	0	0	0	0	0.30		4.80
11 - FISABIO	0	15.50	1	1	0	1	5	0.30		23.80
12 - PUMS	2.70	0	0	0	0	0	5	9.30		17
13 - THL	0	18	1	11	1	1	0	0.30		32.30
14 - OMNI NET	0	12.50	1	1	0	0	0	0.30		14.80
15 - OVGU	0	3.75	1	0	0	0	5	0.30		10.05
16 - INSA	0	8	0	1	0	0	5	0.30		14.30
17 - CHURéunion	0	12	1	1	0	0	5	0.30		19.30
18 - PIH	0	3.25	1	0	0	0	0	0.30		4.55
19 - BIOEF	0	10.50	1	1	0	1	0	0.30		13.80
· BasqueGov	0	0	0	0	0	0	0	0	0	0
20 - BIOMED	0.95	12.35	0	0	0	0	0	0.30		13.60
21 - Redburn	0	0	0	0	0	0	6.22	0		6.22

	WP1	WP2	WP3	WP4	WP5	WP6	WP7	WP8	WP9	Total Person/Months per Participant
22 - SU	0	16.45	0.50	0.50	0.50	0.50	0	0		18.45
Total Person/Months	113.85	330.95	36	65	44	38	148.22	52.35		828.37

1.3.7. WT7 Tentative schedule of project reviews

Review number [19]	Tentative timing	Planned venue of review	Comments, if any
RV1	30	Ethics check	Internal check of ethical documents submitted and available according to ethics management table.

1. Project number

The project number has been assigned by the Commission as the unique identifier for your project. It cannot be changed. The project number **should appear on each page of the grant agreement preparation documents (part A and part B)** to prevent errors during its handling.

2. Project acronym

Use the project acronym as given in the submitted proposal. It can generally not be changed. The same acronym **should appear on each page of the grant agreement preparation documents (part A and part B)** to prevent errors during its handling.

3. Project title

Use the title (preferably no longer than 200 characters) as indicated in the submitted proposal. Minor corrections are possible if agreed during the preparation of the grant agreement.

4. Starting date

Unless a specific (fixed) starting date is duly justified and agreed upon during the preparation of the Grant Agreement, the project will start on the first day of the month following the entry into force of the Grant Agreement (NB : entry into force = signature by the Commission). Please note that if a fixed starting date is used, you will be required to provide a written justification.

5. Duration

Insert the duration of the project in full months.

6. Call (part) identifier

The Call (part) identifier is the reference number given in the call or part of the call you were addressing, as indicated in the publication of the call in the Official Journal of the European Union. You have to use the identifier given by the Commission in the letter inviting to prepare the grant agreement.

7. Abstract

8. Project Entry Month

The month at which the participant joined the consortium, month 1 marking the start date of the project, and all other start dates being relative to this start date.

9. Work Package number

Work package number: WP1, WP2, WP3, ..., WPn

10. Lead beneficiary

This must be one of the beneficiaries in the grant (not a third party) - Number of the beneficiary leading the work in this work package

11. Person-months per work package

The total number of person-months allocated to each work package.

12. Start month

Relative start date for the work in the specific work packages, month 1 marking the start date of the project, and all other start dates being relative to this start date.

13. End month

Relative end date, month 1 marking the start date of the project, and all end dates being relative to this start date.

14. Deliverable number

Deliverable numbers: D1 - Dn

15. Type

Please indicate the type of the deliverable using one of the following codes:

R	Document, report
DEM	Demonstrator, pilot, prototype
DEC	Websites, patent fillings, videos, etc.
OTHER	
ETHICS	Ethics requirement

16. Dissemination level

Please indicate the dissemination level using one of the following codes:

PU	Public
CO	Confidential, only for members of the consortium (including the Commission Services)
EU-RES	Classified Information: RESTREINT UE (Commission Decision 2005/444/EC)
EU-CON	Classified Information: CONFIDENTIEL UE (Commission Decision 2005/444/EC)
EU-SEC	Classified Information: SECRET UE (Commission Decision 2005/444/EC)

17. Delivery date for Deliverable

Month in which the deliverables will be available, month 1 marking the start date of the project, and all delivery dates being relative to this start date.

18. Milestone number

Milestone number:MS1, MS2, ..., MSn

19. Review number

Review number: RV1, RV2, ..., RVn

20. Installation Number

Number progressively the installations of a same infrastructure. An installation is a part of an infrastructure that could be used independently from the rest.

21. Installation country

Code of the country where the installation is located or IO if the access provider (the beneficiary or linked third party) is an international organization, an ERIC or a similar legal entity.

22. Type of access

VA	if virtual access,
TA-uc	if trans-national access with access costs declared on the basis of unit cost,
TA-ac	if trans-national access with access costs declared as actual costs, and
TA-cb	if trans-national access with access costs declared as a combination of actual costs and costs on the basis of unit cost.

23. Access costs

Cost of the access provided under the project. For virtual access fill only the second column. For trans-national access fill one of the two columns or both according to the way access costs are declared. Trans-national access costs on the basis of unit cost will result from the unit cost by the quantity of access to be provided.

History of Changes

Version	Date	Change	Page
1	17/09/2016	"At their first meeting, the SC will finalise an agreement to be signed by all participants and subcontractors, adapted from the DESCA Horizon 2020 Model Consortium Agreement" has been changed to : "A consortium agreement will be developed based on the DESCA Horizon 2020 Model Consortium Agreement. It is planned that this will be signed by all participants before the Grant Agreement is signed."	38
1	17/09/2016	Text added "In particular not all EUROCAT registries are participating in EUROlinkCAT. The registries that are not participating will be kept fully informed about EUROlinkCAT during the Annual Registry Meetings and encouraged to consider participation in the future."	27
1	17/09/2016	Text added "National data on mortality is generally of an extremely high quality with respect to overall completeness and the date of birth and date of death of the child. There are no plans to analyse the cause of death and therefore the accuracy of this is not essential. However, there may be some issues with children being adopted and hence not traceable. This is unlikely to occur often enough to cause a significant bias to our results."	17
1	17/09/2016	Text added "The morbidity of children with congenital anomalies will be estimated using data which is administrative data and will be likely to be incomplete and inaccurate for many variables. For instance it is likely that the number of days in hospital will be well recorded, however the precise codes for the type of surgery may well not be so well recorded and also may differ in accuracy according to country. Such differences will need to be examined and dealt with in a variety of ways. One way is by defining a set of data quality indicators and "measuring" data quality in each data set. For some registries specific linked data sets may not be of sufficient quality to be used. If this occurs part of the work of WP2 includes clearly describing inadequacies in data sources and recommendations for improving them. The large advantage with EUROlinkCAT is that the data on the specific congenital anomalies will be accurate as it is coming directly from the congenital anomaly registries, we will not be relying on this information from the health care databases which we know are less accurate. (see section on information on congenital anomalies in health care databases)."	19
1	17/09/2016	Text added "Similarly to the health care databases educational databases are administrative databases and therefore it is to be expected that such databases may contain inaccurate and/or incomplete information for certain variables. Before commencing the analysis of educational data, the accuracy of the variables to be used must be examined in great detail and its quality taken into account in subsequent conclusions drawn from the data. It is important to evaluate if such educational data can be used and if it is not usable to feed this back to the authorities responsible for the data with constructive suggestions for its improvement."	20
Alterations to Part A	17/09/2016	Additional row has been added to Table 3.2b Poor Quality of the Linked Data Likelihood of occurring in one or more registries in one or more linked data sets : medium All linked data sources will be examined for data quality using specifically developed data quality indicators. Those data sets of too poor a quality will not be included in subsequent analysis. For all work packages the main analyses will involve the variables in the data that will be most robust to poor completion (for example date of death	Table 3.2b

		rather than cause of death will be analysed). If there is insufficient data of a reasonable quality available to perform the analysis this is an important result and the researchers will aim to produce a detailed set of recommendations to improve the data for future use.	
1	17/09/2016	Text added "for developing the data management plan"	38
1	17/09/2016	Text added" An Ethics and Data Protection Advisory Board (EDPB) consisting of two independent advisors with the relevant expertise will monitor all ethical concerns in this project. "	11
1	17/09/2016	Text added "WP1 will also be a repository for all ethics documentation and liase with the independent ethics and data protection board. "	33
1	17/09/2016	Text added " An Ethics and Data Protection Board (EDPB) will be appointed consisting of two professors (or professionals of equivalent standing) who have experience of the issues involved in data linkage projects and are independent from any of the partners. The members of the EDPB will be provided with all documentation concerning ethics or data management. An annual report will be prepared and submitted to the EDPB summarising any existing ethics or data management issues and the EDPB will meet annually face to face with the Management Team to discuss outstanding issues. A report by the EDPB will be submitted with the financial reports. The EDPB will provide advice to ensure that EUROlinkCAT will be compliant with the EU General Data Protection Regulation (Regulation (EU) 2016/679) when it comes into force."	39
1	17/09/2016	The Consultation meeting in Croatia is planned to occur around month 13 or 14 not month 11 /12 as originally specified. This has been altered throughout the text	31,36 , Table 3.1a, 3.1c
Part A	17/09/2016	Additional task has been added to WP1 Task 8 Support the Ethics and Data Protection Board (EDPB). a. QMUL will be responsible for compiling and retaining a complete portfolio of copies of Informed Consent Forms and Information Sheets that cover all aspects of the research by all of the partners of the Consortium throughout the lifetime of the project b. QMUL will be responsible for providing the EDPB with an annual report, ensuring they have been fully informed of any ethical issues and organising one meeting annually.	Table 3.1a
Part A	17/09/2016	Two deliverables in WP1 have been deleted 2. Final Report (QMUL) (Month 60) 3. Documented study archive (QMUL) (Month 60)	Table 3.1a
Part A	17/09/2016	Additional point has been added to WP2 Task 1 • Develop a detailed data management plan conforming to all EU and national legislation.	Table 3.1a
Part A	17/09/2016	WP2 Deliverable 1 (Produce a fully documented Report of the local data sources / content of data..) has been moved to being a milestone	Table 3.1a
Part A	17/09/2016	WP2 Deliverables 2,3,4 and 5 have been combined into one : Provide linked aggregate data (tables and analysis results) to WP3,4,5 and 6. (UU) (Task 3, Month 39)	Table 3.1a
Part A	17/09/2016	WP2 Deliverable 7 : Produce Data Quality Report describing data quality, specificity of … has been moved to being a milestone	Table 3.1a
Part A	17/09/2016	Deliverables in WP3,4,5,6 and 7 are now specified as being reports not peer reviewed papers.	Table 3.1a
Part A	17/09/2016	WP4 deliverables 4 and 5 have been removed (Deliverables 4 and 5 have been removed (Report on Geographic variations in Europe for morbidity and Report on the costs of hospitalisation across Europe during the first 5 years of life for children born with a congenital	Table 3.1a

		anomaly.	
Part A	17/09/2016	WP5 Deliverables 1and 3 have been removed (Report on education across countries of Europe and report on how clinical and sociodemographic factors impact on education for children born with a congenital anomaly?)	Table 3.1a
Part A	17/09/2016	WP6 Deliverables 1 and 3 have been combined as “Report on the evaluation of specific congenital anomaly coding in health care databases (UMCG) including a computer algorithm to improve these codes (UNIFE) (Month 54)”	Table 3.1a
Part A	17/09/2016	WP6 Deliverable 2 has been deleted (Report on coding of terminations of pregnancy for fetal anomalies in mortality and health care databases	Table 3.1a
Part A	17/09/2016	WP7 Deliverables 2,3 and 5 have been combined as “Report evaluating E-Systems for linking researchers, professionals and consumers across Europe”	Table 3.1a
Part A	17/09/2016	WP7 Deliverable 3 has been deleted (Report on the process of translating morbidity and mortality research data into meaningful graphics for e-access)	Table 3.1a
Part A	17/09/2016	WP8 deliverable 4 has been deleted (Report on Creating a European Cohort of Children with Congenital Anomalies)	Table 3.1a
1	17/09/2016	Ethics sections 5.1.1 to 5.1.7 have been added to the document	108-9
1	17/09/2016	Text in 4.2 under QMUL subcontracting altered	107
1	17/09/2016	Text added to Table 3.4b “We declare that selection of subcontractors and entities providing goods, works and services will conform to competitive selection according to H2020 rules, while respecting applicable rules on conflict of interest”	46
1	17/09/2016	Cost of Travel for QMUL in Table 3.4b reduced by €4092 to allow for costs needed at added Participant 22 Swansea University	46
1	17/09/2016	Text amended in 4.2 with respect to Miriam Gatt	107
1	17/09/2016	Text amended in 4.2 Participant 7 (CNR-IFC) estimated costs added	107
1	17/09/2016	Text amended in 4.2 Participant 19 (Asociacion Instituto Biodonostia) estimated costs added	107
1	17/09/2016	Text amended for Participant 19 (Asociacion Instituto Biodonostia)	99
1	17/09/2016	Text for Participant 9: Public Health Wales (CARIS) has been amended to reflect the work done by Participant 22 : Swansea University	75
1	17/09/2016	Swansea University (SU) has been added as Participant 22	105-6.
2	21/09/2016	Text added in 4.2 to clarify third party status of each participant	107
2	27/09/2016	INSERM U953 affiliation has changed to INSERM UMR 1153, Equipe EPOP é.	6,46, 80
2	27/09/2016	109 corrected to 10	44
2	27/09/2016	Wherever possible deleted	52
Part A	27/09/2016	WP1 Location of meetings in London and Milan changed to not specify locations	WP1, 8
2	27/09/2016	Location of meetings in London and Milan changed to not specify locations	40,48
2	27/09/2016	Alterations to Gantt Chart : Additional rows added to identify each deliverable. WP1 website development start Q1 and Q2 Year 1 (not Q3), Aggregate data provided Q2,Q3 Year2 (not Q4 year 2), WP3 Analysis and writing papers start Year2 Q4 (not Q1 Year 3)	37
	27/09/2016	Alterations to figure 6 work package timings : All WPs assumed to go on to month 60 as they will be involved in dissemination. WP6 to start in month 4 (not 24)	38,39
Part A	27/09/2016	WP1 : periodic reports added to Task 3	WP1
Part A	27/09/2016	WP1 : QMUL will be responsible for uploading the content to the	WP1

		website for this project (WP2 will build set up the website and WP8 will provide dissemination material for the website). Title of deliverable changed to website content	
Part A	27/09/2016	WP2 Task 4 : Build the website and install a CMS on the website [BIOMED]	WP2
Part A	27/09/2016	WP8 Task 2 : Design promotional material for the website including an information leaflet and distribute to potential stakeholders. Deliverable 1 : Produce initial information leaflet to promote EUROlinkCAT project . Other deliverables renumbered. Dissemination conference month 58 not 57	WP8
Part A	27/09/2016	WP3,4,5,6 : End month changed to 60 to reflect dissemintaion will continue till end of project	WP3, 4,5,6
Part A	27/09/2016	WP5 Deliverable 5.2 changed from 58 months to 57.	WP5
Part A	27/09/2016	WP6 : Start month corrected to 4	WP6
Part A	27/09/2016	WP7 : Deliverable due 14 months (not 10 months)	WP7
2	27/09/2016	Text added A report will be published to highlight the different legal and ethics requirements for the data linkage across Europe	13,41 ,112
2	27/09/2016	Professor Allan Hackshaw, Deputy Director of the Cancer Research UK and UCL cancer trials centre will head the EDPB	112
2	27/09/2016	Text added : Swansea University will be involved in linking the data from Wales (CARIS).	47
2	30/09/2016	Text added explaining Statistics Denmark	115
2	30/09/2016	Text corrected for Croatia	115
2	30/09/2016	Text corrected for French regsitries	116
2	30/09/2016	Text corrected for Italian registries	116
2	30/09/2016	Text amended to explain CAG for English registries	
2	30/09/2016	Text added “An ethics management table will be completed for each registry to keep a track of all documentation.”	114
2	30/09/2016	PUMS event hosting costs increased by €6400 (€8000 less overheads) as costs previously included under subcontracting (€8000) should have been other direct costs.	Table 3.4b
2	30/09/2016	Text added ahead of table 3.4b to define difference between hosting and travel costs	Table 3.4b
2	30/09/2016	Further details added regarding the QMUL cost for “Parents to Consultation and Dissemination meetings”. Also extended the boxes of the table as formatting was previously obscuring justification text for “other goods”	Table 3.4b
2	30/09/2016	Statement included ahead of table 4.2 to clarify compliance to procurement rules when selecting subcontractors	Table 4.2
2	30/09/2016	PUMS subcontracting details removed from table 4.2 as costs moved to other direct costs.	Table 4.2
2	30/09/2016	In-kind equivalent cost included for Miriam Gatt’s time	Table 4.2
Part A	03/10/2016	Text altered for risk 1 concerning registry funding	Risk
Part A	03/10/2016	Text altered for risk 2 concerning timing ethics permission and availability of data	Risk
Part A	03/10/2016	Additional risk 7 concerning EDPB identifying a serious ethics concern	Risk
2	5/10/2016	Gantt chart revised to be consistent with above changes plus additional rows have been added to identify timings of each deliverable	38
3	21/10/2016	Amended comments about subcontracts as consortium members	39
3	26/10/2016	Extra clarification added that Malta will provide resource free of charge	Table 4.2

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Figures

Tables

1. Excellence

Approximately 130,000 children are born with a congenital anomaly (birth defect) in Europe each year, many of which are rare diseases. [Dolk 2010, EUROCAT 2012a]. Congenital anomalies are a major cause of infant mortality, childhood morbidity and long-term disability [Rosano 2000, Murray 2012]. Although the survival of children with congenital anomalies has improved [Boneva 2001, Tennant 2010, Wu 2013], little is known on the longer term outcomes of these children, particularly for those with rare anomalies, and parental involvement in setting research prorities directly affecting their children with congenital anomalies has been lacking. Parents, health professionals, public health bodies and educational authorities need more information and improved access to existing information to optimise personalised care decisions to ensure these children reach their full potential in society.

The EUROlinkCAT project will greatly enhance the information available on the longer term outcomes of children with congenital anomalies and improve its accessibility through a collaboration of 21 EUROCAT population-based congenital anomaly registries in 13 European countries (including Eastern Europe) with parents and with external experts in areas including health, social care, education, information technology and social media.

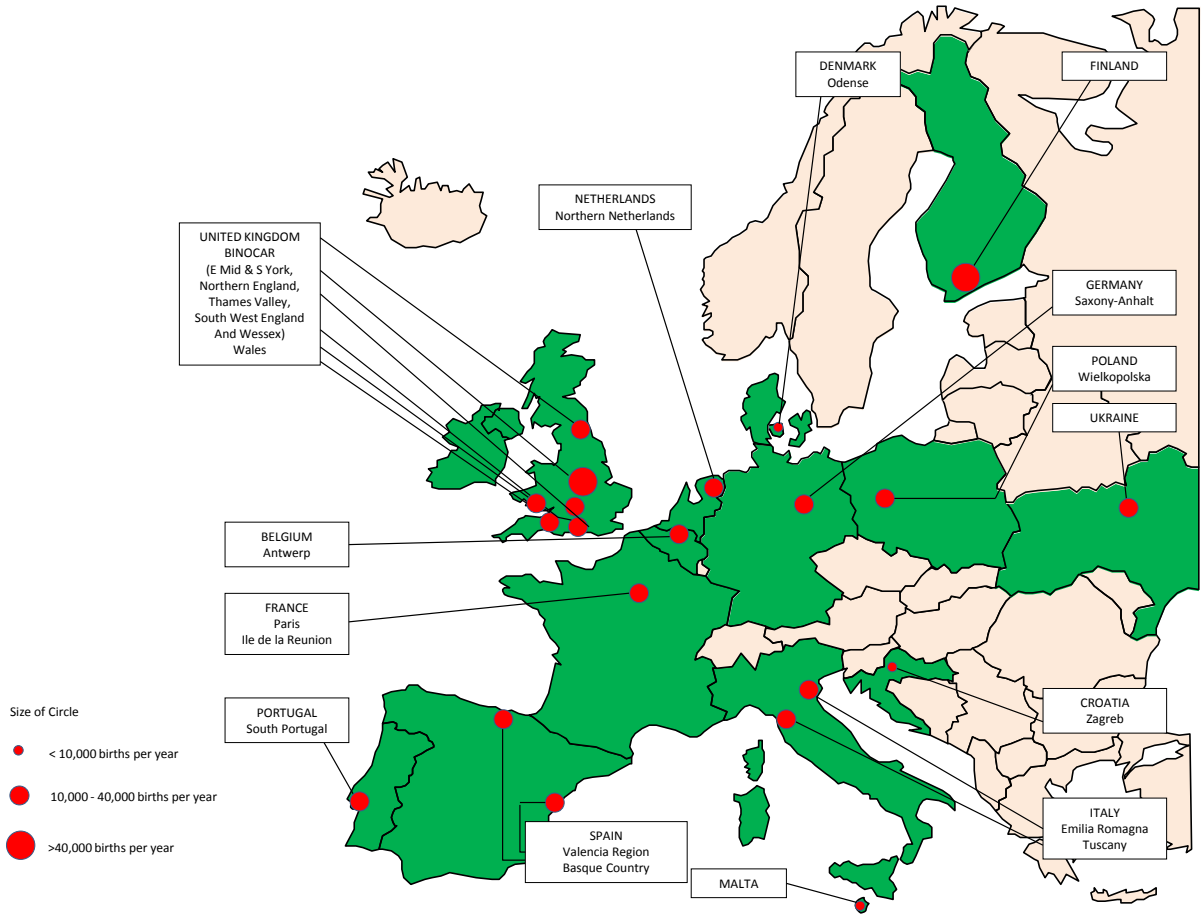
The EUROlinkCAT network covers a population of 9.6 million births from 1995 to 2014 including 200,000 babies born with congenital anomalies (see figure 1). Being able to include such a large population will mean that even rare anomalies can be researched.

The findings will have direct implications for health and social policy development within Europe, provide personalised evidence to optimise prevention and treatment and adress health inequalities. By maximising the exploitation of an existing cohort, data will be harmonised and made readily availble to other researchers across Europe to optimise the impact on clinical practice and public health policy. EUROlinkCAT will provide a platform to which new registries will be able to readily join and collaborate. Without this information, clinical practice and research agendas will not be based on the latest evidence and be responsive to the child and parent's needs.

1.1 Objectives

- To exploit the existing EUROCAT network of population-based congenital anomaly registries to establish a European network of standardised databases containing information on the mortality, health and educational achievements and needs of children up to 10 years of age with congenital anomalies.
- To expand the knowledge on the survival, health, disease determinants and clinical course of specific congenital anomalies while respecting patient privacy and data security issues. Comparing treatment guidelines and recommendations in prenatal, neonatal, infant and childhood care in different European countries will enable identification of "best practice" across Europe to optimise the diagnosis and prevention of complications by personalising the treatments for these children according to their specific anomaly.
- To investigate health inequalities amongst differing socio-economic strata.

Figure 1 : Map of Congenital Anomaly Registries participating in EUROlinkCAT



- To provide an economic evaluation of the costs of hospitalisation across Europe during the first five years of life for children born with a congenital anomaly
- To expand the knowledge on the educational achievements and needs of children with specific congenital anomalies and to provide predictions of their future needs. Differences in educational achievements amongst differing soci-economic strata will be investigated.
- To use social media platforms to establish a sustainable e-forum, "Connect**E**people", for providing regional, national and international support to families with congenital anomalies. "Connect**E**people" will allow a novel approach of connecting researchers with families so that the families can contribute to setting the research priorities in the EUROlinkCAT project.
- To evaluate the accuracy of existing electronic health care databases and make recommendations on their use and on improving their accuracy in countries or regions where congenital anomaly registries are not currently available. This will enable the optimal exploitation of these resources, essential to facilitate epidemiologic and public health research into outcomes of babies with congenital anomalies.
- To engage with the relevant international/national/regional health authorities by establishing an Action Advisory Panel to ensure that relevant findings from the EUROlinkCAT project are implemented and translated into health policy.

- To ensure that the established infrastructure and methodology for this unique research platform continues to be available for local research and future European wide analyses beyond the end of the project.

1.2 Relation to the work programme

This proposal relates to the `SC1-PM-04–2016: Networking and optimising the use of population and patient cohorts at EU level work programme topic' within the `Health, Demographic Change and Well-being' Work Programme 2016-17.

The EUROlinkCAT project will enrich the data from EUROCAT, an established European network of congenital anomaly registries, by taking advantage of new advances in technologies and increased access to electronic data. The project is in a unique position to optimise the use of an existing European infrastructure to link data on over 200,000 live births from 21 EUROCAT registries in 13 European countries from 1995 to 2014 to national data on mortality, eHealth records (hospital discharge diagnoses), prescription databases and educational databases. The existing expertise within the collaborative structure already established over many years in EUROCAT will be utilised to jointly develop standard operating procedures to enable each participating registry to create an independent standardised dataset available as a resource for local research. The harmonisation and standardisation of data across counties offers a unique opportunity for aggregate data and any analytical results from each independent data set to be collectively pooled in a Central Results Repository for pan-European hypothesis-driven analyses whilst respecting patient privacy and data security of such sensitive information.

New technologies such as social media platforms will be used to link regional congenital anomaly registries with families with congenital anomalies that live in their regions. These links will be extended to establish a sustainable e-forum, "Connect**E**people", for providing connections for families to regional, national and international registries and other information sources. "Connect**E**people" will enable the involvement of parents and health professionals early in the project to ensure that the information obtained from linkage with eHealth records and educational records and the subsequent hypotheses investigated are relevant to these stakeholders.

The number and geographical spread of registries contributing to the Central Results Repository will enable new knowledge on the health maintenance, onset and clinical course, in addition to the economic costs of hospitalisations, for many of the rarer congenital anomalies to be evaluated and hence subsequent treatments to be more personalised. The impact of differing treatment guidelines and recommendations in prenatal, neonatal, infant and childhood care in different European countries will enable identification of "best practice" across Europe to optimise diagnosis, prevention and treatment for these children.

This project also provides the unique opportunity to evaluate the accuracy of information on congenital anomalies using a range of existing health care databases. Developing strategies to optimise the use of these existing data where congenital anomaly registries are not established would enable more efficient exploitation of information about children with

congenital anomalies in health care databases across the world not only Europe. In addition, this work would identify which anomalies could be accurately surveyed using only routine health care databases, enabling surveillance of certain anomalies to be performed worldwide.

Results about the morbidity (including co-morbidity and co-infections), mortality and educational achievements of these children will have implications for public health policy across Europe. EUROlinkCAT will establish an Action Advisory Panel lead by Dr Domenica Taruscio (coordinator of EUROPLAN (European Project for Rare Diseases National Plans Development) and EPIRARE (European Platform for Rare Disease Registries) projects, past President of ICORD (International Conferences on Rare Diseases and Orphan Drugs)) to provide advice on how to ensure findings are widely implemented and translated into health policy. EUROCAT's previous experience of working with international/national and regional authorities will also be utilised and extended. EUROCAT is currently working with several potential ERNs (European reference networks for rare diseases) to explore how future collaborations may be fruitful. Globally, the EUROCAT network is held in high esteem as evidenced by requests from the US Centres for Diseases Control and Prevention (CDC) and the WHO to conduct epidemiological surveillance and research on prevalence of microcephaly and the purported association with the Zika virus.

Dissemination is central to our plans; we will ensure that clinical, public health and social care researchers are informed about the availability of this cohort for subsequent hypothesis testing, both locally and at a European level. EUROlinkCAT will provide a platform for new registries across Europe to join and we will provide advice and expertise on how to set up these new cohorts of children with congenital anomalies and link them to existing national data sources.

1.3 Concept and methodology

1.3.1 Concept

EUROCAT has successfully demonstrated over a number of years that there is enormous added value in the collaborative work of congenital anomalies registries across Europe in order to perform research into the epidemiology and aetiology of congenital anomalies. Until now, EUROCAT has focused on the prevalence and the surveillance of live births, stillbirths and terminations of pregnancy for fetal anomaly and the health needs (in terms of surgery) of the surviving infants in the first year of life. With improved survival of children born with a range of congenital anomalies and the establishment of ERNs (European Reference Networks for rare diseases) more personalised information about their lives is needed by parents, health professionals and public health bodies to enable informed decisions to be taken and sufficient support to be made available to ensure these children reach their full potential in society. New advances in technology and the availability of electronic data make it now possible to link data from congenital anomaly registries to national data on mortality, eHealth records, prescription databases and educational databases. All EUROCAT registries are population based, which means that all children with congenital anomalies are included not just those referred to specialist centres. Such linkage also provides the opportunity to create a comparison cohort of children without congenital

anomalies, which for some registries (such as those in Denmark and Finland) will be the whole "unaffected" population. It is well recognised that Europe has some of the most valuable population cohorts but the lack of integration of these cohorts is hampering the optimal exploitation of these resources. The overall concept underpinning the EUROlinkCAT project is to use the existing EUROCAT expertise and infrastructure to establish a set of high quality independent standardised databases across Europe, each containing available information on the health and education for the first 10 years of life for children born with a congenital anomaly and for a set of similar unaffected children or for the whole "unaffected" population. Registries will be supported in using social media platforms to connect with families whose children live with congenital anomalies in their regions. A novel sustainable e-forum, "Connect**E**people", will be established linking these families with local, national and international registries and information resources. "Connect**E**people" will be used to involve these families, through their registries to overcome language issues, in setting research priorities and ensuring a meaningful dissemination of the research results. Specific hypothesis about the morbidity, mortality and educational achievements of children with specific congenital anomalies will be investigated. The costs of hospitalisations for these children will be evaluated. The research results will provide evidence to inform specific national guidelines for prevention and early diagnosis, such as screening programs provided in addition to enabling informed decisions to be made and sufficient support available to help the children reach their full potential in society.

Standard operating procedures will be developed to enable new standardised datasets to be established and for the efficient collaboration of existing datasets to create an invaluable resource for future local and European research. EUROlinkCAT will provide an enduring platform for new registries to join to optimise the impact on clinical practice and public health policy. The e-forum "Connect**E**people", being rooted in the links between regional congenital anomaly registries and the families who live in their regions, will continue past the end of the grant to act as an enabling link between local, national and international registries and information resources.

In summary, by harmonising data from existing population-based registries, enriching this with new data sources and working with parents and health and social care professionals from the outset, EUROlinkCAT will be the largest dataset in the world to provide, for the first time, robust personalised information on the health of children with congenital anomalies.

1.3.2 Positioning of the Project

The project is at TRL 5 – technology validated in relevant environment as some linkage of congenital anomaly registries to mortality data, electronic health records , education and prescription data has been achieved by some registries [(the EUROmediCAT project (http://euromedicat.eu/whatiseuromedicat, Tennant 2010, Iyer 2011, de Jong 2015,Garne 2016 in press, Rankin 2010, Rankin 2012]. However, the majority of the registries have not performed these linkages. Part of the EUROmediCAT project which involved three EUROCAT registries has also used the proposed methodology of analysing independent standardised databases [Garne 2016 in press]. This adds value as the methods have already been developed and tested.

1.3.3 Research and innovation activities linked with the project

EUROCAT will be associated with this project through the participating EUROCAT registries that are able to perform at least one of the linkages. EURORDIS (The voice of rare disease patients in Europe) will also be approached to become involved in the work establishing the "Connet**E**people" e-forum linking families with congenital anomalies to regional registries and other sources of information. This project will also establish collaborative links with the relevant ERNs as they become established in Europe. Linking to ERNs will provide greater insight into the clinical treatment of children with specific congenital anomalies in different parts of Europe. EUROCAT is currently exploring linkage with biobanks and some registries do already have biobanks containing samples of children with CA so that in future it will be possible to study collected data in relation to the genotype of the patients allowing improvement of personalised treatment and risk assessment.

1.3.4 Methodology

EUROCAT was established in 1979. The registries have a long history of working together in a very structured way. EUROmediCAT (an EU FP7 funded project on the safety of medication use in pregnancy) involved 15 EUROCAT registries and demonstrated that congenital anomaly data could be linked to information on the mothers in health care databases to create an invaluable resource for research into the risks of specific congenital anomalies occurring after maternal exposures to medication in utero. Twenty-one EUROCAT congenital anomaly registries from 13 countries will participate in EUROlinkCAT which will link congenital anomaly data to information on the children in health care and educational databases. Researchers within these registries, in addition to other experts in EUROlinkCAT, will obtain the relevant permissions and develop standard operating procedures to enable each participating registry to link over 200,000 births from 1995 to 2014 with congenital anomalies locally to one or more electronic databases on mortality, eHealth records, prescriptions and education to create a linked standardised dataset. Specific protocols and syntax scripts will be developed centrally to create aggregate data and perform specific analyses on each standardised data set. The aggregated data and analytical results will be submitted to the EUROlinkCAT Central Results Repository to enable pan-European analyses to be performed combining the individual aggregated data and analytic results.

The congenital anomaly registries have the correct ethics permission and procedures for data collection and transmission of anonymised data to a central database, according to national guidelines. Local registries follow national legislation as to whether parental consent is needed for registration of babies with anomalies [Busby 2005]. Each registry will be responsible for applying for and obtaining the additional ethics and other permissions required to link their data (see Ethics Annex for more details). An Ethics and Data Protection Advisory Board (EDPB) consisting to two independent advisors with the relevant expertise will monitor all ethical concerns in this project. A report will be published to highlight the different legal and ethics requirements for the data linkage across Europe

EUROCAT registries will be given training in using social media platforms to connect with families with children who live with congenital anomalies in their regions. Links that these families already have to information resources will be investigated, mapped and extended

to create a novel sustainable e-forum, "Connect**E**people", linking these families with local, national and international registries and information resources. Technologies, such as skype and webinar, will be used to involve these families in initial discussions with their registries in their native languages and if possible further discussion in European meetings (some families may need to rely on their registry leaders who all speak excellent English) to set research priorities and ensure a meaningful dissemination of the research results in addition to the usual scientific routes of peer reviewed journals and conferences.

The EUROlinkCAT project has a number of strengths:

- The population-based nature of the data from the congenital anomaly registries avoids bias due to selective referral of patients to centres of expertise, or self-selection into cohorts.
- The geographical spread of the 13 participating countries in Europe including Eastern Europe means results can be applied to the European Union in general, and dissemination of results within the European Union will impact on health and social care practice
- The size of the population coverage: In total registries participating in EUROlinkCAT cover 9.6 million births from 1995 to 2014 (see Table 1.4a). This is essential for the study of congenital anomalies, particularly as many are rare diseases.
- The size of databases and level of detail and accuracy on malformed babies/fetuses and standardisation of the description and coding of congenital anomalies within a single central database is unparalleled, and will allow associations between specific anomalies and outcomes to be studied.
- The EUROlinkCAT researchers have a wide range of expertise in many different disciplines. They have a proven track record of successful collaborations.
- The involvement of each congenital anomaly registry with families with congenital anomalies that live in their areas will mean that many discussions can take place in native languages with registry leaders then being responsible for feeding these results into wider discussions (usually held in English).
- In the project, parents and families will link with researchers locally, nationally and internationally and be empowered to directly contribute to the research agenda.

1.3.5 Consideration of Gender Aspects

The project concerns the lives of children with congenital anomalies, a topic of equal relevance to male and female children and their parents and care givers. A few anomalies only occur in one gender, such as hypospadias in boys and there are differences in the prevalence of specific anomalies in live births in boys compared with girls [Tennant 2011], for example girls with Down syndrome are more likely than boys to have cardiac anomalies [Morris 2014]. Gender differences will be taken into account in all analyses when evaluating their subsequent mortality, morbidity and educational achievements.

Our network of consortium participants is based on complementary expertise. There is a female majority. It is possible that this female majority is due to a greater female professional interest in the topic (congenital anomalies). We have costed and timetabled the project on the basis of normal working weeks (Monday to Friday), and would not expect or encourage the work to encroach on private life. Project meetings will also be held on

weekdays, and skype and phone conferences will replace travel as much as possible, due to environmental, financial and work-life balance grounds.

The EUROlinkCAT consortium have considered equality impact issues and this project will recognise and address the diverse needs of the populations in different regions, ensuring that diversity and inclusion are accommodated in terms of both the development and usability of the solution and the impact of its introduction. All men are treated as equal with women in the project and vice-versa. No inequalities or inequities will be allowed to exist within the project. To ensure the continuous performance of gender issues, all consortium members stated their commitment to gender issues, which will be addressed throughout the project.

1.4 Ambition

1.4.1 Current State of the Art and Proposed Work

- ***European Surveillance of Congenital Anomalies***

EUROCAT (www.eurocat-network.eu) is a European network of 43 population-based congenital anomaly registries in 23 countries covering more than 29% of European births (1.7 million) per year [Boyd 2011, Greenlees 2011]. Congenital anomalies or birth defects include structural defects, chromosomal anomalies, genetic syndromes, skeletal dysplasias and genetic skin disorders. Each registry sends anonymised data on congenital anomalies occurring in all livebirths, fetal deaths from 20 weeks gestation age and terminations of pregnancy for fetal anomaly to a central database. Comprehensive coding instructions (http://www.eurocat-network.eu/content/EUROCAT-Guide-1.4-Full-Guide.pdf) and the use of the EUROCAT Data Management Program (EDMP) ensure standard variables, definitions and coding are used by all registries in the network. The complete dataset has 80 core and non-core variables providing information on the baby and mother, diagnosis, karyotype (if known), exposure, family history, and socio-demographic details. Congenital anomalies are coded locally using the WHO International Classification of Diseases (ICD) 9th or 10th Revision with the British Paediatric Association (BPA) code offering more specificity. Cases which only have minor anomalies are excluded (see EUROCAT Guide 1.4, Minor Anomalies for Exclusion (version 14.10.14)). Registries can code up to nine anomalies for each case (one syndrome and eight malformations) and provide additional information in the specified text fields. Since 2015 the central database is hosted by the European Commission Joint Research Centre in Ispra (Italy). The main objectives of EUROCAT are to provide essential epidemiologic information and surveillance on congenital anomalies in Europe, to evaluate the effectiveness of primary prevention and to assess the impact of developments in prenatal screening [Khoshnood 2011,Loane 2011a,2011b, Garne 2011]. Hence information is mainly only collected up to a baby's first year of life.

The aim of EUROlinkCAT is to extend the remit of surveillance of congenital anomalies by linkage to electronic databases to include information on the first 10 years of the children's lives and extend measures of their health to include their educational experiences. The first 10 years has been chosen to enable enough children to be identified and followed up for a reasonable period of time (a longer follow-up would mean less children would be eligible as

currently electronic sources often do not go back more than 10 years). This proposal concerns an estimated 200,000 live births with congenital anomalies born from 1 January 1995 up to 31 December 2014 registered in 21 of the EUROCAT congenital anomaly registries. (see Table 1.4a and Table 1.4b).

Table 1.4a : Congenital anomaly registries in EUROlinkCAT : start year, births in population to 2014, live births with an anomaly to 2014 and ability to link to mortality, health care, prescription and education data

Congenital Anomaly Registry	Start year	Estimated total births in population to 2014	Estimated live births with an anomaly up to 2014	Linkage is possible to :			
				Mortality	Health Care	Prescription	Education
Belgium: Antwerp	1995	372394	8083	Y	N	N	N
Croatia : Zagreb	1995	136979	2232	Y	Y	N	N
Denmark : Odense	1995	106026	2418	Y	Y	Y	Y
Finland	1995	1179314	44869	Y	Y	Y	Y
France : Ile de la Reunion	2002	189647	3855	Y	Y	N	N
France : Paris	1997	598208	13335	Y	N	N	N
Germany : Saxony-Anhalt	1995	308747	8821	Y	N	N	N
Italy : Emilia Romagna	1995	674044	11447	Y	Y	Y	Y
Italy : Tuscany	1995	565131	9827	Y	Y	Y	N
Malta	1995	84769	2470	Y	N	N	N
Netherlands : Northern	1995	373474	8567	Y	Y	Y	N
Portugal : South	1995	358617	3425	N	Y	N	N
Spain : Basque	1995	318788	4883	Y	Y	Y	N
Spain : Valencia	2007	409296	7438	Y	Y	Y	N
UK : East Midlands	1998	1151533	18549	Y	Y	Y	Y
UK : North	2000	484393	8617	Y	Y	Y	Y
UK : South West	2005	500374	11671	Y	Y	Y	Y
UK : Thames Valley	1995	362051	5142	Y	Y	Y	Y
UK : Wales	1998	572558	18239	Y	Y	Y	Y
UK : Wessex	1995	561192	7771	Y	Y	Y	Y
Ukraine : West	2005	306980	6166	Y	Y	Y	N
Total		9,614,515	207,825	20Y	17Y	14Y	9Y

Table 1.4b : Live births : number and prevalence per 10,000 births of all 95 standard EUROCAT subgroups for 21 registries involved in EUROlinkCAT, 1995-2014.

Anomaly	Live births	Prevalence	Anomaly	Live births	Prevalence
All Anomalies	207825	216.2			
Nervous system	12226	12.7	**Respiratory**	3601	3.7
Neural Tube Defects	2107	2.2	Choanal atresia	784	0.8
Anencephalus and similar	207	0.2	Cystic adeno malf of lung	840	1.0
Encephalocele	294	0.3	**Oro-facial clefts**	13555	14.1
Spina Bifida	1606	1.7	Cleft lip with or without palate	7429	7.7
Hydrocephalus	2950	3.1	Cleft palate	6126	6.4
Microcephaly	2469	2.6	**Digestive system**	16270	16.9
Arhinencephaly	297	0.3	Oesophageal atresia	2307	2.4
Eye	6209	6.5	Duodenal atresia or stenosis	1255	1.3
Anophthalmos/ micropthalmos	869	0.9	Atresia or stenosis of other parts of small intestine	946	1.0
Anophthalmos	156	0.2	Ano-rectal atresia and stenosis	2401	2.5
Congenital cataract	1394	1.4	Hirschsprung's disease	1465	1.5
Congenital glaucoma	363	0.4	Atresia of bile ducts	370	0.4
Ear, face and neck	3446	3.6	Annular pancreas	204	0.2
Anotia	246	0.3	Diaphragmatic hernia	2062	2.1
Congenital heart defects	70221	73.0	Abdominal wall defects	3518	3.7
Severe CHD	16805	19.7	Gastroschisis	2217	2.3
Common arterial truncus	493	0.5	Omphalocele	1221	1.3
Double outlet right ventricle	553	0.8	**Urinary**	27669	28.8
Transposition of great vessels	2986	3.1	Bilateral renal agenesis including Potter syndrome	303	0.3
Single ventricle	559	0.6	Multicystic renal dysplasia	3005	3.1
Ventricular septal defect	36903	38.4	Congenital hydronephrosis	10865	11.3
Atrial septal defect	13861	14.4	Bladder exstrophy and/or epispadia	524	0.5
Atrioventricular septal defect	3080	3.2	Posterior urethral valve and/or prune belly	865	0.9
Tetralogy of Fallot	2890	3.0	**Genital**	16621	17.3
Tricuspid atresia and stenosis	550	0.6	Hypospadias	14797	15.4
Ebstein's anomaly	453	0.5	Indeterminate sex	537	0.6
Pulmonary valve stenosis	4457	4.6			
Pulmonary valve atresia	863	0.9			
Aortic valve atresia/stenosis	1488	1.7			
Mitral valve anomalies	780	1.2			
Hypoplastic left heart	1515	1.6			
Hypoplastic right heart	334	0.4			
Coarctation of aorta	4148	4.3			
Aortic atresia	226	0.3			
Total anomal pulm venous return	611	0.6			
PDA as only CHD in term infants	2133	2.5			

Table 1.4b cont : Live births : number and prevalence per 10,000 births of all 95 standard EUROCAT subgroups for 21 registries involved in EUROlinkCAT, 1995-2014.

Anomaly	Live births	Prevalence	Anomaly	Live births	Prevalence
Limb	36624	38.1	**Teratogenic syndromes with malformations**	1218	1.4
Limb reduction defects	3995	4.2	Fetal alcohol syndrome	738	0.8
Club foot - talipes equinovarus	9095	9.5	Valproate syndrome §	83	0.1
Hip dislocation and/or dysplasia	6565	7.8	Maternal infections resulting in malformations	370	0.4
Polydactyly	8935	9.3	**Genetic syndromes + microdeletions**	3923	4.7
Syndactyly	4785	5.0	**Chromosomal**	15175	15.8
Skeletal dysplasias	1040	1.2	Down Syndrome	8891	9.2
Craniosynostosis	2838	3.0	Patau syndrome/trisomy 13	349	0.4
Congenital constriction bands/amniotic band	339	0.4	Edward syndrome/trisomy 18	786	0.8
Situs inversus	459	0.5	Turner syndrome	625	0.7
Conjoined twins	18	0.0	Klinefelter syndrome	490	0.6
Congenital skin disorders	2374	2.5			

Twenty registries currently link or will be able to link their data to mortality records with 17 being able to link to electronic health care records and 14 to prescription records for the morbidity analyses. Nine will be able to link to education records. Table 1.4b demonstrates that the EUROlinkCAT data is large enough to include sufficient numbers of babies with rare congenital anomalies to be analysed individually. This enables analysis stratification and the subsequent personalisation of disease determinants.

This use of electronic databases is an extremely efficient use of resources as it is exploiting the data already available which contributes to substantial savings in terms of study costs and researcher time. A further advantage of using electronic databases is that it offers the opportunity to create a matched set of children without congenital anomalies (controls) for comparison purposes. The use of such a comparison set of control children is novel and will support the researchers, health professionals and parents in interpreting the results. The selection of controls is dependent on the data providers responsible for individual databases within an organisation in each country. Scandinavians countries are advanced in data linkage studies and they are able to simultaneously request cases and matched controls from the registry area with little additional effort on the part of the data providers. In contrast, in England the healthcare database is the Hospital Episode Statistics database and will, by default, only include children who have been in hospital. Hence it is not possible to select controls from a population of all children without anomalies using the Hospital Episode Statistics database. Instead a control set of children will be requested from the educational database and these children will then be identified in the Hospital Episode Statistics database to ascertain if they have been in hospital or not.

- ***Mortality of children with Congenital Anomalies***

There is a large variation in child death rates across Europe; in 2013 the child death rates (age 0-14 years) were 60% higher in the UK and Belgium compared to Sweden, with an additional 10 countries being 30% higher than Sweden [Wolfe 2013]. Congenital anomalies are a leading cause of perinatal and infant mortality, especially in developed countries [Rosano 2000]. In 2013, congenital anomalies were associated with about one quarter of all child deaths in the UK [Kurinczuk 2010]. Congenital anomalies are therefore associated with a substantial burden of child mortality which merits detailed investigation to identify potentially preventable and remedial causes and to understand the source of the variations in child death rates across Europe including whether there are health inequalities in mortality across Europe.

Advances in fetal and neonatal care have improved outcomes for individuals with some congenital anomalies, for example Down syndrome [Wu 2013, Rankin 2012], and cardiac anomalies [Boneva 2001, Gordon 2008], but there is a lack of detailed information about the survival for various specific congenital anomalies. One recent study did report on a large number of specific congenital anomaly groups [Tennant 2010]. However, this study analysed the twenty year survival rates for children born in one region of England, and as indicated above, the mortality rates are likely to vary considerably across Europe. It has been shown that relying on death certificates as a source of information on mortality due to congenital anomaly does not provide an accurate assessment of the mortality for children with specific congenital anomalies as death certificates state the cause of death which may be infection, seizures or others and therefore may not mention the congenital anomaly [Copeland 2007]. Copeland et al (2007) concluded that the only way to accurately study mortality and survival in children with rare congenital anomalies is to pool data across congenital anomaly registries and link these to death certificates. No analysis comparing the mortality of children with congenital anomalies above the age of one across Europe has been published.

The aim of WP3 (Mortality associated with Congenital Anomalies) is to expand the knowledge on the survival of livebirths with congenital anomalies for the first 10 years of life and to evaluate the potential benefit of prenatal diagnosis on survival and risk factors for survival in Europe, in particular any social inequalities in survival. Estimates of survival will be stratified and personalised according to specific congenital anomaly and other risk factors such as gender and gestational age at birth.

Some EUROCAT registries already obtain information on children's deaths (in Scandinavia for example) and other registries have already linked their data to national death registries/registrations (for example in North East England and Wales). Therefore, no major problems are foreseen with this linkage for the remaining registries.

National data on mortality is generally of an extremely high quality with respect to overall completeness and the date of birth and date of death of the child. There are no plans to analyse the cause of death and therefore the accuracy of this is not essential. However,

there may be some issues with children being adopted and hence not traceable. This is unlikely to occur often enough to cause a significant bias to our results.

- ***Morbidity of children with Congenital Anomalies***

Several studies have shown that children with congenital anomalies account for a very high proportion of all hospital admissions [Muranjan 2014, McCandless2004]. However, there is much less information on the length of hospital stay for individual children with specific congenital anomalies, with most studies concerning children with Down syndrome, orofacial clefts or congenital heart disease [Shetty 2016]. Often hospital stays are investigated for the first two or three years of a child's life [Weiss 2009, Fitzimmons 2013, So 2007, Derrington 2013]. However, Wehby et al (2012) showed that hospital admissions for those born with oral clefts were increased at all ages up to 60 years of age. Larsen et al (2011) examined hospital admissions up to 12 years of age for children with congenital heart surgery. Frid et al (2002) also investigated the length of stays of children with Down syndrome up to ten years of age and Zhu et al (2012) included adults in his cohort when analysing length of stay. Rarely has length of hospital stay been related to other factors, such as social class. Two studies (Derrington 2013 in the USA to 3 years of age and Hung 2011 in Taiwan for all ages) both identified other factors such as ethnicity and socio- economic factors as important influences on the length of inpatient stays in children and adults with Down syndrome.

The aim of WP4 (Morbidity associated with Congenital Anomalies) is to expand the knowledge on the health and clinical course of children with congenital anomalies up to the first 10 years of life and to evaluate different treatment guidelines and recommendations in prenatal, neonatal, infant and childhood care in different European countries to optimise the diagnosis and prevention of complications by personalising the treatments for these children according to their specific anomaly.

The morbidity of children with specific congenital anomalies will be measured by the number of days in hospital, occurrence of surgery, days in intensive care units and outpatient contacts. In addition, a measure of the co-morbidity of these children can be obtained from the prescription of medications, particularly for infections and respiratory illness, as they are an indication of the occurrence of infections outside hospital. The available sample size within EUROlinkCAT (Tables 1.4a and 1.4b) will enable the morbidity of many rare anomalies to be evaluated for the first time. Furthermore, investigations into possible explanations for variations in morbidity will be explored, particularly whether prenatal diagnosis improves the health of selected subgroups of anomalies (spina bifida, transposition of the great arteries, diaphragmatic hernia, gastroschisis). The morbidity of children according to social class will also be examined for evidence of social inequalities. Geographic variations in morbidity across Europe for specific congenital anomalies and possible explanations will be investigated. Information on length of stay and operations performed will enable an economic analysis of the costs of hospitalisation for specific congenital anomalies to be evaluated [Shetty 2016]. The costs for children with and without a prenatal diagnosis will be compared. Where possible, this information will be compared to the same data for the control populations.

Several EUROCAT registries have already linked their data to hospital episode data (for example Emilia Romagna (Italy), Wales, Norway, Finland and Denmark). Therefore, no major problems are foreseen with this linkage for the remaining registries.

The morbidity of children with congenital anomalies will be estimated using data which is administrative data and will be likely to be incomplete and inaccurate for many variables. For instance it is likely that the number of days in hospital will be well recorded, however the precise codes for the type of surgery may well not be so well recorded and also may differ in accuracy according to country. Such differences will need to be examined and dealt with in a variety of ways. One way is by defining a set of data quality indicators and "measuring" data quality in each data set. For some registries specific linked data sets may not be of sufficient quality to be used. If this occurs part of the work of WP2 includes clearly describing inadequacies in data sources and recommendations for improving them. The large advantage with EUROlinkCAT is that the data on the specific congenital anomalies will be accurate as it is coming directly from the congenital anomaly registries, we will not be relying on this information from the health care databases which we know are less accurate. (see section on information on congenital anomalies in health care databases).

- ***Educational needs of children with Congenital Anomalies***

The proportion of children born with a congenital anomaly surviving beyond infancy is increasing [Tennant 2010, Wu 2013]. How these children are performing in school and their additional educational needs is therefore becoming increasingly important; as there may be a growing population of children and young people requiring additional support and resources in the future. However, apart from the more common genetic syndromes, there is a paucity of information about this. The American Heart Association reviewed the literature on children with congenital heart defects (CHD) and concluded that they are at an increased risk of developmental delay, even once the frequent occurrence of genetic syndromes has been taken into account, particularly neonates or infants requiring open heart surgery [Marino 2012]. Wehby et al (2015) also showed that children with isolated oro-facial clefts were at a much greater risk of low achievement at school than their classmates. Hansen et al (2015) compared the academic achievements of a cohort of children in Denmark who had all undergone neurosurgeries as infants with an age-matched cohort of children who had not and concluded that neurosurgery in infancy was associated with significantly impaired academic achievements in adolescence. The authors recommended that overall conclusions on the effects of surgery ignoring the specific anomalies are not meaningful, but that the effects of surgery should be considered separately for each specific anomaly. This finding agrees with their earlier studies showing that inguinal hernia or pyloric stenosis repairs in infancy were not associated with subsequent impaired academic achievements. [Hansen 2011, 2013]. EUROlinkCAT will have a large enough sample so that combining information from children with different congenital anomalies is not necessary and the educational achievements can be stratified for each congenital anomaly.

The EUROCAT Congenital Anomaly Register and Information Service (CARIS) in Wales has linked their data on girls born with Turner syndrome to data on education and found that 45% had no special needs, 35% required some additional classroom or after school support and 20% required a significant amount of special education needs, essential information for the planning of educational resources [Iyer 2011].

The aim of WP5 (Educational achievements of children with Congenital Anomalies) is to expand the knowledge on the educational achievements and needs of children with specific congenital anomalies and to provide predictions of their future needs. Issues in combining data on education across the different countries will need to be addressed to enable a pan-European analysis of education achievements and needs to be performed. Increasing the understanding of educational attainment of children born with a congenital anomaly, as well as what factors influence attainment, has the potential to provide information that could lead to the development of early intervention strategies which would have substantial positive effects on the children and young people's health and wellbeing. The comparisons with a set of children without anomalies will aid in interpretation.

Electronic educational data are available in Wales, Denmark, Finland, Italy and England. Both Wales and Denmark have examined educational achievement of children with a few selected congenital anomalies [Hansen 2011, Hansen 2013, Hansen 2015, Iyer 2011] and in England linkage between health and education data has occurred as part of the ALSPAC study, but this study was not investigating the attainment of children with congenital anomalies [(Avon Longitudinal Study of Parents and Children (ALSPAC) 2011]. Finland is not likely to have any significant problems with this linkage.

Similarly to the health care databases educational databases are administrative databases and therefore it is to be expected that such databases may contain inaccurate and/or incomplete information for certain variables. Before commencing the analysis of educational data, the accuracy of the variables to be used must be examined in great detail and its quality taken into account in subsequent conclusions drawn from the data. It is important to evaluate if such educational data can be used and if it is not usable to feed this back to the authorities responsible for the data with constructive suggestions for its improvement.

- ***Information on Congenital Anomalies in health care databases***

Electronic health care data are increasingly being used by researchers to investigate the epidemiology of congenital anomalies, rather than using information from congenital anomaly registries. Such health care data have often been found to be incomplete [Boulet 2005]. Recent studies in the USA estimated that 93% of babies with any congenital anomaly would be identified [Salemi 2015, Wang 2010], but that the proportions identified with specific anomalies is much lower with, for example only 54% with reduction deformities of the lower limb being identified. [Salemi 2015]. Andrade et al (2013) found only 37% for pregnancies affected with anencephaly were recorded. Frohnert et al (2003) found only 50% of atrial septal defects were identified and 21.7% of patent ductus arteriosus. A recent Canadian study reported slightly higher accuracy, but this was based on a very restricted set of congenital anomalies [Blais 2013]. A large limitation in hospital discharge databases is

that, by definition, they are restricted to information on live births only. For pregnancies with a congenital anomaly, many may result in a termination, a late fetal loss or a stillbirth. Both Tairou et al (2006) and Cronk et al (2003) concluded that medical records need to be examined in addition to using hospital discharge databases and infant death and stillbirth certificates when studying trends in neural tube defect pregnancies and congenital heart disease respectively. In the UK, Devine et al (2008) found that the General Practice Research Database could not be used to identify all pregnancies affected with a neural tube defect; it identified only 47% of spina bifida cases.

For many populations, a congenital anomaly register may not exist. It is therefore important to develop a set of codes / algorithms that would enable the maximum information from electronic health care data to be obtained. It is essential to develop such algorithms in regions where a congenital anomaly registry exists in order to ensure that the algorithms used to identify cases / clinical diagnoses will not include differential or unconfirmed diagnoses. The inclusion of suspected or unconfirmed clinical diagnoses will over-estimate the prevalence of congenital anomalies. Identifying which specific congenital anomalies can be accurately identified using only routine health care databases will enable the surveillance of these anomalies to be performed worldwide not just in regions with congenital anomaly registries. In addition, in regions where a congenital anomaly registry does exist the use of these algorithms on electronic health care data will provide an additional source of ascertainment and hence will improve the coverage and quality of data in the registries. One study has developed an algorithm which has been tested using data from one single health care database in Europe [Astolfi 2013]. A second study reports an algorithm from the USA which may not be accurate when transferred to Europe [Wang 2005].

A related problem with national electronic health care data is the distinction between late terminations, fetal losses and still births, with terminations often being incorrectly classified in the health care databases as fetal losses or vice versa [Draper 2012]. This is of particular importance to congenital anomalies as it is often these pregnancies that will result in a late termination due to late detection by prenatal screening. Accurate information on the risk of a fetal loss or still birth is very important to parents who have been told their fetus has a congenital anomaly and are facing the decision about whether to terminate the pregnancy or not. It is also important to evaluate the extent to which misclassification is occurring across Europe, particularly when comparing the prenatal detection rates for different prenatal screening programs. EUROCAT data can distinguish between terminations and birth as the variables “birth type” and “civil registration” are filled in locally based on a common EUROCAT definition.

The aims of WP6 (Accuracy of health care databases) are to evaluate the accuracy and the quality of the ICD coding of congenital anomalies in health care databases compared to EUROCAT data, to develop algorithms for use of health care data in the surveillance of congenital anomalies to improve the quality of the data and to evaluate the accuracy and the quality of data on terminations of pregnancy for fetal anomalies from health care databases in different countries and provide advice on how to improve it.

- ***Using social media to empower parents of children with congenital anomalies***

The definition of social media is "websites and applications that enable users to create and share content or to participate in social networking" (Oxford Dictionaries 2016). Globally, the use of social media is increasing. The world population in 2016 is 7.4 billion and 46% (3.4 billion) of these have Internet access (see figure 2), with increasing penetration rates rising from one billion users in 2005 to three billion in 2014 (Internet Live Stats 2016). The choice of device to connect to the Internet has also changed with increased usage of smart technologies such as i-phones or androids. The eMarketer (2016) estimates that the proportion of people in Western Europe who access the internet from a mobile phone will double from 32% in 2012 to 66% in 2017.

The escalation in growth and the relevance of using the Internet for linking people with rare diseases is best evidenced in the internationally renowned and award winning website "Patients Like Me" (https://www.patientslikeme.com/) established 10 years ago by an individual suffering from Lou Gehrig's disease. Parents connecting with parents is another common benefit of the Internet such as the US site "Understood" (https://www.understood.org/en/about) where information and support for carers of children and young people aged 3-20 with learning difficulties can be accessed with a small fee. However, none of these excellent resources offer a direct link to the researchers working in their specialist field, nor do they offer free access to a menu of social media apps tailored to specific congenital anomalies.

Figure 2 : A snapshot of the world's key digital statistic indicators

It is fundamental to involve parents, not only in their children's treatment, but also to incorporate their needs in the design of new technologies and healthcare services. Participatory Design is a design approach which actively involves all stakeholders (for example researchers, health care professionals and parents) in the whole process to help ensure the result meets their needs. Research has shown promising results of the use of Participatory Design in Health Science in terms of patient outcomes (e.g. empowerment, self-efficacy and security) and new healthcare services (Clemensen 2007, Holme KG 2016, Lubberding 2015). For example a recent study used the Participatory Design approach to develop an eHealth application for cancer survivors to improve their access to supportive cancer care (Lubberding 2015).

The aim of WP7 (ConnectEpeople) is to use Participatory Design techniques to create new ways of connecting parents and families with researchers locally, nationally and internationally and to other information resources and thereby empower them to obtain the best care for their children and to contribute to the research agenda to improve their children's lives in the future. The sustainable e-connections developed between people and the social media apps tailored to specific congenital anomalies created by Redburn Solutions Limited as part of the e-forum "ConnectEpeople" will be designed to last beyond the life of this project.

This project is unique as it will provide an e-forum where the power of social media will equalize the balance between parents who are 'experts in the lived experience of caring for children with a congenital anomaly' and renowned "expert" researchers.

- ***Using comparisons with children without congenital anomalies***

The use of comparison groups (controls) is standard in medical statistics, particularly in clinical trials involved in testing new medications or treatments or in case control studies comparing prior exposures in people with a disease (cases) and those without (controls). Two EUROCAT registries (Denmark and Finland) have the whole population of children without congenital anomalies available as controls. Three EUROCAT registries have identified sets of children (controls) whom are compared with the children in the registry with congenital anomalies (Saxony-Anhalt; Germany, Emilia Romagna; Italy and Ukraine (OMNI-NET)). The linkage procedures will provide the opportunity for additional registries to select a set of control children. The availability of controls and how the selection of controls has been done will be compared between registries. Usually the main aim of having a comparison group or treatment is to determine if the new treatment is "better" than the old one. The involvement of children without congenital anomalies will determine if there is a difference between the two groups of children. However, perhaps more importantly, it will be investigated if the presence of a comparison group enables parents and professionals to interpret the group differences in a more meaningful way. Differences in outcomes in the two groups are often presented as relative risks and absolute risks, but these two measures can give contradictory impressions of the size of the difference. For example, a preventive intervention that reduces the risk of a disease by 70% confers an absolute risk reduction of only 0.7% if the prevalence of the disease without treatment were 1%. The Connect**E**people virtual forum will provide the opportunity to work with parents to determine measures that

are meaningful to them and will use info graphics, wordles and other visualisation software to enhance the interpretation and transferability of complex data across cultures.

- ***Analysing aggregated data***

  Many congenital anomaly registries are given permission to link to mortality data, electronic health records, education and prescription data on condition that the resulting individual case data, which will contain a large amount of personal information, is not released to a central registry. The EUROmediCAT project (http://euromedicat.eu/whatiseuromedicat) overcame this issue by analysing aggregated data and individual analytical results from the independent standardised databases (Garne 2016 in press). A similar methodology will be used in this project.

  In order to clarify and illustrate the processes involved in the EUROlinkCAT project the precise steps required are listed for one of the planned analyses in WP3: Mortality associated with Congenital Anomalies in figure 3.

Figure 3 : Analysis Process for Survival of children with Tetralogy of Fallot

Tetralogy of Fallot (TOF) is a severe congenital heart defect which is treated with corrective surgery, usually within the first year of life, but presents with long-term problems and requires repeat operation. TOF can be diagnosed prenatally with an ultrasound scan. If the survival of babies with TOF improves with a prenatal diagnosis the routine use of ultrasound scans in Europe could be recommended.

Steps	***Details***	***Examples***
*Specify hypothesis clearly (WP2, WP3 informed by parental views gained from "Connect**E**people" forum)*	*Decide which variables are the relevant ones*	*Date of birth, Date of death, prenatal diagnosis, gestational age at birth, gender, karyotype, socio-economic status etc …*
	Check that the coding / definition of the variables is consistent in different registries	*Do all diagnoses have a karyotype so that chromosomal cases and non-chromosomal cases can be clearly distinguished?*
	Check if collected sufficiently in all registries	*Is prenatal diagnosis variable completed > 80% ?* *Is karyotype completed > 80% ?*
	Check if reasonable answers in all registries	*Would expect over 90% to survive more than 1 year*
Specify cross tabulations of variables required (WP3)	*Cross tabulation for checking consistency of data*	*Number live births, still births and fetal losses and terminations of pregnancy by registry*
	Cross tabulations of interest	*Amongst live births : survival >1 year by registry and by prenatal diagnosis*
Specify analysis to be performed (WP3) Check syntax script consistent all registries (WP2)	*Analysis on aggregate data : adjusted and unadjusted*	*OR (survival > 1 year) if prenatal diagnosis unadjusted and adjusted for time of surgery, registry, year of diagnosis*
Perform cross tabulations and analysis (WP2, WP3) and Place results in Central Results Repository. UNEW will receive data from Central Results Repository for Pan Europe analysis All pregnancy outcomes analysed to consider natural history of the congenital anomaly		
Perform Pan Europe Analysis (WP3) to investigate determinants of survival such as gender, socioeconomic status, prenatal diagnosis etc.	*Combine cross tabulations*	*to determine if survival differs by registry*
	Perform random effect meta-analysis of adjusted and unadjusted odds ratios / hazard ratios	*to determine if prenatal diagnosis does improve survival and if effect differs by country*
Write up analysis (WP3)		
*Present and discuss results on "Connect**E**people" e-forum (WP3,WP7,WP8)*	*If survival varies considerably in different registries, partly explained by age at surgery*	*Work in WP7 may inform about results and parents can give input how to disseminate this further /contact to scientific organisations/surgeons*
Data placed in Central Repository section of website (no public access) (WP2)	*Aggregate cross tabulations of results from each registry*	*Number live births, still births and fetal losses by registry by prenatal diagnosis*
Data placed in Public area of website (WP3, WP8)	*Plain English summary of results and any recommendations*	*Total number live births, still births and fetal losses by prenatal diagnosis*

1.4.2 Summary of Progress beyond Current State of the Art

The proposed work will be the first to establish a comprehensive set of independent standardised databases containing consistently coded and verified information on the morbidity, mortality and educational experiences of children with congenital anomalies up to age 10 across Europe. It will be an invaluable resource for research to be conducted to improve the survival and morbidity of these children and will also establish a platform for continued data collection and collaboration across Europe. EUROlinkCAT is built on an existing European resource but takes advantage of new data types and new technologies to develop the largest database of information on children with congenital anomalies in the world and which has the potential to provide real impact in clinical, public health and socio-economic research.

The proposed work will be the first to quantify and investigate in detail risk factors for and variations in the survival and morbidity of children with congenital anomalies across Europe. It will demonstrate that by setting up the correct infrastructure, protocols and coding guidelines, data and expertise can be truly shared and analysed across Europe obtaining enough information on often rare diseases to inform and optimise personalised care and treatment decisions for these children. This is the first project that aims to determine the educational achievements and needs of children with congenital anomalies.

The proposed work will be the first to exploit the enormous potential of electronic health records in a standardised manner across Europe. Not only will the study provide guidance on research for congenital anomalies, but it will also provide a template for how to establish other European cohorts such that routine electronic data can be used for both research and surveillance. It will also determine the feasibility of using a comparison set of children without congenital anomalies and establish if it yields additional information or helps in the interpretation of results.

The proposed work will be the first project to use social media to enable families of children with congenital anomalies to become members of an e-forum ("Connect**E**people") linking them to local, national and international congenital anomaly registries and other sources of information. "Connect**E**people" will involve these families, through their registries to overcome language issues, in setting shared research priorities and ensuring a meaningful dissemination of results.

2. Impact

2.1 Expected impacts

2.1.1 Novel information on onset and course of diseases for children with congenital anomalies, with a view to tailor diagnosis and optimise prevention and treatment.

This will be achieved by the results from WP3 Mortality and congenital anomalies (tasks 1-4) and WP4 Morbidity associated with Congenital Anomalies (tasks 1-4). The survival of babies with specific congenital anomalies will be determined and associations with risk factors, treatment received (including for example the potential benefit of a prenatal diagnosis) and

geographical variations will be evaluated. The morbidity of children with specific congenital anomalies will be measured by the number of days spent in hospital, occurrence of surgery, days in intensive care units, outpatient contacts and prescriptions of medicine (which give a strong measure on the occurrence of infections and respiratory illness). These measures of morbidity will be related to the same factors as mortality. The size of the population coverage (registries wishing to participate in EUROlinkCAT cover 9.6 million births from 1995 to 2014, Table 1.4a) enables, for the first time, information about even rare congenital anomalies to be available. The geographical spread of the 13 countries in Europe contributing means results can be applied to the European Union in general. The population-based nature of the data avoids bias due to selective referral of patients to centres of expertise, or self-selection into cohorts.

2.1.2 Novel information about the educational achievements and needs of children with Congenital Anomalies.

This will be achieved by the results from WP5 Educational achievements and needs of children with Congenital Anomalies (tasks 2, 3). These results will also be combined with information about survival to predict the number number of children with congenital anomalies up to 10 years of age with potential educational needs (task 4). This will enable more efficient resource planning to occur and parents to make more informed decisions about their children's future. Specific emphasis will be given to identifying socio-economic differences as they have been shown to have a significant impact on the education children with congenital anomalies receive.

2.1.3 Major methodological and analytical contributions towards integrative cohorts and their efficient exploitation.

One of the major impacts of EUROCAT has been the establishment of a standardised coding system for Congenital Anomalies (detailed in EUROCAT Guide 1.4) which has been adopted around the world [De la Paz 2010]. The same procedures will be used in EUROlinkCAT to create a set of agreed variables standardised across Europe with full details of all standardisation and linkage procedures being freely available on the internet (WP2: Building EUROlinkCAT Central Results Repository). In particular not all EUROCAT registries are participating in EUROlinkCAT. The registries that are not participating will be kept fully informed about EUROlinkCAT during the Annual Registry Meetings and encouraged to consider participation in the future. The dissemination of these methodological and analytical methods, occurring at a time before such linkage and standardisation in Europe is common, will be an efficient way to help future projects to combine similar data in Europe. In addition, the issues needed to be overcome to obtain consistency across countries will be used to inform future national data collection structures in European countries that have not yet established such databases. (WP6 task 4; WP8 tasks 6, 7).

2.1.4 Major methodological and analytical contribution towards the efficient exploitation of existing national hospital discharge databases

This will be achieved by the results from WP6: Accuracy of anomaly coding in health care databases (tasks 1- 4). This algorithm will enable identification of which specific congenital anomalies are accurately recorded in health care databases, which can be identified given

new algorithms and which are not accurately enough recorded to be identified. This will improve future research using these databases. Recommendations on how to improve the recording of congenital anomalies in these databases will be widely disseminated (Deliverable 2). Work will be done with the Poland Health Registry, who do not have a national data collection system, to determine if there are specific areas in which EUROlinkCAT could provide information on best practice in other European countries. This work will influence our recommendations for future data collection in other countries which have not set up national data collection systems yet. (WP6 tasks 4; WP8 tasks 6, 7).

2.1.5 Provide the evidence base for the development of policy strategies for early diagnosis, prevention and treatment, with an economic evaluation of interventions

This will be achieved by the results from the WP3 Mortality associated with Congenital Anomalies (tasks 2- 4) and WP4 Morbidity associated with Congenital Anomalies (tasks 2, 4). The geographical spread of countries in Europe contributing to EUROlinkCAT means that public health policies, such as prenatal and newborn screening programmes, can be evaluated in order to recommend best practice to optimise prevention of subsequent health issues (such as further operations) and the treatment of them for these children. Geographic variations in morbidity and mortality will be examined across Europe to determine the extent of the health inequalities and possible explanations will be investigated using the information on age at diagnosis, parental socio-economic status, the length of stay in hospital and numbers of operations for children with specific congenital anomalies. The costs of hospital stays will be calculated and compared across Europe (WP4 task 5). The costs for those children who had received a prenatal diagnosis and those who had not, will be compared for certain congenital anomalies.

2.1.6 Major conceptual contributions towards integrative cohorts and their efficient exploitation.

One of the main obstacles to this work is overcoming the conceptual fear that linking data from national databases carries a risk of identifying individuals and does not yield useful research results. The dissemination of the results and the methodology to be used in this project will make a major conceptual contribution in overcoming this fear and will act as a catalyst to enable more congenital anomaly registries to obtain permissions to link their data and combine aggregated data in a secure manner to allow pan-European analysis.

2.1.7 Optimise the use of population cohorts in defining/improving clinical practice and public health policy

The richness and importance of the results from this project will emphasize the importance of registries and databases of congenital anomalies coordinated at European level in defining clinical practice and public health policy. The availability of all standardisation and linkage procedures will optimise the future use of such cohorts and inspire researchers to initiate more. The importance of sustainable surveillance and continued linkage of congenital anomalies with other databases across Europe will continue to be demonstrated due to population characteristics, morbidity and environment constantly changing over time. For example, information on any changes in the prevalence of microcephaly (of

interest due to the emergence of the Zika Virus) are available on the internet for all European countries with EUROCAT registries (see the prevalence tables on the EUROCAT website : http://www.eurocat-network.eu/accessprevalencedata/prevalencetables).

2.1.8 Enable parents of children with congenital anomalies to access the information they want on the internet and influence the research priorities and dissemination methods.

This will be achieved by the establishment of the "Connect**E**people" forum in WP7. This forum will link these parents with local, national and international congenital anomaly registries and other sources of information. The training of the registries in the use of social media and helping them to establish links with local families with congenital anomalies will have a long term impact on the relationship between the registries and their key stakeholders, the families.

2.2 Measures to maximise impact

2.2.1 Audience

The audience for EUROlinkCAT project outcomes includes all those interested in congenital anomalies. A stakeholder analysis identified the following groups and individuals that will be interested in the project outputs, or whose support/approval is essential for further development of the EUROlinkCAT project activities:

- ***Internal stakeholders***
  - Associated and collaborative partners of the EUROlinkCAT project – the dissemination plan aims to keep all the partners well informed about different aspects of the project. It will ensure sharing of methodology and results within the project, across work packages, and getting feedback from partners facing similar problems and issues, or working on the same problem from different perspectives.
  - *Joint Research Centre of the European Commission (JRC)* – The JRC hosts the EUROCAT Central Registry on the Platform for Rare Disease Registries. All the partners of the EUROlinkCAT project submit their data on congenital anomalies to the Central Registry. The JRC are very supportive of this project and will be regularly informed about its progress The JRC will use its own dissemination strategies to provide relevant and timely information about the EUROlinkCAT achievements.

- ***External stakeholders***
  - *Health professionals*, e.g., pediatricians, obstetricians, paediatric surgeons, orthopaedic surgeons, ophthalmologists, medical geneticists, genetic counselors, midwives and other medical professions actively involved in the care of children with congenital anomalies and/or pregnant women.
  - *Public health professionals* and those involved in *health service planning* at regional, national, EU and WHO levels.

- *Professionals who are involved in resource planning for special education* at national/regional levels
- Parent and *Patients' organizations*
- *Governmental/public regulation agencies* in several domains (health, education, medications).
- *Scientific research community* in the areas such as epidemiology and public health, pediatrics, clinical genetics, embryology.
- *Politicians and policy makers*.

· ***The community***

Some of the outputs of this project will also be of interest also to the wider community, e.g., the importance and safety aspects of the linkage and analysis of personal data collected for clinical purposes and its efficient aggregation across Europe, evaluation of the effectiveness of methods of secondary prevention (e.g., prenatal ultrasound or biochemical screening), etc.

· ***Communication activities***

To get the right message to the right audience, we plan to use a wide variety of dissemination methods (see Table 2.2a) and will convene an Action Advisory Panel lead by Dr Domenica Taruscio (coordinator of EUROPLAN (European Project for Rare Diseases National Plans Development) and EPIRARE (European Platform for Rare Disease Registries) projects, President of ICORD (International Conferences on Rare Diseases and Orphan Drugs)) to provide advice on how to ensure findings are widely implemented and translated into health policy.

Table 2.2a: Planed Dissemination Methods

Method	**Purpose**	**Target audience**	**Month of delivery (if applicable)**
Project website	Awareness Information Engagement Promotion	Open access for different audiences – internal and external stakeholders, wider community. Restricted access – for internal stakeholders	Continuous monthly update
Connet**E**People e-forum	Awareness Information Engagement Promotion	Families with children with congenital anomalies	Continuous
Promotional leaflet (electronic and print version)	Awareness Information Engagement Promotion	Internal and external stakeholders, wider community	3

Newsletter	Awareness Information	Internal and external stakeholders, wider community	12, 24, 36,48,60
Annual meetings during the EUROCAT Registry Leaders Meetings (RLM) at ISPRA, Varese	Awareness Information Engagement	Internal stakeholders, JRC EUROCAT Central Registry representatives and invited representatives of other networks	6, 18, 30,42,54
Workshops	Engagement	Internal stakeholders and invited representatives from different stakeholders groups	6, 18, 30,42,54 as part of EUROCAT RLMs
Consultation meeting	Awareness/ Engagement	Patient organizations	14
Dissemination conference : European Symposia on Congenital Anomalies	Information Engagement Promotion	Scientific/clinical research community. Governmental/ public regulation agencies Politicians and policy makers.	58
Conference presentations and posters	Information Promotion	Scientific/clinical research community	As appropriate
Peer-reviewed journals	Information Promotion	Scientific/clinical research community	17 scientific papers
Reports and other documents	Information	JRC Newsletters and publications, public health officials, scientific/clinical community	Final Report 60 Data quality report, 24 Distributed database manual, 54
Report on recommendations for improving and standardizing coding for CA in Hospital Discharge Data	Information	Public health officials responsible for Hospital Discharge Data	58
EUROlinkCAT Communications	Information Engagement	Internal stakeholders	Quarterly
Press releases	Awareness	Community	Ad hoc
Work of the Action Advisory Panel	Awareness Information Engagement	Governmental/public regulation agencies Politicians and policy makers.	Ad hoc

The dissemination strategy will ensure that the project has a high profile, the community learns from its achievements, and outputs are embedded and adopted. A Steering Committee will discuss the ways to collaborate on dissemination. The dissemination strategy outlined here will be discussed and evaluated at Steering Committee meetings (2/year). The available outcomes of WPs 3-7 will be reviewed and consensus decisions made on the best ways to present the results.

2.2.2 Collaboration

Co-ordination of liaison with other networks, organizations and committees, especially those involved in rare diseases, exploring the possibilities of joint projects, exchange of information, experience and expertise will be developed. Liaison officers have been nominated as follows:

Table 2.2b : Proposed liaisons

Network/organization	**Liaison Partner Institute**
International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR)	CNR-IFC
European Conference on Rare Diseases	KDB
The Voice of Rare Disease Patients in Europe (EURORDIS)	Action advisory panel CNR-IFC
The European Society of Human Genetics (ESHG)	KDB
Non European Networks/experts	UNIFE
EUROPERISTAT	UMCG
Surveillance of Cerebral Palsy in Europe (SCPE)	RSD
Innorare (http://innorare.eu/) Irdirc consotium http://www.irdirc.org/	UNIFE
Medication Safety in Pregnancy (EUROmediCAT)	UU
European networks of reference for rare diseases (ERNs) including EUROcleftNet	UNIFE
Child health charities and patient groups	UU
International Spina Bifida and hydrocephalus association	UNIFE
International Conference on Rare Diseases (ICORD)	Action advisory panel
European, National and regional government bodies and health authorities	UNIFE Action advisory panel Registry Leaders at regional/National level

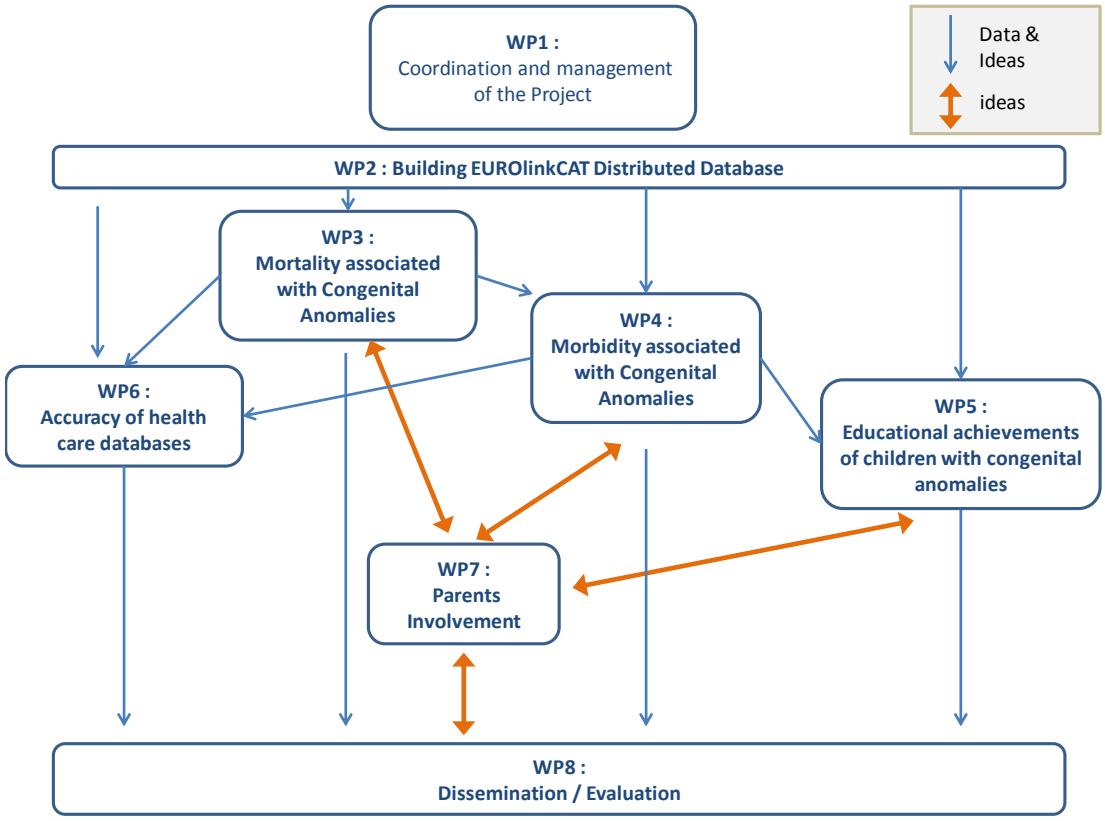
3. Implementation

3.1 Work plan — Work packages, deliverables

3.1.1 Overall structure of the work plan

WP1 (coordination and management) will provide the infrastructure needed for success. QMUL will lead financial management, provide scientific coordination and will co-ordinate the dissemination of progress and results and organise meetings (see figure 4). WP1 will also be a repository for all ethics documentation and liase with the independent ethics and data protection board. WP2 (infrastructure) will develop the structure, provide advice on linkage, document the linked independent standardised databases and co-ordinate the transfer of aggregated data and analysis results to the EUROlinkCAT Central Results Repository. WP2 will also provide guidance in the selection of suitable local cohorts of children without congenital anomalies. WP3, WP4 and WP5 respectively will be responsible for analysing the aggregated data to investigate specific hypothesis about the mortality, morbidity, and educational achievements and needs of children with congenital anomalies compared to unaffected children. They will work together with WP2 to ensure consistency in methodology across these work packages. WP6 will be responsible for using the results from WP3 and WP4 and additional analyses to evaluate the limitations of using health care databases and develop algorithms to overcome these weaknesses of mortality and health care databases covering populations were congenital anomaly registries are not available. WP7 will be responsible for developing links with families with children with congenital anomalies and working with them to enhance their use of the internet for information. Early consultations with parents in WP7 will influence the analyses performed in WPs 3, 4 and 5. While dissemination tasks are ongoing across all work packages, WP8 is specifically responsible for a consultation workshop near the start of the project to ensure input from families with children with congenital anomalies and other stakeholders in the work of WPs 3,4,5 and 7 and a dissemination conference at the end aimed at maximising the impact of the EUROlinkCAT results. The overall strategy of the consortium work plan is to develop a method of maximising the use of routinely collected health care data available across Europe for children with congenital anomalies, to demonstrate that the method works and the data are relevant and essential in making informed decisions and to provide a research resource and mechanisms for its continued growth for future use.

Figure 4 : Work Package Collaboration



3.1.2 Timing of the different work packages

Figure 5 : Gantt chart for EUROlinkCAT

Gantt Chart	Year 1				Year 2				Year 3				Year 4				Year 5			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
WP1 : Co-ordination and Management																				
Initial Website online (D1.1)		D																		
WP2 : Building EUROlinkCAT distributed database																				
Build website (D2.1)	D																			
Ascertain individual registry capacity to link																				
Standardise variables, data quality checks																				
Create & check linked dataset - mortality																				
Create & check linked dataset - morbidity (hospital)																				
Create & check linked dataset - morbidity/prescriptions																				
Create & check linked dataset - education																				
Provide the aggregate data to WP3-WP6 (D2.2)													D							
Develop Interactive Website Tables (D2.3)														D						
Produce manual describing data held in Central Results Repository (D2.4)																	D			
WP3: Mortality associated with Congenital Anomalies																				
Develop protocols for registry ethical approval																				
Develop protocols for analysis																				
Analysis and writing of 2 reports : Survival (D3.1) and Geographical variations in Survival (D3.2)													D	D						
Dissemination																				
WP4: Morbidity associated with Congenital Anomalies																				
Develop protocols for registry ethical approval																				
Develop protocols for analysis																				
Analysis and writing of 3 reports : Hospitalisations (D4.1), Infections (D4.2) and Prenatal Diagnosis (D4.3)														D			D	D		
Dissemination																				
WP5: Educational achievements of children with congenital anomalies																				
Identify and address issues in combining education data across countries of Europe																				
Develop protocols for registry ethical approval																				
Develop protocols for analysis																				
Analysis and writing of 2 reports : Education (D5.1) and Numbers of children (D5.2)																		D	D	
Dissemination																				
WP6: Accuracy of health care databases																				
Develop protocols for registry ethical approval																				
Develop protocols for analysis																				
Analysis and writing of report on coding (D6.1)																		D		
Develop algorithm for congenital anomaly data from hospital discharge databases																				
Dissemination																				
WP7: ConnectEpeople																				
Formation of e stakeholder forum "ConnectEpeople" (D7.1) and its continued development					D															
Report evaluating E-Systems (D7.2)																				D
WP8: Dissemination and Evaluation																				
Infromation leaflet (D8.1)	D																			
Consultation Meeting (D8.2)					D															
Report for guidelines on coding (D8.3)																			D	
Continued dissemination ensuring website current etc																				
Final dissemination incl dissemination meeting (D8.4)																				D

Figure 6: Proposed plan of work of the Congenital Anomaly Registries.

Month of start	Work Package	Tasks for Registries [Delivery number]
1	WP2	Find datasets for linking and determine coverage, years and opportunity for selecting controls
1	WP2	For each data set create a "dictionary" of every variable in the data with its name, description/definition, coding instructions and values in English. This should be available for all national data sets already but may not be in English
1	WP2	Determine quality of the data to be linked for example completeness of each variable. This may require specific queries
1	WP7	Find out details of parent support groups on spina bifida, congenital heart disease, Down syndrome and Clefts.
4	WP2/3/6	Write applications for ethics and research governance to conduct linkage studies for mortality (WP3) and accuracy of coding (WP6). Protocols will be provided but you will have to fill in your local application forms
4	WP2/4/6	Write applications for ethics and research governance to conduct linkage studies for hospital discharge data (WP4a) and accuracy of coding (WP6).
4	WP2/4/6	Write applications for ethics and research governance to conduct linkage studies for WP4b – medication data (WP4b) and accuracy of coding (WP6).
4	WP8	Disseminate information on EUROlinkCAT to relevant contacts
7	WP7	Find out how parents obtain information on the anomalies their children have ?
9	WP2	A set of rules to create standardised variables will be suggested. Check they will work with the data - frequencies/ crosstab tables
9	WP2	A set of rules to select controls will be suggested. Check they will work with the data
13	WP2/5	Write applications for ethics and research governance to conduct linkage studies for WP5 - education.
13	WP2/3	A set of syntax scripts to create standard aggregated tables and analysis for mortality will be suggested. You need to check they will work with your data
14	WP7/8	Attend consultation meeting to talk to parents about what they want out of research [D8.2]
16	WP2/3	Run the registry-specific syntax scripts to generate the required output aggregated tables and analytical results for WP3 analysis – mortality and geographical variations – It is extremely likely that several runs will be required
19	WP2/4	Run syntax scripts WP4a analysis - hospital stays & geographic variations
24	WP7	Report: Evaluation of research priorities from key stakeholder group will be written and circulated for your comments
25	WP2/4	Run syntax scripts WP4b analysis - hospital stays & prescriptions

27	WP2/3	Report: Survival and risk factors for survival [D3.1]
33	WP2/3	Report: Geographical variations in survival in Europe [D3.2]
34	WP2/5	Run syntax scriptsWP5 analysis - education
36	WP2/4	Report: Hospitalisations/number of days in hospitals [D4.1]
40	WP2/6	Run syntax scripts to evaluate specific congenital anomaly coding and termination coding
40	WP2	Check aggregate tables on website are correct before publication
42	WP2/5	Report: Education needs and achievements of children with congenital anomalies [D5.1]
42	WP2/6	Report: Coding registration status and anomaly coding [D6.1]
43	WP6/8	Algorithm for using congenital anomaly data from health care databases
43	WP2/4	Report: Infections and respiratory illness [D4.2]
46	WP2/4	Report: Is there a relation between prenatal diagnosis and morbidity [D4.3]
48	WP2/5	Paper: How do clinical and sociodemographic factors influence education achievements in children with congenital anomalies ?
49	WP2/4	Paper : The costs of hospitalisation
49	WP2/5	Report : Predictions of the number of children needing educational support [D5.2]
51	WP7	Paper : Process of translating morbidity and mortality research data into meaningful graphics for e-access
55	WP8	Report guidelines for improving the quality of the congenital anomaly coding [D8.3]
56	WP8	Disseminate information on EUROlinkCAT to relevant contacts
56	WP7	Report: Evaluating e-systems for linking researchers, professionals, policy makers and consumers [D7.2]
58	WP8	Attend dissemination meeting [D8.4]

3.2 Management structure, milestones and procedures

3.2.1 Management Structure

The Consortium consists of twenty two beneficiary institutions, referred to as "consortium members". Seventeen of the consortium members are EUROCAT congenital anomaly registry leaders who will be responsible for the linkage of their congenital anomaly data to other databases and for providing the required aggregate data. The majority of the consortium members have worked closely together before on both EUROCAT and EUROmediCAT projects and have a long history of successful collaboration and trust.

The Management Team (WP1) will consist of the project Co-ordinator (Morris, QMUL), a data Co-ordinator (Loane, UU) and a clinical Co-ordinator (Garne, RSD). The Co-ordinator will undertake financial management of the project, be responsible for reports to the funders, oversee the running of the project as a whole, co-ordinate dissemination and organise meetings. The co-ordinator will monitor progress towards the milestones and deliverables in all the work packages and in addition act as statistical advisor. The data co-ordinator, as leader of WP2, will be responsible for applying for relevant ethics permissions for the Central Results Repository, for supporting registries in local data linkage, for developing the data management plan, for ensuring standardised linked datasets for use in other work packages and for co-ordinating and providing pooled results for analysis. The clinical co-ordinator will give input on clinical issues and function as congenital anomaly coding and classification advisor.

The Steering Committee (SC) will consist of the Co-ordinator and the leaders and deputy leaders from each work package (12 people). The SC will be supported by WP1. SC documents, agendas and minutes will be managed via the internal website. The SC will meet every six months; they will meet annually during the EUROCAT Registry Leaders Meeting which the majority of the SC will be attending, during the Consultation meeting in the first year and the Dissemination Conference in year 5 and an additional three times. Phone conferences will provide the balance, so that there are at least three meetings, in person or by phone, per year. If there are any unforeseen issues then additional phone conferences will be organised by QMUL. The SC will track progress according to milestones and deliverables, approve publications for submission, create a detailed dissemination and evaluation strategy, and carry out the provisions of the Consortium agreement. A special responsibility of the SC will be to seek ways to continue the consortium as a sustainable network after the end of the project, and to set up mechanisms by which external researchers can apply for access to data in the EUROlinkCAT Central Results Repository in addition to data being available on the website. The SC will generally operate by consensus agreement, but where no consensus can be reached, voting will take place as specified in the consortium agreement.

A consortium agreement will be developed based on the DESCA Horizon 2020 Model Consortium Agreement (www.DESCA-2020.eu). It is planned that this will be signed by all participants before the Grant Agreement is signed. This will cover governance, financial responsibilities, meetings, withdrawal procedures, decision making, dispute resolution, as well as authorship guidelines. The governance structure in the DESCA model will be

modified as specified here. Authorship of publications will follow appropriate international guidelines. All actual or potential conflicts of interest will be declared at the outset, and will be made publicly available on the website.

Work package Committees, led by each Work package leader, will be set up to manage the work of the separate tasks in each work package and will arrange phone conferences as required. Each Work package Committee will provide a yearly progress report to be circulated to all members, and will also present progress at annual meetings for discussion. Work package Committees will meet at annual meetings. Each work package will have a section on the website (external and internal). There will also be clear signposting of important issues and deadlines.

WP2 will establish a Standardisation Committee to agree the common data model and to standardise variables. This group will consist of the data Co-ordinator (Leader of WP2), Clinical Co-ordinator and 3 registry leaders involved in the data collection.

An Ethics and Data Protection Board (EDPB) will be appointed consisting of two professors (or professionals of equivalent standing) who have experience of the issues involved in data linkage projects and are independent from any of the partners. The members of the EDPB will be provided with all documentation concerning ethics or data management. An annual report will be prepared and submitted to the EDPB summarising any existing ethics or data management issues and the EDPB will meet annually face to face with the Management Team to discuss outstanding issues. A report by the EDPB will be submitted with the financial reports. The EDPB will provide advice to ensure that EUROlinkCAT will be compliant with the EU General Data Protection Regulation (Regulation (EU) 2016/679) when it comes into force. A final report suitable for publication will be produced highlighting the different legal and ethics requirements for the data linkage across Europe.

An Action Advisory Panel (AAP) led by Dr Domenica Taruscio (co-ordinator of EUROPLAN (European Project for Rare Diseases National Plans Development) and EPIRARE (European Platform for Rare Disease Registries) projects, Past President of ICORD) will be appointed to provide advice on how to ensure findings are widely implemented and translated into health policy. The AAP will have a major role in creating a cascade for implementing in the real world the policy and practice benefits that result from the project (e.g. in primary prevention, prenatal screening to improve neonatal outcomes, inequalities in treatment throughout Europe, education, parent and patient needs).

The structure of the EUROlinkCAT website will be modelled on the EUROCAT website with a public (external) structure, and an internal website visible only to members who log in with their passwords. The “internal website” will be the major internal communication tool, together with email communications. The internal website will contain all financial documents for the convenience of project participants, and to facilitate awareness of financial rules and agreements.

All meetings, whether face to face or by phone, will be minuted, and the minutes made available on the internal website.

3.2.2 Appropriateness of Management Structure

There is much interest in and enthusiasm for this collaborative project, with 21 Congenital Anomaly Registries participating. The consortium brings together experts from throughout Europe contributing different expertise, who have all collaborated together either on EUROCAT or EUROmediCAT. The management structure is built up from the work package committees consisting of all those people involved in a specific work package who are completing the work and are therefore best placed to make decisions pertaining to their own specific tasks. For each work package (apart from WP2), the leader or deputy leader is also a congenital anomaly registry leader. This ensures that the work packages are very aware of the work and implications for the congenital anomaly registries that will be providing the data. Each work package has a leader and deputy leader in order for the two people to provide support for each other and also to ensure that if one is unable to complete their work package the other person will be able to take over. For WP7 RSD will be able to take over if UU is struggling to meet the deadlines. As the results from WP2 are essential for WP3, WP4, WP5 and WP6 there is an additional backup plan that if the work is suffering serious delays then additional resources from QMUL would be available (Professor Morris has experience of such data management projects and the Research Fellow at QMUL will already be working on the data for the five English registries). BioMedical Computing would also be able to increase their contribution.

Each Work package committee will have representation on the SC (through their Leaders and Deputy Leaders). The SC will therefore be close enough to the people performing the work, but will consist of all WPs so that they will be well placed to make overall decisions pertaining to the collaboration of the individual work packages, and to provide unified decisions across all work packages. Face to face meetings will occur at least every 6 months providing opportunity for decisions involving many members to be made by consensus agreement.

The small management team of Morris (QMUL), Garne (RSD) and Loane (UU) is sufficient to oversee the whole project and hopefully identify potential problems and issues in time to offer additional support to ensure the success of the whole project. These three members work well together with their main areas of expertise in epidemiological methods, clinical knowledge of congenital anomalies, and extensive expertise and knowledge of the management of data complementing each other. A comprehensive set of milestones has been defined (see table 3.2a) in order for everyone involved to have a clear idea of observed and expected progress.

3.2.3 Innovation management

The initial part of the project will involve finding out detailed information about the data available for linkage, standardising and assimilating this information from 21 registries in 13

countries and deriving protocols that can be used to apply for ethics permission to obtain the linkage. The project is novel in that researchers in WP7 will use this time and take advantage of new technologies to establish links and collaborations with parents and parent support groups of children with congenital anomalies to try and obtain information as to what research questions are important to them. This innovation management aspect will allow the specific research questions posed to be altered during the initial phase of the project to ensure that they are more relevant to the members of the public. The involvement of parents will also be exploited later by developing methods of dissemination that will be effective for parents.

3.2.4 Critical risks for implementation

Table 3.2b summarises the main risks to implementation of EUROlinkCAT. In general, this is a low risk project, given that there is considerable experience among the participants in developing algorithms and protocols, analysing the databases contributing to the project, and a history of successfully working together. The EUROmediCAT FP7 funded project can be considered a "pilot project" for many of the core elements of EUROlinkCAT, in terms of methodology and consortium management. Many of the registries also have experience of linking to some of the data sources, for example for three registries (Finland, Denmark and Wales) linkage has already occurred between all the suggested data sources.

The project uses existing databases from congenital anomaly registries, mortality databases, disease cohorts (such as hospital discharge databases) and prescription databases. The outcome of the project will therefore not depend on the participation of patients or health care professionals.

The feasibility of all the work packages has been discussed thoroughly with the work package leaders and the partners from each work package, who are fully committed to the work packages in which they participate.

3.3 Consortium as a whole

3.3.1 Complementarity of the participants and extent to which the consortium as whole brings together the necessary expertise

The EUROlinkCAT consortium consists of 21 EUROCAT congenital anomaly registries from 13 countries together with researchers who are associated with EUROCAT. Representation in many countries is essential to explore the diversity in morbidity and mortality in Europe, to assess the implications of the research on a Europe-wide basis, and to disseminate the results so that it has an impact on national policy and practice.

Across the consortium, we have expertise in congenital anomalies, obstetrics, paediatrics, medical genetics, midwifery, nursing, pharmacoepidemiology, pharmacy, public health, epidemiology, statistics and computing skills, providing the full range of expertise necessary for research on mortality, morbidity and educational in children with congenital anomalies. In addition WP7 : Connect**E**people is led by Professor Sinclair, who is an expert in the use of

social media to enable patients to find out about their illnesses. Two specialist IT companies are also partners to ensure the full range of IT expertise is available.

Many of the consortium members have worked within the EUROmediCAT project and are also members of the EUROmediSAFE consortium, and thus have experience of working together for a common aim, good communication, trust, ability to jointly meet deadlines, and productivity. The group have jointly published many papers on the epidemiology of congenital anomalies and also the risks of medication exposure in pregnancy. In addition, Biomedical Computing Ltd have provided database and web applications for EUROCAT since 2001. They have produced the EUROCAT data management program, for central and registry use, worked on the EUROmediCAT project and are also currently supporting the redesign of the EUROCAT website. This long collaboration results in many cost savings as Biomedical Computing Ltd are extremely familiar with the issues concerning congenital anomaly data.

The data that will be used in EUROlinkCAT has already been subject to considerable standardisation work within the framework of EUROCAT. Four registries have experience of linking with health care databases in the EUROmediCAT project.

The collaboration of congenital anomaly registries from at least 10 countries is essential for the setting up of the e-forum Connet**E**people as it will be built on the initial contacts between registries and the families with congenital anomalies in their areas. This has the enormous advantage of overcoming language and cultural differences as each registry will be directly liaising within their own country.

3.3.2 Appropriateness of the allocation of tasks, ensuring that all participants have a valid role and adequate resources in the project to fulfil that role

The co-ordinating institution (**QMUL**) has considerable experience of managing EU projects. A full time project manager will manage this project. The co-ordinator of this Project (Professor Joan Morris) is the scientific leader of EUROCAT and in addition to overall scientific co-ordination of the project, as a statistician, she will be working closely with the research fellow at QMUL and other statisticians in each work package to ensure consistency of methodology. She will be contributing 30 months. The research fellow at QMUL will be responsible for collating the data from the 5 English congenital anomaly registries. A PhD student will be investigating the advantages and disadvantages of using of a comparison set of children without congenital anomalies.

Ulster University (**UU**) will be responsible for WP2 – Building the central results repository. The data co-ordinator (Dr Maria Loane) is Leader of the standardisation committee and a member of the management team. She brings fifteen years of experience of managing the EUROCAT and EUROmediCAT databases and epidemiologic data analysis relating to congenital anomalies. She will be contributing 30 months and will be assisted by a full-time research assistant.

Biomedical Computing Ltd (**BIOMED**) will be responsible for many of the tasks in WP2- Building the central results repository. Biomedical Computing Ltd provides specialised bespoke programming to various customers in the medical research and biotechnology fields and have an established track record of successful working with the applicants through EUROCAT. Their programmers will be contributing 13 months.

Ulster University (**UU**) will also be responsible for WP7 – connecting parents with researchers. The work package leader (Professor Marlene Sinclair) has considerable experience in research on the use of the internet by health professionals and pregnant women and also in developing electronic tools for data collection. She will be contributing 18 months and will be assisted by a research assistant (48 months).

Redburn Solutions Ltd (**REDBURN**) will be responsible for providing IT support and training for registry Leaders and Parents in setting up and administrating Facebook, Twitter and Skype accounts and running Webinars in WP7. They specialise in portals, mobile and Business Intelligence with a focus on Health and Education, delivering EU research to public and commercial organisations. UU has worked with them on previous successful collaborations. They will design a Logo for EUROlinkCAT and will generate 4 infographics for the four specific congenital anomalies chosen (Down syndrome, congenital heart defects, spina bifida and clefts). They will contribute 6 months.

Dr Ester Garne (**RSD**) is the clinical co-ordinator and will be responsible for ensuring clinical validity and standardisation in all work performed. Dr Garne is a paediatrician and neonatologist who alongside her clinical work, has worked with the EUROCAT Central Registry for 15 years as leader of the Classification and Coding Committee and is extremely experienced and effective in ensuring different registries and researchers all work to common standards. In addition she will lead two work packages (WP4 concerning morbidity and WP6 concerning the accuracy of data in databases) and is Registry Leader of the Odense congenital anomaly register. She will be contributing 15 months and will be assisted by a statistician who has worked on the EUROmediCAT project (36 months). In addition Professor Jane Clemensen, who has more than 13 years' experience with telemedicine research and Participatory Design, will lead one task in WP7 Connect**E**people (15 months).

Newcastle University (**UNEW**) will be responsible for work packages 3 concerning mortality and work package 5 concerning education. Professor Judith Rankin, as an experienced epidemiologist and Registry Leader of the Northern Congenital Abnormality Survey (NorCAS) congenital anomaly register and member of the EUROCAT Management Committee, will contribute 12 months and will be assisted by Dr Svetlana Glinianaia who is an experienced researcher with 20-years' experience of working with congenital anomaly data and involvement in linking large datasets. (48 months).

University of Ferrara **(UNIFE)** will be responsible for work package 8 : Dissemination. Amanda Neville as a Registry Leader of IMER registry will contribute 35 months and will be assisted by a computer programmer and data analyst (20 months). Amanda Neville is also deputy leader of WP5.

Anna Pierini **(CNR-IFC)** is responsible for one task in work package 3 concerning mortality, is a member of the standardisation committee and is registry leader of the Tuscany Registry of Congenital Defects for the EUROmediCAT project. She will contribute 9 months.

Dr Hermien de Walle **(UMCG**) is responsible for one task in work package 4 concerning morbidity, is a member of the standardisation committee and is registry leader of the Northern Netherlands Registry of Congenital Defects for the EUROmediCAT project. She will contribute 16 months.

Professor Mika Gissler **(THL)** has been working more than 25 years with the Finnish Reproductive Health Registers and is responsible for one task in work package 4 concerning morbidity of children with congenital anomalies. . He will contribute 10 months.

PUMS will be responsible for the dissemination , with a particular responsibility for the final dissemination conference in Posnan. Professor Latos Bielenska is a medical geneticist who set up the registry of Wielkopolska collaborating in this project, and a larger registry covering most of Poland. Apart from contributing data to this project, she and the PUMS team of clinicians will be particularly active in the dissemination of results at Polish and European level. She will contribute 10 months.

KDB will be responsible for the dissemination , with a particular responsibility for the consultation meeting early in the work package. Professor Ingeborg Barisic is a clinical geneticist and also Registry Leader of the Zagreb Registry. She will contribute 10 months.

The following registries will supply data to the project. Each Registry Leader is responsible for overseeing the linkage at a local level. This is essential as they are familiar with their own data and their participation will ensure the resulting model is acceptable and consistent across Europe. These registry leads will also be responsible for commenting on interpretation, contributing their country perspective, contributing their disciplinary perspective, and helping to disseminate the findings in their countries. They will contribute between 5 and 18 months depending on the number of different data sets they are able to link to:

Wales : Congenital Anomaly Register and Information Service (**CARIS**)
France : Paris Registry of Congenital Malformations (**INSERM UMR 1153, Equipe EPOP é**)
Spain : Valencia Congenital Anomaly Registry (**FISABIO**)
Spain : Basque Congenital Anomaly Registry (**BIOEF**)
Portugal : South Portugal Congenital Anomaly Registry (**INSA**)
Finland : Finland Congenital Anomaly Registry (**THL**)
Germany: Malformation Monitoring Centre Saxony-Anhalt (**OVGU**)
Belgium : Antwerp Congenital Anomaly Registry (**PIH**)
France : Ile de la Reunion Congenital Anomaly Registry (**ILDR**)
Ukraine : OMNI-Net Ukraine Birth Defects Program (**OMNI-NET**)

Congenital Anomaly registry subcontractors: These registries together with NorCAS (previously based at Newcastle University) all collaborate and at present a copy of their data is stored at QMUL. A research fellow based at QMUL will be responsible for linking all their data at the same time:
England : East Midlands and South Yorkshire Congenital Anomaly Register
England : South West Congenital Anomaly Register
England : Thames Valley Congenital Anomaly Register
England : Wessex Congenital Anomaly Register

The Maltese Congenital Anomaly registry will also provide data on mortality for this project.

Swansea University will be involved in linking the data from Wales (CARIS).

3.4 Resources to be committed

3.4.1 Other direct cost items

Table 3.4b: 'Other direct cost' items

We declare that selection of subcontractors and entities providing goods, works and services will conform to competitive selection according to H2020 rules, while respecting applicable rules on conflict of interest

Travel: Consortium Trips planned: 5 Steering Committee Meetings and 5 Standardisation Committee Meetings 1/yr, tagging onto end of annual Registry Leaders Meeting so most people will already be there; most partners are only asking for funds for 1 night accommodation and 1 day subsistence); **3 Steering Committee Meetings & 2 Standardisation Committee Meetings Consultation Meeting** in Croatia**; Dissemination Meeting** in Poland**; Travel to conferences for wider dissemination**

To clarify, "Hosting Costs" refer to event organisation costs incurred when a partner will host a meeting or event at their institution; "Travel Costs" refer to costs associated to travel to a meeting or event in a different location.

None of the partners have any equipment costs in their budgets.

Participant 1 QMUL	Cost (€)	Justification
Travel	€90626	**PI** to all meetings except Standardisation Committee Meetings (€9030.50); **Project Manager** to Steering Committee Meetings, Consultation Meeting and Dissemination Meeting and conferences (€10430.5); **Researcher** to Dissemination Meeting (€1560.5); **PhD Student** to Dissemination Meeting (€1560.5); **Administrator** subsistence to London evening meetings (€454.50); **Miriam Gatt** in the Malta Government (third party providing resources in-kind free of charge) to Consultation Meeting and Dissemination Meeting (€2126); **Advisory panel** to Dissemination Meeting (€6636) **Parents & other professionals** to Consultation and Dissemination meetings (€58828). We have budgeted for 40 people to be invited to the Consultation Meeting. We are hoping to have 4 different groups of parents corresponding to the four anomalies: Down syndrome, severe congenital heart defects, spina bifida and cleft lip with cleft palate. As 11 registries are involved in working with parents/carers in this work package this assumes that most of the registries will recruit 1 person for each anomaly group. In addition there are some European parent associations that we wish to involve. We felt approx. 10 parents per anomaly would be an efficient use of resources. We have budgeted for 20 people to be invited to the dissemination meeting. This is less than the consultation meeting as by the time of the dissemination meeting we will have established the ConnectEpeople forum and would expect most parents to participate using webinar and skype. The 20 would include other professionals.

Other goods and services	€108115	Hosting costs for project meetings held in London (€2550); Consumables (e.g. printing leaflets for workshops, laptop for researcher to be used solely on the project) (€4200); Data licenses (€7500); Open access costs (€6000); Audit fee (€3250); Data access fees (€84615)
Total	**€198741**	
Participant 3 RSD	**Cost (€)**	**Justification**
Travel	€31053	**PI & Researcher** travel to Steering Committee Meetings, Standardisation Meetings, Consultation Meeting, Dissemination Meeting and conferences
Other goods and services	€37499	Open access (€12000); Data access and linkage (€21999); Audit fee (€3500)
Total	**€68552**	
Participant 5 UNIFE	**Cost (€)**	**Justification**
Travel	€20760	**PI** travel to Steering Committee Meetings, Consultation meeting, Dissemination Meeting and travel to conferences (€20760)
Other goods and services	€31500	Data Access (€28000); Open access (€3000); Consumables (€500)
Total	**€52260**	
Participant 6 KDB	**Cost (€)**	**Justification**
Travel	€17160	**PI** travel to Steering Committee Meetings, Dissemination Meeting and conferences (€17160)
Other goods and services	€15000	Hosting costs for Consultation meeting in Croatia (€15000);
Total	**€32160**	
Participant 12 PUMS	**Cost (€)**	**Justification**
Travel	€12260	**PI & Researcher** Travel to Steering Committee Meetings and Consultation meeting (€12260)
Other goods and services	€33760	Hosting costs for Dissemination Meeting including catering and event organisation (€33760)
Total	**€46020**	
Participant 13 THL	**Cost (€)**	**Justification**
Travel	€3626	**PI** travel to Consultation meeting and Dissemination Meeting (€3626)
Other goods and services	€65000	Open access costs (€3000); Data linkage and access (€62000)
Total	**€68626**	
Participant 14 OMNI-NET	**Cost (€)**	**Justification**
Travel	€2126	**PI** travel to Consultation meeting and Dissemination Meeting (€2126)
Other goods and services	€3926	Data linkage and access (€3426), Consumables (€500)
Total	**€6052**	

Participant 15 OVGU	Cost (€)	Justification
Travel	€10000	**PI** travel to Consultation meeting and Dissemination Meeting and conferences (€10000)
Other goods and services	€8109	Data linkage and access costs (€8109)
Total	**€18109**	
Participant 20 BIOMEDICAL	**Cost (€)**	**Justification**
Travel	€11110	**PI** Travel to Project meetings, Consultation meeting and Dissemination Meeting (€11110)
Other goods and services	€10800	Computer licences & website hosting (10800)
Total	**€21910**	
Participant 21 REDBURN	**Cost (€)**	**Justification**
Travel	€4000	**PI** Travel to Consultation meeting and support at webinar meetings (€4000)
Other goods and services	€10070	Webinar licence costs (€2070); Project logo and upload (€4000); Generating 4 InfoGraphics (€4000)
Total	**€14070**	

4. Members of the consortium

4.1 Participants

Participant No 1 : Queen Mary University of London (QMUL)

Queen Mary University of London is one of the UK's leading research-focused higher education institutions, with around 17,840 students, 4,000 staff and an annual turnover of £300m. This project will be located in the Wolfson Institute of Preventive Medicine (WIPM), which is one of five institutes within Barts and the London Medical School. The results of the most recent national assessment of research – the Research Excellence Framework (REF 2014) ranked QMUL 9th in the UK among multi-faculty universities and Barts and The London Medical School within the top 5 medical schools in the country.

Tasks

- WP1 : Project Management

  During the period of FP7, WIPM held 7 European funded projects (6 under FP7, 1 under DG SANCO), and are currently leading on three of them (COFI GA:602645; ENNAH GA:226442; EUGATE: DG SANCO). Excluding EU projects, WIPM currently holds 116 research grants from other funders (notably Cancer Research UK, NIHR and MRC).). Queen Mary University of London has been awarded ≈77 European grants under the period of H2020 so far, and held ≈204 EU projects prior to H2020. QMUL is therefore practiced in managing European funded grants.
- WP1 : Co-ordinate scientific content of the work packages

  The focus in the WIPM is on research dedicated to the reduction of disease and disability. WIPM has led many international multi-centre clinical trials including

screening and treating hypothyroidism in pregnancy and the subsequent cognitive development of the child. WIPM is a leader in the field of antenatal screening for Down's syndrome and houses an Antenatal Screening Service providing 50,000 screening tests per year for Down's syndrome and open neural tube defects including the new reflex DNA screening test in 2015.

- WP2 : Linkage of Congenital anomaly registry data from English registries

  WIPM housed the BINOCAR Hub and has the experience of collating data from the five regional congenital anomaly registries in England that will be contributing data to EUROlinkCAT.

- Statistical and Economic contributions to WP3,WP4,WP5,WP6

  WIPM provides a statistical advisory service to Barts and The London Medical School. WIPM has also been providing the statistical expertise to the EPICURE cohorts (Extremely Premature Babies) since 1995. WIPM is involved in many cost-effectiveness analyses of preventive medicine.

- WP8 : Dissemination

  The focus in the WIPM is on the translation of research into public health strategies and their practical implementation. WIPM houses Britain's leading advocacy group into salt and sugar intake reduction (CASH) and one of the leading smoking cessation research and treatment centres globally (TDRU).

Joan Morris, Professor of Medical Statistics. **Gender: Female**

Joan is the co-ordinator of this Project, and will lead WP1 and provide statistical and epidemiological support to WP2, 3, 4, 5 and 6 in addition to overall guidance of all WPs

Achievements include:

- Scientific leader of EUROCAT having previously been a work package leader for EUROCAT FP7 funded project.
- Co-ordinator of EUROmediSAFE (one of the five research consortium selected by the EMA to respond to their research proposals).
- Director of the National Down Syndrome Cytogenetic Register (NDSCR).
- Director of the British Isles Network of Congenital Anomalies HUB since 2010 which produced the National Congenital Anomaly Statistics for England and Wales from 6 regional and 2 national congenital anomaly registries.
- Member of EUROmediCAT project linking EUROCAT registries to prescription and health care databases.
- Statistician on the EPICURE cohort studies, evaluating the morbidity of extremely premature births up to 18 years of age.

She is committed to the sustainability of EUROCAT as a network supporting activities related to the primary prevention of congenital anomalies in Europe.

Project Manager / Administrator : To be appointed

They will be responsible for the administration of the project. Someone with previous experience project managing a large grant will be sought.

Research Fellow / Statistician : To be appointed

They will be responsible for the linkage of the five congenital anomaly registries in England which will all occur through the BINOCAR HUB (established in the WIPM in 2010). They will also be responsible for ensuring consistency of statistical analysis and methodology across the

workpackages and for collating interim and final reports from all workpackage leaders. Someone with a statistical background and experience of working in a collaborative group will be sought.

PhD Student : To be appointed

When appointing staff members, QMUL Equal Opportunities Policy will be followed at all times. “Staff will be treated equitably and will not be accorded less favourable treatment because of age, marital/civil partnership status, sex, disability, race, colour, ethnic or national origin, sexual orientation, family circumstances, religious or political beliefs and transgender status”. This policy will be applied throughout the project.

Relevant Previous Publications

1. Morris, J. K., Rankin, J., et al. (2015). Prevention of neural tube defects in the UK: a missed opportunity. Archives of disease in childhood. doi:10.1136/archdischild-2015-309226
    - Successful dissemination of collaborative work from BINOCAR registries: By quantifying the number of affected pregnancies that could have been prevented , this paper achieved wide publicity with interviews on BBC news programmes.
2. Wald NJ, Luteijn JM, Morris JK et al. (2016) . Cost-benefit analysis of the polypill in the primary prevention of myocardial infarction and stroke. European journal of epidemiology
    - Cost-benefit analysis of preventive treatment.
3. Morris, J. K., Grinsted, M., & Springett, A. L. (2015). Accuracy of reporting abortions with Down syndrome in England and Wales: a data linkage study. Journal of public health (Oxford, England). doi:10.1093/pubmed/fdv022
    - Linkage of National Down Syndrome Cytogenetic Register to sensitive national data on abortions to enhance both data sets and recommendations to improve national data collection.
4. Calzolari, E., Barisic, I., Loane, M., Morris, J.K et al (2014). Epidemiology of multiple congenital anomalies in Europe: A EUROCAT population-based registry study. Birth Defects Research Part A: Clinical and Molecular Teratology, 100(4), 270-276. doi:10.1002/bdra.23240
    - Epidemiological and clinical approach for classification of cases to improve the quality and accuracy of Multiple Congenital Anomaly data
5. Boyle, B., Morris, J. K., McConkey, R., Garne, E., Loane, M., Addor, M. C., . . . Dolk, H. (2014). Prevalence and risk of Down syndrome in monozygotic and dizygotic multiple pregnancies in Europe: Implications for prenatal screening. BJOG: An International Journal of Obstetrics and Gynaecology, 121(7), 809-820. doi:10.1111/1471-0528.12574
    - Analysis of data from EUROCAT collaboration to provide clinical information to improve the performance of screening for Down syndrome in twins.

Relevant Previous Projects

1. EUROCAT: Led from Belfast Funded under Health Programme European Union 2008-2014; QMUL led Prenatal Diagnosis WP 2008-2013. EUROCAT now hosted at ISPRA, Milan. Professor Morris is the Scientific Leader 2015- . The current proposal builds on the established EUROCAT infrastructure and involves many of the EUROCAT registries and will hopefully be as successful in establishing standards for coding and analysing data concerning congenital anomalies.

2. EUROmediCAT: FP7 funded 2011-2014. The current proposal is adopting much of the methodology of EUROmediCAT which was a successful partnership of congenital anomaly registries which linked their data with hospital discharge data and prescription data to produce innovative research on medication use in pregnancy.

3. National Down Syndrome Cytogenetic Register: funded by Department of Health through Health Quality Improvements Program 1989-2015. Professor Morris was the Director which

involved collecting congenital anomaly data, linking the data to other sources and also performing research using it (over 40 peer reviewed papers).

4. British Isles Network of Congenital Anomaly Registers (BINOCAR) HUB: funded by Department of Health through Health Quality Improvements Program 2010-2014. Professor Morris was responsible for establishing standard operating procedures to enable aggregation of data from 8 congenital anomaly registries in England and Wales to provide national data on the prevalence of anomalies, creating and using the HUB as a research resource and disseminating this information nationally.

5. EPICURE Cohorts: funded by the MRC since 1995 to evaluate the long term outcomes in a cohort studies of babies born extremely premature in the UK in 1995. The experience in analysing and evaluating long term outcomes in a cohort of babies, many with serious morbidity at birth, will aid in the EUROlinkCAT analysis.

Participant No 2: Ulster University (UU)

Ulster University (UU) is the largest single university on the island of Ireland with 20,000 full-time and part-time students. The Institute of Nursing and Health Research (INHR) http://www.science.ulster.ac.uk/inhr/, located within UU's Faculty of Life and Health Sciences, has acquired a reputation which ranks it among the best in the United Kingdom. This research will be undertaken in the Centre for Maternal, Fetal and Infant Research (MFIR), one of five centres within INHR. The Research Excellence Framework (REF) 2014 results show that 96% of nursing and health sciences research at UU is of international excellence or 'world leading,' and 100% of our research impact and 100% of our research environment are also recognised as world leading or internationally excellent.

Tasks

WP1: Member of the core scientific management team.

- Experienced in management of other large EU funded projects: EUROCAT and EUROmediCAT.

WP2: Central Results Repository

- The MFIR perinatal epidemiology research cluster has focused on epidemiological surveillance of congenital anomalies.
- Responsible for central database and surveillance work-packages in previous EU projects. Produced all deliverables, Reports and scientific papers on time.
- Responsible for developing and implementing Data Quality Indicators within EUROCAT network

WP4: Responsible for 2 scientific papers relating to morbidity

- Experience in pharmacoepidemiology research. Research included risk assessment studies of maternal exposures to specific drugs in relation to the risk of congenital anomalies.
- Have published extensively on geographical variations in congenital anomalies.
- Co-Author on previous publications on cost-benefit analyses.

WP7: ConnectEpeople

- Extensive project management experience
- Experienced in applied research using the Internet, social media and the use of technologies such as mobile apps by pregnant women. Internet based research (online survey and online focus groups in EuroMediCAT) and developing online apps and conducting an online survey in (OptiBirth).
- Experienced in classic phenomenology, interpretative phenomenology and ethnography to explore women's experiences and behaviours

Maria Loane, Reader in Public Health. **Gender: Female**

Maria is the EUROlinkCAT project Data Co-ordinator responsible for supporting registries in local data linkage, for ensuring standardised linked datasets for use in other work packages and for co-ordinating and providing pooled results for analysis. She will lead WP2 "Building EUROlinkCAT Central Results Repository".

Achievements include:

- Member of EUROCAT Steering Group since 2005. Responsible for the EUROCAT central database and surveillance activities/ work packages up to 2014
- Member of EUROmediCAT consortium, led the Central Database and Software Development WP

- Member of EUROmediSAFE consortium (one of the five research consortium selected by the European Medicines Agency to respond to their research proposals).
- Member of the Northern Ireland Administrative Data Research Centre network conducting data linkage studies using available administrative data.
- Core member of the NI Baby Hearts Study conducting a case-control study investigating risk and protective factors for congenital heart disease
- She has also contributed to a number of European reports as an expert on congenital anomalies. This included the Global Burden of Disease project, of which she co-authored 2 papers subsequently published in the Lancet.

Marlene Sinclair, Professor of Midwifery Research. **Gender: Female**
She will lead WP7 and establish a sustainable e-forum "Connect**E**People" to provide regional, national and international support to families with congenital anomalies as well as involving these families in setting out research priorities across Europe.

- Head of the Maternal Fetal and Infant Research Centre at Ulster University.
- A practicing midwife
- Panel member of UK Research Excellence Framework (REF2014)
- Chair of a HTA Working Group for the European Medicines Agency in 2013.
- Personal funding record is over £2m
- Founder and President of the Doctoral Midwifery Research Society
- Founder and editor of the *Evidence Based Midwifery* Journal.
- Member of OptiBirth consortium 2012 and led WP2: "Translation of Optibirth intervention into an on-line format"
- Member of EUROmediCAT consortium, led WP 7: "Implications of the Internet in relation to medication access and safety information"
- Member of EUROmediSAFE consortium (one of five research consortium selected by the EMA for future research proposals)

Research Assistant (WP2). **To be appointed.** They will be responsible for documenting the various European datasets available for linking, standardising data, running the Central Results Repository and the populating the website interactive tables.
Research Associate (WP4). **To be appointed.** They will be responsible for conducting literature review and the pooled analysis using morbidity data linked to prescription data.
Research Associate (WP7). **To be appointed.** They will be responsible for liaising with the registries to scope existing links and networks for parents of children with select congenital anomalies.

Relevant Previous Publications

1. Linda de Jonge; Ester Garne; Rosa Gini; Sue Jordan; Kari Klungsoyr; Maria Loane; et al. Improving information on maternal medication use by linking prescription data to congenital anomaly registers: A EUROmediCAT Study. Drug Safety **DOI:** 10.1007/s40264-015-0321-9
    - This study showed that information on maternal medication use in the first trimester of pregnancy was improved when local congenital anomaly data were linked to local prescription databases, and is highly relevant to the current proposal.
2. Dolk H, Jentink J, Loane M, Morris JK et al. (2016) Lamotrigine use in pregnancy and risk of orofacial cleft and other congenital anomalies. Neurology (published online April 2016: DOI 10.1212/WNL.0000000000002540)
    - This study was based on the EUROCAT Antiepileptic Drugs (AED) database which has underpinned research into medication safety in pregnancy. No evidence of an increased risk of isolated orofacial clefts following first trimester exposure to the anti-epileptic drug (AED) lamotrigine was found. The findings have significant public health implications for women of childbearing age with epilepsy.
3. Dolk H, de Jong-van den Berg LTW, Pierini A, Morris J, Bakker M, Jordan S, Garne E, Klungsoyr K, Loane M, Charlton R, Luteijn M, Sinclair M, Latos-Bielenska A (2015). EUROmediCAT Recommendations for European Pharmacovigilance Concerning Safety of Medication use in Pregnancy. P*harmacoepidemiology & Drug Safety* 24(S2): 3-7. DOI:10.1002/pds.3865
    - Recommendations, arising from the entire FP7 EUROmediCAT project, were disseminated to improve future reproductive pharmacovigilance research. These have been endorsed by the ENCePP (European Network of Centres for Pharmacoepidemiology) Special Interest Group (Pregnancy).
4. Lagan B, Dolk H, White B, Uges D and Sinclair M (2014). Assessing the availability of the teratogenic drug isotretinoin outside the pregnancy prevention programme: a survey of e-pharmacies. *Pharmacoepidemiology and Drug Safety,* 23 (4): 411-418. DOI: 10.1002/pds.3565
    - Online surveys and focus groups explored the availability of purchasing highly teratogenic drugs such as isotretinoin on the internet without a prescription. This study highlighted the importance of investigating women's medication-related behaviour, and their use of the internet for information.
5. Lagan B M, **Sinclair M**, Kernohan WG (2011). What is the impact of the internet on decision-making in pregnancy? A global study. Birth (Berkeley, Calif.), 38(4), 336-345. doi: 10.1111/j.1523-536X.2011.00488.x

Relevant Previous Projects

1. **EUROCAT**: Led by Ulster University (UU) 2001-2014, funded under DG Sanco Health Programme. Dr Loane managed the EUROCAT central database holding data on more than 600,000 cases of congenital anomalies received from 38 registries in 20 countries, 2002-2014. She led the EUROCAT Registration, Central Database and Surveillance WP 2004-2014 and has been a member of the EUROCAT Steering Group since 2005. She has extensive experience of database management, and was involved in the planning, design, and implementation of data quality indicators within the network. The current proposal builds on this work by linking data from congenital anomaly registries to existing databases to assess mortality, morbidity and educational outcomes.
2. **EUROmediCAT**: Led by UU 2011-2014, FP7 funded project. Dr Loane led the EUROmediCAT Central Database and Software Development WP and was responsible for the effective transfer of the congenital anomaly data from 15 registries to other WP leaders to perform risk assessment studies of medications relating to specific malformations. Data Quality Indicators were produced to assess the quality of the data. She was involved in the Diabetic cohort study and linking congenital anomaly data to prescription databases. This experience highlights the importance of standardising data across registries at the beginning of a project, and will be invaluable for the current proposal. Prof Sinclair led the WP on internet use and drug safety.
3. **Administrative Data Research Centre NI** (ADRC-NI): funded by the Economic and Social Research Council, 2013-2018. Dr Loane is a core member of an UU team conducting data linkage studies using available administrative data. She is responsible for the research strand relating to Medication use in pregnancy and its risks/consequences in terms of birth outcome and later child development outcomes. This research again will inform the current proposal, as it concerns data linkage studies.
4. **"OptiBirth"**. A cluster randomised trial in Ireland, Germany and Italy, with 15 clusters of 94 women, the OptiBIRTH study will attempt to increase VBAC rates from 25 to 40% through increased women-centred care and women's involvement in their care. The intervention involves an online resource that is evidence-based and facilitates shared decision making by women and clinicians. Professor Sinclair leads WP2: "Translation of Optibirth intervention into an on-line format".
5. **Horizon2020 Funding January 2016. "mHealth4Afrika - Community-based ICT for Maternal Healthcare in Africa"** Professor Sinclair is part of the Ulster research team working with IIMC, Ireland University of Gondor, Ethiopia, Strathmore University, Kenya, University of Malawi, Baobab Health Trust, Malawi, University of Oslo, Nelson Mandela Metropolitan University, South Africa, UU Computer Science Research Institute and UK Ireland contributing to the Research and evaluate the potential impact of co-designing an open source, multilingual mHealth platform to support quality community-based maternal and Newborn healthcare delivery at clinic level, based on end-user requirements. This project has just commenced and Professor Sinclair will be involved in identifying and evaluating a range of sensor technologies for maternity health data collection in Africa.

Participant No 3 : Region Syddanmark (Hospital Lillebaelt)(RSD)

Hospital Lillebaelt, one of four hospitals in Region Syddanmark, serves as teaching hospital for University of Southern Denmark and has 14 professorships. The hospital cares for more than 200,000 patients per year, has 4,500 FTE positions and a yearly expenditure of 429m Euros. Both patient care and research focuse on evidence based treatment and care. The hospital prioritizes communication and patient involvement, and has established a research unit mainly focusing on studies on how to improve patient communication, implement shared decision-making, and patient involvement.

Tasks

- WP1: member of the core scientific management team
  Previously involved in the management of EUROCAT and EUROmediCAT projects
- WP2: Linkage of the Danish Congenital anomaly registry data to data in Statistics Denmark for use in WP3-6.
  Responsible for the same task in the EUROmediCAT study
- WP3: contribute with mortality data for children with congenital anomalies
  Has written several papers about mortality for liveborn infants with congenital anomalies
- WP4: leader of this WP on morbidity and responsible for 1 scientific papers
  Has been WP leader in several EUROCAT contracts and in the EUROmediCAT study. Has been leading several EUROCAT studies on morbidity for specific congenital anomalies
- WP5: contribute with data on education for children with congenital anomalies
  Experience in working with linked data from Statistics Denmark
- WP6: leader of this WP on accuracy of coding and responsible for 1 scientific paper
  Same as WP4. For many years been Chair for EUROCAT coding and Classification Committee
- WP7: Responsible for 1 scientific paper
  Centre of Innovative Medical Technologies is part of RSD and has experience of telemedicine research
- WP8: Dissemination. Responsible for report to EU institutions hosting health care databases with guidelines for improving the quality of the congenital anomaly coding
  Has written many coding guides to the EUROCAT network.
  Experienced in coding of diseases at hospital level

Ester Garne, Consultant Paediatrician. **Gender: Female**
Ester Garne is responsible for two workpackages in the study and for providing data from the Danish registries.
Achievements include:
Consultant Paediatrician (neonatology and paediatric echocardiography), Paediatric Department, Lillebaelt Hospital, Denmark
Associate Professor, Institute of Regional Health Research, University of Southern Denmark
Member of European Union Committee of Experts on Rare Diseases (EUCERD) 2010-13
Registry leader of EUROCAT Registry for congenital malformations for Funen County
Chair of EUROCAT Coding and Classification Committee
Member of Steering Committees in EUROCAT and EUROmediCAT
Database manager for Neobase, Lillebaelt Hospital (neonatal quality of care database)

Jane Clemensen, Associate Professor. **Gender: Female**
Jane Clemensen is responsible for contributing to WP7 : ConnectEpeople with her experience of telemedicine research and Participatory Design.
Achievements include
Associate Professor and head of research: Centre for Innovative Medical Technology (CIMT) Odense University hospital/SDU.
Head of Centre for Clinical Nursing Research in the Region of Southern Denmark.
Responsible for two modules at the Master's Degree in Clinical Nursing; a) Health Technology and Innovation (b) Flipped Healthcare

Statistician/research fellow: to be employed.
This is likely to be Anne Vinkel Hansen (Female), a statistician who worked on the EUROmediCAT study

Relevant Previous Publications

1. **Garne E**, Hansen AV, Morris J et al. Use of asthma medication during pregnancy and risk of specific congenital anomalies: A European case-malformed control study. J Allergy Clin Immunol. 2015; 136: 1496-1502
2. **Garne E,** Dolk H, Loane M et al. Paper 5: Surveillance of multiple congenital anomalies: Implementation of a computer algorithm in European registers for classification of cases. Birth Defects Research (Part A) 2011; 91:S44-S50
3. **Garne E**, Olsen MS, Johnsen SP on behalf of the Danish Register of Congenital Heart Disease. How do we define congenital heart defects for scientific studies? Congenit Heart Dis 2012:46-9
4. **Garne E**, Khoshnood B, Loane M et al. Termination of pregnancy for fetal anomaly after 23 weeks of gestation: A European register-based study. BJOG 2010;117:660-6
5. Danbjorg DB, Wagner L, Kristensen, BR, **Clemensen J**: "Nurses' experience of using an application to support new parents who are discharged early postnatal - an intervention study". International Journal of Telemedicine and Applications. Volume 2015 (2015), Article ID 851803.

Relevant Previous Projects

1. EUROCAT : Leader of EUROCAT registry for Funen County since 1988. From 2002 to 2014 worked part time as paediatric epidemiologists for the Central EUROCAT database in Belfast.

Member of EUROCAT Steering Committee and Chair of EUROCAT Coding and Classification Committee.

2. EUROmediCAT: FP7 funded 2011-2014. Leading a WP on use of asthma medication and SSRI during pregnancy using different methodologies.
3. DRCHD (The Danish Register for Congenital Heart Disease): member of the Steering Group. Developing algorithms for use in the National Discharge Database.
4. Patterns of Birth Defects in a Saudi population- A 3 years prospective cohort study. Riyad, Saudi Arabia
5. Neobase. A Danish database for quality of care in neonatology

Participant No 4 : Newcastle University (UNEW)

Newcastle University (UNEW) is a member of the prestigious Russell Group, comprising 24 leading research institutions in the UK and in the year ended 31 July 2014, its total research income equalled €138 million. UNEW is one of the UK's leading research-focused higher education institutions. UNEW is a thriving international community of more than 17,000 undergraduate and 6,000 postgraduate students from over 130 countries worldwide and 5,670 employees of which 2,567 are academic or research staff. Our mission as a world-class civic university means we apply our academic excellence to real-world challenges. UNEW is very active in EU funding and has had around 235 FP7 projects worth over €100million. So far, the University has nearly 60 projects awarded under Horizon 2020. This project will be located in the Institute of Health & Society (IHS), which is one of five research institutes within the Faculty of Medical Sciences. In the results of the most recent national assessment of research, the Research Excellence Framework (REF2014), our research ranked 8th in England for combined "Medical" Units of Assessment and Medical Schools with a total of 85% judged as world leading (4*) or internationally excellent (3*). Newcastle ranked in the top 10 for clinical medicine, biological sciences, and neuroscience & psychology. UNEW holds a bronze Athena SWAN charter award which recognises excellent working practices to support women in STEMM; the applicant (Rankin) is the University's Dean of Diversity. UNEW also holds the EU approved HR Excellence in Research Award.

Tasks

- WP3 : Linkage of congenital anomaly data to mortality data
    - The IHS conducts translational research aimed at promoting evidence-based policy and practice for the benefit of patient and population health. The Applied Epidemiology research theme (led by Rankin) contributes to the understanding, prevention and treatment of chronic non-communicable diseases across the life course nationally and internationally. The work is multidisciplinary and adopts a broad range of methodological approaches. Researchers within IHS have undertaken a number of data linkage studies involving the design and analysis of large datasets. This includes the applicant's own work on linking congenital anomaly data to national mortality data and linkage of congenital anomaly data to the region's childhood cancer register.
- WP5 : Linkage to educational data
    - The IHS child development team is a leader in the field of child development including work on cognitive development and achievement. The IHS hosts several high quality cohorts including Dasl^{ne} for children with autism and is known internationally for its work on transition from pediatric to adult services. IHS researchers work closely with the Dept of Speech and Language development and has relevant expertise on educational attainment.
- WP7 : Connect**E**people
    - IHS has a long and established track record of involving parents and patients (PPI) in its research. It houses the NIHR Research Design Service which has a PPI group. Rankin has led a number of projects on sensitive topics including feticide for congenital anomaly and termination of pregnancy which have involved close working with health professionals and parents, as well as a project which has co-

developed guidelines for health professionals when there has been a loss from a multiple pregnancy.

- Epidemiological contributions to WP2,WP4,WP6
    - Rankin leads the Applied Epidemiology research theme within IHS and will provide epidemiological input as needed. Rankin will also provide comments on all papers resulting from the workpackages.
- WP8 : Dissemination
    - The focus of the IHS is to conduct translational research aimed at promoting evidence-based policy and practice for the benefit of patient and population health. This involves the translation of research into public health strategies and their practical implementation. IHS hosts Fuse, the Centre for Translational Research in Public Health which is a UK Clinical Research Collaboration which aims to reduce inequalities by tackling major and emerging public health challenges, and is a partner in the School for Public Health Research.

Judith Rankin, Professor of Maternal & Perinatal Epidemiology. **Gender: Female**

Lead WPs 3 and 5, as well as provide epidemiological support to WPs 2, 4, 6 and advice working with parents and patients in WP7 and give support to the dissemination activities in WP8.
Achievements include:

- Work package contributor for the EUROCAT Joint Action funded project
- Director of the Northern Congenital Abnormality Survey (NorCAS), one of the British Isles Network of Congenital Anomalies Registers (BINOCAR) and EUROCAT register
- Academic Director, Regional Maternity Survey Office which hosts five surveys of maternal and perinatal health
- Has led a number of data linkage projects to clinical information including datasets of mortality, obesity, diabetes and childhood cancer
- Active member of BINOCAR, EUROCAT and is an invited member of the UK National Congenital Anomaly and Rare Diseases Scientific Committee

She is committed to the sustainability of EUROCAT as a network supporting activities related to the primary prevention of congenital anomalies in Europe.

Dr Svetlana Glinianaia , Research Fellow. **Gender: Female**

Dr Svetlana Glinianaia is an experienced perinatal epidemiologist with particular experience in congenital anomalies, has worked with NorCAS, BINOCAR and EUROCAT data, has been involved in data linkage studies and working within a collaborative group. She will be responsible for ensuring the accuracy of the linkage (in WP2) of the NorCAS register, for analysing the results and ensuring consistency of statistical analysis and methodology across the participating registers with WP3 and 5, for collating interim and final reports for WP3 and 5, drafting papers and liaising with all other workpackage leaders to coordinate the submission of the papers.

Relevant Previous Publications

1. Khoshnood B, Loane M, de Walle H, Arriola L, et al. Long term trends in prevalence of neural tube defects in Europe: population based study. *BMJ* 2015;**351:**h5949: DOI: 10.1136/bmj.h5949

- Successful dissemination of public health relevant collaborative work from EUROCAT registries; this paper discussed the lack of progress in reducing neural tube defects in Europe and the need for folic acid supplementation.

2. Morris, J. K., Rankin, J., et al. Prevention of neural tube defects in the UK: a missed opportunity. Archives of Disease in Childhood Fetal & Neonatal Edition 2015; doi:10.1136/archdischild-2015-309226
    - Successful dissemination of collaborative work from BINOCAR registries: By quantifying the number of affected pregnancies that could have been prevented, this paper achieved wide publicity with interviews on BBC news programmes.
3. Jardine J, Glinianaia SV, McConachie H, Embleton ND, Rankin J. Self-Reported Quality of Life of Young Children With Conditions From Early Infancy: A Systematic Review. *Pediatrics* 2014, **134**(4), e1129-e1148: DOI: 10.1542/peds.2014-0352
    - Systematic review of the international evidence on self-reported quality of life in children with congenital anomalies demonstrating that even for younger children, both child and parent perspectives are essential to understanding the impact of a condition on a child's quality of life.
4. Tennant PWG, Pearce MS, Bythell M, Rankin J. 20-year survival of children born with congenital anomalies: a population-based study. *Lancet* 2010;**375**(9715), 649-656: DOI: 10.1016/S0140-6736(09)61922-X
    - Linkage of population-based data from the Northern Congenital Abnormality Survey to national mortality records to provide accurate estimates of survival for children born with a congenital anomaly by subtype.
5. Rankin J, Tennant PWG, Stothard KJ, Bythell M, Summerbell C, Bell R. Maternal body mass index and congenital anomaly risk: a cohort study. *International Journal of Obesity* 2010;**34**(9):1371-1380: DOI: 10.1038/ijo.2010.66
    - Linkage of data from the Northern Congenital Abnormality Survey to clinical information on body mass index; demonstrated an association of obesity with particular congenital anomaly subtypes.

UNEW will provide the infrastructure support to ensure delivery of the programme of work. Computing facilities and maintenance will also be provided.

Relevant Previous Projects

1. EUROCAT: Led from Belfast Funded under Health Programme European Union 2008-2014; UNEW contributed to several workpackages. EUROCAT now hosted at ISPRA, Milan. Professor Rankin is a member of the EUROCAT Scientific Committee 2015- . The current proposal builds on the established EUROCAT infrastructure and involves many of the EUROCAT registries. It will establish standards for coding and analysing data concerning congenital anomalies as well as build a lasting infrastructure and methodology for European-wide research on children with congenital anomalies.
2. British Isles Network of Congenital Anomaly Registers (BINOCAR) HUB: funded by Department of Health through Health Quality Improvements Program 2010-2014. Professor Morris was responsible for establishing standard operating procedures to enable aggregation of data from 8 congenital anomaly registries in England and Wales to provide national data on the prevalence of anomalies, creating and using the HUB as a research resource and disseminating this information nationally.
3. Congenital Anomaly and obesity study: First UK study to demonstrate an association between certain congenital anomaly subtypes and maternal obesity. Involved linking data from a congenital anomaly register to clinical information held by hospitals.
4. Survival of children born with a congenital heart defect: investigated survival and risk factors for survival for children born with congenital heart disease (CHD) by CHD subtype; involved linking data from a congenital anomaly register with mortality data.
5. Exposure to potentially teratogenic medications and outcome of pregnancy in women with diabetes: investigated exposure of statins and ACES in women with diabetes who became pregnant, reviewing different pregnancy outcomes including congenital anomalies.

Participant No 5 : University of Ferrara (UNIFE)

The University of Ferrara (UNIFE), founded in 1391, is a medical science orientated university. It consists of twelve Departments including the Department of Medical Science which hosts the interdepartmental Center for Clinical and Epidemiological Research and IMER the Emilia Romagna Regional congenital anomaly register. UNIFE has around 18,000 students, of which 6% are international students, with 230 Socrates/Erasmus partners.

Tasks

- WP1 : Project Management
  - UNIFE gained 41 international research projects funded by FP7, of which 4 coordinated by UNIFE and has 12 projects funded by Horizon 2020, 1 as Coordinator, and 4 Individual Marie Skłodowska-Curie Fellowship. Several other European research programmes are ongoing with around 500 international cooperation agreements.
- WP1 : Co-ordinate scientific content of the work packages
  - UNIFE has hosted IMER since 1978. IMER was a founder member of EUROCAT in 1980 and has been a partner in numerous EUROCAT research projects. UNIFE provides a service to other Regional Health authorities to support CA registries through the use of a patented algorithm.
- WP2 : Linkage of Congenital anomaly registry data
  - UNIFE receives funding for the IMER registry from the Regional Health authority to whom it reports. The IMER database accesses through algorithms the regional hospital databases and is an integral part of the public health information system. The CA registries in Puglia, Campania, Calabria and Mantova have all used the UNIFE expertise to achieve linkage and create compatible CA registries from hospital data systems.
- Contributions to WP3,WP4, WP5 WP6and WP7
  - UNIFE through IMER has experience in linkage to mortality and morbidity data and will widen the timeframe and quality of the data through this project. It has proven experience in assessing data quality (see publications) and creating filters to algorithms to ensure quality based on EUROCAT guidelines. The contribution to WP7 builds on consiladated experience in this area in the EUROmediCAT project. In WP5 coordination and magaement support will be the main contribution.
- WP8 : Dissemination
  - UNIFE is actively engaged in the translation of research into public health policies and their practical implementation facilitated by its integration in the Regional Health Authority, EUROCAT, and Italian national Steering Committees, for example for prevention of CA through folic acid use.

Amanda Julie Neville, Senior Research Fellow and EUROCAT Registry Leader for Emilia Romagna.
Gender: Female
Amanda will lead WP8, co-lead WP5 and be a partner in WP2,3,4, and 6 and 7 so helping WP1 to have a holistic view.
Achievements include :

- Member of the JRC- EUROCAT Steering Committee having previously been a partner for EUROCAT FP7 funded project
- Consortium member of EUROmediSAFE (one of the five research consortium selected by the EMA to respond to their research proposals).
- Member of the Governing Board of the Center for Clinical and Epidemiological Research, University of Ferrara, Ferrara , Italy
- Member of EUROmediCAT project linking EUROCAT registries to prescription and health
- Member of the Steering Committee of the National Folic Acid Network under the Superior Institute of Health.(ISS) Rome, Italy
- EUROCAT Member of the International Conference on Rare Diseases and Orphan Drugs (ICORD)

She is committed to the sustainability of EUROCAT as a network supporting activities related to the primary prevention of congenital anomalies in Europe.

Gianni Astolfi, Database and IT expert. **Gender: Male**

Gianni is the inventor of a patented algorithm SIAE 009325 intellectual property of UNIFE used to ascertain CA cases from hospital discharge records. He has a proven track record in creating data linkage between the CA registry cases and other health care databases (prescriptions, mortality, hospital discharge records, birth assistance certificates). He created and has over 15 years experience of the IMER database.

Secretary/Assistant. **To be appointed**

He/she will be responsible for providing general and communication support to the IMER registry to enable timely actions to ensure the deliverables and milestones agreed are met.

Relevant Previous Publications

1. Taruscio D, Arriola L, **Neville A** et al. *European Recommendations for Primary Prevention of Congenital Anomalies: A Joined Effort of EUROCAT and EUROPLAN Projects to Facilitate Inclusion of This Topic in the National Rare Disease Plans. Public Health Genomics. 2014;17(2):115-23.*
    - Ability to translate research into policy action for public health in Europe

2. Charlton RA, Pierini A, Klungsøyr K, **Neville AJ** et al. *Asthma medication prescribing before, during and after pregnancy: a study in seven European regions. BMJ Open. 2016 Jan 19;6(1):e009237.*
    - *S*uccessful Linkage of EUROCAT registries to prescription data in EUROmediCAT.

3. Astolfi G, Bianchi F, Lupi C, Napoli N, **Neville A,** Verdini E, Verzola A, Calzolari E. *[Using hospital discharge records, birth certificates and a birth defects registry for epidemiological and public health purposes: experience in Emilia-Romagna region (northern Italy)]. Epidemiol Prev. 2013Jul-Oct;37(4-5):279-88. Italian.*
    - Successful linkage of patient cohorts for public health and research

4: Calzolari E, Barisic I, Loane M, **Neville AJ** et al. *Epidemiology of multiple congenital anomalies in Europe: a EUROCAT population-based registry study. Birth Defects ResA Clin Mol Teratol. 2014 Apr;100(4):270-6.*
    - Epidemiological and clinical approach for classification of cases to improve the quality and accuracy of Multiple Congenital Anomaly data

5. Khoshnood B, Loane M, , **Neville AJ** et al. *Long term trends in prevalence of neural tube defects in Europe: population based study. BMJ. 2015 Nov24;351:h5949.*

- Dissemination of the long term effect of public health policy and reccomendation for improvement

Relevant Previous Projects

1. **EUROCAT** : Led from Belfast Funded under Health Programme European Union 2008-2014. UNIFE is a founder member from 1980, has provided Coding and Classification committee and WG members and a past President of EUROCAT. UNIFE is a full member for surveillance and Research. EUROCAT now is now hosted at JRC ISPRA, Italy. Dr Neville is EUROCAT Registry Leader for Emilia Romagna (a population of 4.5 million EU residents) and Member of the JRC-EUROCAT Joint Management Committee. She also leads the JRC-EUROCAT joint workgroup on Website development. The current proposal builds on EUROCATs consolidated network of partners and infrastructure.
2. **EUROmediCAT** : FP7 funded 2011-2014. The current proposal is adopting much of the methodology of EUROmediCAT which was a successful partnership of congenital anomaly registries which linked their data with hospital discharge data and prescription data to produce innovative research on medication use in pregnancy.
3. **IMER** (**I**ndagine delle **M**alformazione congenite in **E**milia-**R**omagna) started in 1978, is the longest running research and public health project financed by the Emilia Romagna Regional Health authority. The database covers 21,000 cases of CA and 1 million births. Case are ascertained using multiple sources including healthcare database linkage. Dr Neville has been a researcher for the registry for over 15 years.
4. **ESPEA** (Emilia Romagna Study on Pregnancy Exposure to Antiepileptic drugs) An Italian nationally funded project **RF-2010-2315893** creating datalinkage between CA cases and epileptic mothers in a EURAP Epilepsy register and clinical setting
5. **RISCRIPRO** An Italian nationally funded project lead by Dr F Bianchi at the CNR investigating CA and fetal health outcomes in highly polluted areas of Italy. This project lead to the adoption of an algorithm invented at UNIFE to identify CA cases in hospital discharge databases in areas where CA registries did not exist

Participant No 6: Klinika za dječje bolesti Zagreb (KDB)

Established in 1917, the University of Zagreb School of Medicine is the oldest, most respected and largest institution offering medical studies in the Republic of Croatia. Children's hospital Zagreb (KDB) is the largest children's hospital in Croatia and a central institution for health care for children and adolescents. KDB offers multidisciplinary approach to the diagnostics and treatment of patients with congenital anomalies. KDB hosts Centre of Excellence of the Croatian Ministry of Health for Monitoring Congenital Anomalies, a major stakeholder in the promotion and organization of programs for the health of children with congenital defects in the country. The Centre hosts Registry of Congenital Anomalies Zagreb which is a is member of the European Network for Surveillance of Congenital Anomalies-EUROCAT since 1989 and has a long standing experience in the field of surveillance and research on congenital anomalies.

Tasks

- WP 2,3,4,6: Linkage of congenital anomaly registry data from Croatian registries to datasets on mortality/hospital discharge data, provision of aggregated tables and appropriate analysis. Contribution to any papers that subsequently use data provided and checking that any aggregated data on the website is correct.
    - KDB is hosting Zagreb Registry of Congenital anomaly and has the experience of collating data from the five regional congenital anomaly registries that will be contributing data to EUROlinkCAT.
- WP7: ConnectEpeople - contacting parents and carers of children with selected congenital anomalies and creating a network linking them with local, national and international registries and information resources.
    - As a Centre of reference for congenital anomalies, KDB has very good contacts with patient's organisations. Members of the Centre are on many boards of these organisations, helping organise activities, meetings and health care pathways.
- WP8 : Dissemination
    - The translation of research in the field of congenital anomalies into public health strategies is one of the major tasks of KDB. The Referral Centre of the Ministry of Health of the Republic of Croatia for Monitoring Congenital Anomalies aims to target: aetiology, diagnosis and treatment of congenital anomalies; development and validation of diagnostic tools and new treatment protocols for congenital anomalies; epidemiology and prevention, optimisation of approaches to data collection/validation, evaluation of existing preventive strategies and proposal of the new ones based on research results; dissemination and exploitation of research results (guidelines and recommendations, disseminating information to health professionals and families on prevention, diagnosis and treatment of congenital anomalies). All these objectives fit into the general framework of the EUROlinkCAT project.

Ingeborg Barišić, Professor of Paediatrics and Medical Genetics. Gender: Female
Dr Barisic is a deputy leader of WP8, oversees collection of statistical and epidemiological data to WP 2, 3, 4 and 6 and participates in the WP7 activities for Croatia
Achievements include:

- President of EUROCAT Association
- Member of European Commission Expert Group on Rare Diseases
- Member of the Orphanet Management Board and coordinator of Orphanet Croatia
- Member of COMP (Committee on Orphan Medicinal Products) at European Medicine Agency, nominated by EC
- Representative of the National Society of Human Genetics at the European Society of Human Genetics
- President of the Croatian Society of Human Genetics of the Croatian Medical Association
- President of the Croatian Society for Rare Diseases of the Croatian Medical Association
- Collaborating partner in EUROmediCAT project linking EUROCAT registries to prescription and health care databases
- Collaborating partner in EPIRARE and EUROPLAN I and II EU Public Health projects working on the integration of national information sources and the collation and exchange of data on rare disease registries at the Community level
- Leader of Zagreb Registry of Congenital anomalies since 1997

  Dr Barisic is a member of EUROCAT Coding Committee and Multiple Malformation Working Group. She is committed to the sustainability of EUROCAT as a network supporting activities related to the rare diseases and primary prevention of congenital anomalies in Europe.

Dr Ljubica Boban, resident in paediatrics at KDB and researcher. Gender: Female.
Dr Boban will be involved in WP 2,3,4,6 activities. She has experience with statistical-epidemiological methods for surveillance of congenital anomalies and will be responsible for the activities of congenital defects coding, management of the database and data analysis for the surveillance of births in Zagreb registry.

Research Fellow / Statistician/IT person : To be appointed
The appointed person will be responsible for the linkage of the five congenital anomaly registries in Croatia.

Relevant Previous Publications

1. Khoshnood B, Loane M, Walle Hd, Arriola L, Addor MC, Barisic I et al. (2015). Long term trends in prevalence of neural tube defects in Europe: population based study. BMJ 351 : h5949. doi: 10.1136/bmj.h5949.
2. Garne E, Hansen AV, Morris J, Zaupper L, Addor MC, Barisic I et al. (2015). Use of asthma-medication during pregnancy and risk of specific congenital anomalies –A European case-malformed control study. J Allergy Clin Immunol 136 : 1496-1502.e7. doi: 10.1016/j.jaci.2015.05.043
3. Barisic I, Boban L et al. (2015). Meckel-Gruber Syndrome: a population-based study on prevalence, prenatal diagnosis, clinical features, and survival in Europe. Eur J Hum Genet 23:746-52. Wu J, Morris JK (2013). The population prevalence of Down's syndrome in England and Wales in 2011. Eur J Hum Genet 21:1016-9. doi:10.1038/ejhg.2012.294.
4. Barisic I, Odak L, Loane M, Garne E, Wellesley D, Calzolari E, Dolk H, Addor MC, Arriola L, Bergman J, Bianca S, Doray B, Khoshnood B, Klungsoyr K, McDonnell B, Pierini A, Rankin J,

Rissmann A, Rounding C, Queisser-Luft A, Scarano G, Tucker D (2014). Prevalence, prenatal diagnosis and clinical features of oculo-auriculo-vertebral spectrum: a registry-based study in Europe. Eur J Hum Genet 22:1026-1033.

5. Calzolari, E., Barisic, I., Loane, M., Morris, J.K et al (2014). Epidemiology of multiple congenital anomalies in Europe: A EUROCAT population-based registry study. Birth Defects Research Part A: Clinical and Molecular Teratology, 100(4), 270-276. doi:10.1002/bdra.23240

Relevant Previous Projects

1. **EUROCAT**: a network of European registries of congenital anomalies, funded by several EU Health Programmes. In JA - EUROCAT (2011- 2013) KDB lead WP (Dissemination) in and in Operating grant (2013-2014) WP 2 (Sustainability), WP 3 (Dissemination), WP 10 (New Registries/Network Expansion/Registry Advisory Service). EUROCAT is now hosted at Joint Research Centre in ISPRA, Milan within the European Platform for Rare Disease Registries.
1. Professor Barisic is the President of EUROCAT Association from 2011. The current proposal builds on EUROCAT infrastructure and experience involving many of the EUROCAT registries.
2. **EUROmediCAT:** FP7 funded 2011-2014. The current proposal is implementing the methodology of EUROmediCAT used for linking their data with hospital discharge data and prescription data to produce innovative research on medication use in pregnancy. KDB was a collaborating partner.
3. **EPIRARE** (European Platform for Rare Disease Registries), a project co-funded by the European Commission within the EU Program of Community Action in the field of Public Health (2011-2013). KDB was collaborating partner. The specific objectives of the projects were to define the needs of the EU registries and databases on rare diseases, the state of the art of existing registries, and key issues to prepare a legal basis to assess the feasibility of an EU legal instrument to allow the integration of national information sources and the collation and exchange of data at the Community level in compliance with the EU Directive 45/96 and with other relevant provisions; to agree on a Common data set and elaborate procedures for quality control; to define a minimum data set for all rare diseases; to define criteria for quality assessment of data, data sources and procedures in the registries, to agree on the Register and Platform Scope, Governance and long-term sustainability. All these issues are relevant to the present project proposal.
4. **Orphanet** is the reference portal for information on rare diseases for all audiences. KDB is a partner and coordinator for Croatia. Orphanet's aim is to help improve the diagnosis, care and treatment of patients with rare diseases. As 80% of congenital anomalies are rare, this portal is a valuable source of information regarding classification and coding, expert resources - clinics, medical laboratories, ongoing research projects, clinical trials, registries, networks, technological platforms and patient organisations in the field of congenital anomalies in Europe.
5. **EUROPLAN:** The European Project for Rare Diseases National Plans Development (EUROPLAN) was a project co-funded by the EU Commission (DG-SANCO) (2008-2011, 2012-2015) to promote and implement National Plans or Strategies to address rare diseases, to share relevant experiences within countries, linking national efforts with a common strategy at European level ensuring that progress is globally coherent and follows common orientations throughout Europe. One of the main areas of National plans is setting up of registries, monitoring of data quality and their linking at national and international level at the JRC Platform for Rare Diseases. KDB was collaborating partner in both calls.

Participant No7: Consiglio Nazionale delle Ricerche - Institute of Clinical Physiology (CNR-IFC)

The CNR Institute of Clinical Physiology (IFC) is the largest biomedical institute for clinical research of the National Research Council (CNR), with over 500 “professionals”, 118 of them permanent researchers and technologists, mostly based in Pisa. A multidisciplinary team from different academic and scientific backgrounds, including medicine, biology, chemistry, bioengineering, physics, mathematics and IT, has turned the underlying idea into reality, adding the concept of measurement – previously confined to physiological research – to medical practice. The Institute’s work may be aptly defined as a synergism of four key areas of interest: 1) preclinical biology and the mechanisms of illness, 2) clinical physiopathology and risk factors for health, 3) bio-techno-science and “modelling", 4) epidemiology and health promotion. IFC has a long standing experience in the field of surveillance and research on congenital anomalies, as coordinator of the Tuscany Registry of Birth Defects since 1979. The Registry is member of the European Network for Surveillance of Congenital Anomalies-EUROCAT since 1980 and member of the International Clearinghouse for Birth Defects Surveillance and Research-ICBDSR since 1995. By an active collaboration with the Regional Health Agency all the requested healthcare data for the linkage with data on congenital anomalies will be provided.

Anna PIERINI BSc. Researcher. Gender : Female
Experience with reproductive epidemiology, particularly on congenital defects, and with statistical-epidemiological methods for birth defects surveillance. Responsible for the activities of congenital defects coding, management of the database and data analysis for the surveillance of births in Tuscany. Registry Leader for the Tuscany Registry of Congenital Defects for the EUROmediCAT project. Project manager for ICBDSR. Member of the EUROCAT Antiepileptic Drug Working Group.

Fabrizio BIANCHI BSc PhD in Hygiene and Public Health. Gender : Male
Specialized in Health Statistics and Epidemiology. Head of Environmental Epidemiology and Diseases Registries Research Unit – IFC CNR, EU research project design and coordination, scientific coordinator of the CNR national project on Environment and Health, coordinator of the Tuscany Registry of Birth Defects and of the Tuscany Registry of Rare Diseases, professor in-charge for teaching in University masters.

Anna Maria ROMANELLI BSc. Researcher Gender : Female .
Practice areas: population studies, epidemiological studies in environmentally sensitive areas, creation and management of integrated archives and their epidemiological applications, clinical epidemiology, disease registries.

Silvia BALDACCI BSc. Researcher Gender : Female
15 years of experience in epidemiological evaluation of the healthcare activity, healthcare management, clinical governance and health information, epidemiological studies on congenital heart defects.

Liliana CORI BA. Researcher. **Gender : Female**
In charge of internal and external communication activities, with specific reference to studies in high risk areas, including human biomonitoring studies, and in producing instruments to bridge science and policy. Project management. Project preparation. Report drafting. Budget management.

Michela RIAL MA, MSMP. Researcher **Gender : Female** .
Head of the Grant Office of CNR IFC, research adviser and senior project manager, she has an extensive knowledge and expertise in the management and controlling of EU-funded projects. Since 2004 she has been active in Equal Opportunity and Work Life Balance projects and has gained wide competence in gender issues and gendered innovation.

Relevant Previous Publications

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1. Helen Dolk, Lolkje de Jong-van den Berg, **Anna Pierini**, Joan Morris, Marian Bakker, Sue Jordan, Ester Garne, Kari Klungsoyr, Maria Loane, Rachel Charlton, Michiel Luteijn, Marlene Sinclair, Anna Latos Bielenska. EUROmediCAT Recommendations for European Pharmacovigilance concerning safety of medication use in pregnancy. Pharmacoepidemiology and drug safety 2015; 24:3–7. Published online in Wiley Online Library (wileyonlinelibrary.com) DOI: 10.1002/pds.3866
   - Recommendations set out from the FP7 EUROmediCAT project for European and national medicines regulatory agencies, public health authorities and professional clinical bodies. These recommendations concentrate particularly on safety in early pregnancy in relation to the risk of congenital anomalies.
2. Khoshnood B, Loane M, Walle Hd, Arriola L, Addor MC, Barisic I, Beres J, **Bianchi F**, et al. Long term trends in prevalence of neural tube defects in Europe: population based study. BMJ. 2015 Nov 24;351:h5949. doi: 10.1136/bmj.h5949.
   - Successful dissemination of collaborative work from EUROCAT registries quantifying that in the absence of mandatory fortification, the prevalence of NTD has not decreased in Europe despite longstanding recommendations aimed at promoting peri-conceptional folic acid supplementation and existence of voluntary folic acid fortification
3. Garne, E, Hansen, AV, Morris, JK, Zaupper L, Addor MC, Barisic I, Gatt M, Lelong N, Klungsøyr K, O'Mahony M, Nelen V, Neville AJ, **Pierini A**, Tucker D, de Walle H, Wiesel A, Loane M, Dolk H.et al.(2015). Use of asthma medication during pregnancy and risk of specific congenital anomalies: A European case-malformed control study.. The Journal of allergy and clinical immunology, 136(6), 1496-1502.e7. doi:10.1016/j.jaci.2015.05.043
   - Successful Linkage of EUROCAT registries to prescription data in EUROmediCAT.
4. Jorieke E.H. Bergman, Maria Loane, Martine Vrijheid, **Anna Pierini**, JM Nijman, Marie-Claude Addor, Judit Beres, Paula Braz, Judith Budd, Virginia Delany, Miriam Gatt, Babak Khoshnood, Kari Klungsøyr, Amanda J. Neville, Ljubica Odak, Mary O'Mahony, Carmen Martos, Carmel Mullaney, Annette Queisser-Luft, Hanitra Randrianaivo, Anke Rissmann, Catherine Rounding, Guy Thys, David Tucker, Diana Wellesley, Natalya Zymak-Zakutnia, Marian K. Bakker, Hermien E.K. de Walle. Epidemiology of hypospadias in Europe: a registry-based study. World J Urol 2015 Dec;33(12):2159-67. DOI 10.1007/s00345-015-1507-6
   - Successful dissemination of collaborative work from EUROCAT registries. The study shows both the advantages and disadvantages of using birth defect registry data to investigate prevalence and trends in hypospadias.

5. RA Charlton, **A Pierini**, K Klungsøyr, A Neville, S Jordan, L T W de Jong-van den Berg, D Thayer, HJ Bos, A Puccini, AV Hansen, R Gini, A Engeland, H Dolk, E Garne. Asthma medicine prescribing before, during and after pregnancy: a study in 7 European regions. BMJ Open 2016;6:e009237 doi:10.1136/bmjopen-2015-009237
    - To explore utilisation patterns of asthma medication before, during and after pregnancy as recorded in seven European electronic healthcare databases.

Relevant Previous Projects

1. European Network for the Surveillance of Congenital Anomalies **- EUROCAT** : Member since 1980. Fabrizio Bianchi was previously President and member of the Steering Committee for the 2013-2017 period.
2. Safety of medication use in pregnancy in relation to risk of congenital malformations - **EUROmediCAT** (contract number 260598): Seventh Framework Programme study funded by the European Union in 2011-2014 with the aim to make more systematic use of electronic healthcare databases in combination with EUROCAT congenital anomalies data. Partner.
3. International Clearinghouse for Birth Defects Surveillance and Research-**ICBDSR**. Member since 1995.
4. **National Rare Diseases Registry** coordinated by the Centre for Rare Diseases at the Italian Health Institute in Rome (Italy).
5. **RISCRIPRO-SENTIERI**: CCM public health project funded by the Italian Ministry of Health mainly aimed at describing the reproductive health in the Italian National Priority Contaminated Sites.

The Institute features a Grant Office having significant experience in the management of FP6, FP7 and H2020 projects.

Participant No 8: University Medical Center Groningen (UMCG)

The University Medical Center Groningen (UMCG; www.umcg.nl) was established in 2005 as a joint activity of the University of Groningen and the Academic Hospital Groningen (AZG). The UMCG is one of the largest hospitals in the Netherlands and the largest employer in the Northern Netherlands at present. More than 10,000 employees provide patient care, are involved in medical education and perform cutting-edge scientific research. This project will be located in the Department of Genetics, which has a large, international staff and a broad spectrum of activities.

Tasks
To work in WP2 to link data from the "EUROCAT Northern Netherlands Registry" to datasets on mortality/hospital discharge data/prescriptions and to provide aggregated tables and analysis. To help with the interpretation and provide comments on any papers that subsequently use the data provided and check that any aggregated data on the website is correct. To work in WP6 as deputy leader to evaluate the accuracy and the quality of coding of congenital anomalies and terminations of pregnancy for fetal anomalies in health care databases compared to EUROCAT data.
To work in WP7 connecting with Parent Support Groups and becoming part of the e-forum ConnectEpeople

Hermien de Walle, Associate Professor. **Gender : Female**
Hermien has a long standing experience in the field of surveillance and research on congenital anomalies, as coordinator of the Northern Netherlands Registry of Birth Defects since 1999. The Registry has been a member of the European Network for Surveillance of Congenital Anomalies (EUROCAT) since it began in 1981. She is an associate professor and supervisor of the EUROCAT database which contains information on more than 15.000 children. EUROCAT is well known for its detailed and precise information on children and fetuses with birth defects, risk factors in pregnancy and individual information on prenatal tests and diagnosis.Her PhD was on the awareness and use of periconceptional folic acid in the Netherlands. Since then she continued to study this topic with a focus on neural tube defects (NTDs), congenital heart defects and clefts.
During the period 2000-2003 she was Secretary and vice Chair of the Executive Committee of the International Clearinghouse for Birth Defects Monitoring Systems, a worldwide system of birth defect registries. She was also member of the Project Management Committee of EUROCAT International (European network of birth defects registries) and chair of the international EUROCAT Working Group on Folic Acid (Ulster, UK). Dr De Walle was from 2002-2006 part of the Steering Committee NACCG (Dutch Association Community Genetics and Public Health Genomics) and Stichting Preconceptiezorg Nederland. She was a member of the Dutch Health Council, committee 'Prenatal exposure to Dusts' and currently of the committee 'Prenatal Screening'.

Relevant Previous Publications

1. Khoshnood B, Loane M, **de Walle H**, Arriola L, Addor MC, Barisic I, Beres J, Bianchi F, Dias C, Draper E, Garne E, Gatt M, Haeusler M, Klungsoyr K, Latos-Bielenska A, Lynch C, McDonnell B, Nelen V, Neville AJ, O'Mahony MT, Queisser-Luft A, Rankin J, Rissmann A, Ritvanen A, Rounding C, Sipek A, Tucker D, Verellen-Dumoulin C, Wellesley D, Dolk H. Long term trends in the prevalence of neural tube defects in Europe: population based study. BMJ. 2015 Nov 24;351
2. Luteijn JM, Addor MC, Arriola L, Bianchi F, Garne E, Khoshnood B, Nelen V, Neville A, Queisser-Luft A, Rankin J, Rounding C, Verellen-Dumoulin C, de Walle H, Wellesley D, Wreyford B, Yevtushok L, de Jong-van den Berg L, Morris J, Dolk H.The Association of H1N1 Pandemic Influenza with Congenital Anomaly Prevalence in Europe: An Ecological Time Series Study. Epidemiology. 2015 Nov;26(6):853-61
3. Garne E, Hansen AV, Morris J, Zaupper L, Addor MC, Barisic I, Gatt M, Lelong N, Klungsøyr K, O'Mahony M, Nelen V, Neville AJ, Pierini A, Tucker D, de Walle H, Wiesel A, Loane M, Dolk H. Use of asthma medication during pregnancy and risk of specific congenital anomalies: A European case-malformed control study. J Allergy Clin Immunol. 2015 Jul 25.
4. Bergman JE, Loane M, Vrijheid M, Pierini A, Nijman RJ, Addor M, Barisic I, Béres J, Braz P, Budd J, Delany V, Gatt M, Khoshnood B, Klungsøyr K, Martos C, Mullaney C, Nelen V, Neville AJ, O'Mahony M, Queisser-Luft A, Randrianaivo H, Rissmann A, Rounding C, Tucker D, Wellesley D, Zymak-Zakutnia N, Bakker MK, de Walle H.E. Epidemiology of hypospadias in Europe: a registry-based study. World J Urol. 2015 Dec;33(12):2159-67
5. de Jonge L, de Walle HE, de Jong-van den Berg LT, van Langen IM, Bakker MK. Actual Use of Medications Prescribed During Pregnancy: A Cross-Sectional Study Using Data from a Population-Based Congenital Anomaly Registry. Drug Saf. 2015 Aug;38(8):737-47

Relevant Previous Projects

1. **EUROCAT** : Led from Belfast Funded under Health Programme European Union 2008-2014; QMUL led Prenatal Diagnosis WP 2008-2013. EUROCAT now hosted at ISPRA,Milan. Professor Morris is the Scientific Leader 2015- . The current proposal builds on the established EUROCAT infrastructure and involves many of the EUROCAT registries and will hopefully be as successful in establishing standards for coding and analysing data concerning congenital anomalies.
2. **EUROmediCAT** : FP7 funded 2011-2014. The current proposal is adopting much of the methodology of EUROmediCAT which was a successful partnership of congenital anomaly registries which linked their data with hospital discharge data and prescription data to produce innovative research on medication use in pregnancy.
3. **International Clearinghouse for Birth Defects Surveillance and Research:** International Clearinghouse Centre, located in Rome - Italy, is the Central Office of the ICBDSR, coordinating the surveillance activities and collaborative research studies of the Organisation. EUROCAT Northern Netherlands Registry has been a member of the ICBDSR since 1993.
4. **Research Institute SHARE**: Research Institute SHARE is one of the five Research Institutes of the University Medical Center Groningen. The mission of the Research Institute SHARE is to elucidate factors related to health, notably healthy ageing. Research on determinants and

consequences of illness and ageing, quality of life, care and cure is conducted within multiple interdisciplinary research programs. EUROCAT Northern Netherlands is part of SHARE.

5. **ROAHD:** EUROCAT Northern Netherlands is part of the ROAHD (Reproductive Origins of Adult Health and Disease) program of the UMCG. ROAHD researchers are studying factors that influence the health of mother, father and child before, during and after pregnancy.

Participant No 9: Public Health Wales (CARIS)

Public Health Wales
Public Health Wales was established as an NHS trust on 1st October 2009, with the aim of protecting and improving health and wellbeing and reducing health inequalities in Wales. The Congenital Anomaly Register and Information Service (CARIS) is based at Singleton Hospital, Swansea and in 2009 became part of Public Health Wales NHS trust.

Tasks
To work in WP2 to link data from the "Congenital Anomaly Register and Information Service for Wales" to datasets on mortality/hospital discharge data/prescriptions/education data and to provide aggregated tables and analysis. This will be done by providing data analysts from SAIL database at Swansea University Medical School with the information on all births with congenital anomalies. The data analysts will be perform the linkage. CARIS will help with the interpretation and provide comments on any papers that subsequently use the data provided and check that any aggregated data on the website is correct.

David Tucker, Manager of the Congenital Anomaly Register and Information Service for Wales.
Gender : Male
David Tucker holds a Masters degree in Public Health and has a long standing experience in the field of surveillance and research on congenital anomalies, as Manager of the Congenital Anomaly Register and Information Service for Wales since 1998. The Registry has been a member of the European Network for Surveillance of Congenital Anomalies (EUROCAT) since 1998.

Relevant Previous Publications

1. Bergman JEH, Loane M, Vrijheid M, Pierini A, Nijman RJM, Addor M-C, Barisic I, Beres J, Braz P, Budd J, Delany V, Gatt M, Khoshnood B, Klungsoyr K, Martos C, Mullaney C, Nelen V, Neville A, O'Mahony M, Queisser-Luft A, Randrianaivo-Ranjatoelina H, Rissmann A, Rounding C, **Tucker D**, Wellesley D, Zymak-Zakutnya, N, Bakker M and de Walle H (2015). Epidemiology of hypospadias in Europe: a registry-based study. *World Journal of Urology*.
2. Calzolari E, Barisic I, Loane M, Morris J, Wellesley D, Dolk H, Addor M-C, Arriola L, Bianchi F, Neville A, Budd J, Klungsoyr K, Khoshnood B, McDonnell R, Nelen V, Queisser-Luft A, Rankin J, Rissmann A, Rounding C, **Tucker D**, Verellen-Dumoulin C, de Walle H and Garne E (2014). Epidemiology of multiple congenital anomalies in Europe: a EUROCAT population-based registry study. *Birth Defects Research (Part A)*. 100: 270-276.
3. Luteijn M, Dolk H, Addor M-C, Arriola L, Barisic I, Bianchi F, Calzolari E, Draper E, Garne E, Gatt M, Haeusler M, Khoshnood B, McDonnell R, Nelen V, O'Mahony M, Mullaney C, Queisser-Luft A, Rankin J, **Tucker D**, Verellen-Dumoulin C, de Walle H and Yevtushok L (2014). Seasonality of Congenital Anomalies in Europe. *Birth Defects Research (Part A)*. 100: (260). 269
4. McGivern M, Best KE, Rankin J, Wellesley D, Greenlees R, Addor M-C, Arriola L, de Walle H, Barisic I, Beres J, Bianchi F, Calzolari E, Doray B, Draper E, Garne E, Gatt M, Haeusler M, Khoshnood B, Klungsoyr K, Latos- Bielenska A, O'Mahony M, Braz P, McDonnell R, Mullaney C, Nelen V, Queisser-Luft A, Randrianaivo-Ranjatoelina H, Rissmann A, Rounding C, Sipek A, Thompson R, **Tucker D**, Wertelecki W and Martos C (2014). Epidemiology of congenital diaphragmatic hernia in Europe: a register-based study. *Archives of Disease in Childhood - Fetal and Neonatal Edition*. epub: F1-F8.

5. Morris J, Garne E, Wellesley D, Addor M-C, Arriola L, Barisic I, Beres J, Bianchi F, Budd J, Dias C M, Gatt M, Klungsoyr K, Khoshnood B, Latos- Bielenska A, Mullaney C, Nelen V, Neville A, O'Mahony M, Queisser-Luft A, Randrianaivo-Ranjatoelina H, Rankin J, Rissmann A, Rounding C, Sipek A, **Tucker D**, de Walle H, Yevtushok L, Loane M, Dolk H and Stoianova S (2014). Major Congenital Anomalies in Babies Born with Down Syndrome: A EUROCAT Population-Based Registry Study. *American Journal of Medical Genetics Part A*.

Relevant Previous Projects

1. **European Network for Surveillance of Congenital Anomalies** (EUROCAT, http://www.eurocat-network.eu/). Led from Belfast Funded under Health Programme European Union 2008-2014; QMUL led Prenatal Diagnosis WP 2008-2013. EUROCAT now hosted at ISPRA, Milan.
2. **EUROmediCAT** (http://euromedicat.eu/). FP7 funded 2011-2014. The current proposal is adopting much of the methodology of EUROmediCAT which was a successful partnership of congenital anomaly registries which linked their data with hospital discharge data and prescription data to produce innovative research on medication use in pregnancy.
3. **International Clearinghouse for Birth Defects Surveillance and Research** (ICBDSR, http://www.icbdsr.org/). The International Clearinghouse Centre, located in Rome - Italy, is the Central Office of the ICBDSR, coordinating the surveillance activities and collaborative research studies of the Organisation. CARIS has been a member of the ICBDSR since 2004.
4. **British and Irish Network of Congenital Anomaly Researchers** (BINOCAR, http://www.binocar.org/). a group of researchers who work closely with regional and disease-specific registers across the United Kingdom and the Republic of Ireland, with the aim of providing expert advice on research into the epidemiology, frequency, nature and outcomes of congenital anomalies for the population of the British Isles by means of national, regional and disease-specific registers of congenital anomalies.
5. **Implementation of screening programmes in Wales**. The CARIS register has worked closely with Antenatal Screening Wales to ensure the successful implementation and monitoring of antenatal ultrasound screening and Down screening in Wales.

Participant No 10: Paris Registry of Congenital Malformations (NSERM UMR 1153, Equipe EPOPé)

Since 1981, the Paris registry of congenital malformations registers all cases of birth defects and chromosomal anomalies among live-births, still-births (≥ 22 weeks of gestation), and pregnancy terminations. The registry is population-based and its coverage area includes the population of women who live in Paris and deliver or have a termination of pregnancy for foetal anomaly in a Parisian maternity unit. The annual number of deliveries in our population is approximately 25,000. The Paris registry is a member of the European network of registries of congenital malformations (European Surveillance of Congenital Anomalies, EUROCAT) and of the International clearinghouse for birth defects surveillance and research. The registry follows the EUROCAT methodology and quality of data is routinely monitored by both EUROCAT and the French National Committee of Registries. Review of procedures regarding confidentiality of data is overseen by both the National Committee of Registries and the National Committee of Informatics and Freedom (CNIL). Data are based on medical records and are collected from several sources including maternity units, neonatology wards, cytogenetic, and pathology laboratories. The registry is part of the Obstetrical, Perinatal and Pediatric Epidemiology Research Team of INSERM (French National Institute of Health and Medical Research) Unit 1153, Center for biostatistics and epidemiology.

Tasks

To work in WP2 to link data from the "Paris Registry of Congenital Malformations" to datasets on mortality data and to provide aggregated tables and analysis. To help with the interpretation and provide comments on any papers that subsequently use the data provided and check that any aggregated data on the website is correct.

Babak Khoshnood, medical epidemiologist. Gender : Male

Babak Khoshnood is Registry Leader of the Paris Registry of Congenital Malformations, served as a member of the Steering Committee of EUROCAT during 2009-2014 and has a long standing experience in the field of surveillance and research on congenital anomalies.

Nathalie Lelong, statistician. Gender : Female

Nathalie Lelong is Registry co-Leader of the Paris Registry of Congenital Malformations and has a long standing experience in the field of surveillance and research on congenital anomalies.

Relevant Previous Publications

1. **Khoshnood B,** Loane M, De WH, Arriola L, Addor MC, Barisic I, Beres,J, Bianchi,F, Dias,C, Draper,E, Garne,E, Gatt,M, Haeusler,M, Klungsoyr,K, Latos-Bielenska,A, Lynch,C, McDonnell,B, Nelen,V, Neville,A.J, O'Mahony,M.T, Queisser-Luft,A, Rankin,J, Rissmann,A, Ritvanen,A, Rounding,C, Sipek,A, Tucker,D, Verellen-Dumoulin,C, Wellesley,D, Dolk H (2015). Long term trends in prevalence of neural tube defects in Europe: population based study. *BMJ* ; 351:h5949.
2. **Khoshnood B**, Loane M, Garne E, Addor M-C, Arriola L, Bakker M, Barisic I, Bianca S, Boyd P, Calzolari E, Doray B, Draper E, Gatt M, Haeusler M, Klungsoyr K, Latos- Bielenska A, McDonnell R, Mullaney C, Nelen V, O'Mahony M, Pierini A, Queisser-Luft A, Randrianaivo-Ranjatoelina H, Rankin J, Rissmann A, Salvador J, Tucker D, Verellen-Dumoulin C, Wellesley D, Zymak-Zakutnya, N and Dolk H (2013). Recent decrease in the prevalence of congenital heart defects in Europe. Journal of Pediatrics. 162: (1). 108-113.
3. **Khoshnood B**, Greenlees R, Loane M, Dolk H, EUROCAT Project Management Committee and EUROCAT Working Group (2011). Paper 2: EUROCAT public health indicators for congenital anomalies in Europe. Birth Defects Research (Part A). 91: S16-S22.

4. Tararbit K, **Lelong N**, Thieulin A-C, Houyel L, Bonnet D, Goffinet F, Khoshnood B and EPICARD Study Group, (2013). The risk for four specific congenital heart defects associated with assisted reproductive techniques: a population-based evaluation. Human Reproduction. 28: (2). 367-374.
5. Khoshnood B, **Lelong N**, Houyel L, Thieulin A-C, Jouannic J-M, Magnier S, Delezoide A-L, Magny J-F, Rambaud C, Bonnet D, Goffinet F and EPICARD Study Group, (2012). Prevalence, timing of diagnosis and mortality of newborns with congenital heart defects: a population-based study. Heart. 98: (22). 1667-1673.

Relevant Previous projects

1. **European Network for Surveillance of Congenital Anomalies** (EUROCAT, http://www.eurocat-network.eu/). Led from Belfast Funded under Health Programme European Union 2008-2014; QMUL led Prenatal Diagnosis WP 2008-2013. EUROCAT now hosted at ISPRA, Milan.
2. **EUROmediCAT** (http://euromedicat.eu/). FP7 funded 2011-2014. The current proposal is adopting much of the methodology of EUROmediCAT which was a successful partnership of congenital anomaly registries which linked their data with hospital discharge data and prescription data to produce innovative research on medication use in pregnancy.
3. **International Clearinghouse for Birth Defects Surveillance and Research** (ICBDSR, http://www.icbdsr.org/). The International Clearinghouse Centre, located in Rome - Italy, is the Central Office of the ICBDSR, coordinating the surveillance activities and collaborative research studies of the Organisation. Paris Registry has been a member of the ICBDSR since 1982.

Participant No 11: Valencia Region Registry (FISABIO)

Institution: Foundation for the Promotion of Health and Biomedical Research in the Valencian Region (FISABIO). FISABIO has a long standing experience in the field of surveillance and research on congenital anomalies, as coordinator of the Valencia Region Registry of Birth Defects since 2010. The Registry is member of the European Network for Surveillance of Congenital Anomalies-EUROCAT since 2011. Currently it contains data since 2007. By an active collaboration with the Regional Health Agency all the requested healthcare data for the linkage with data on congenital anomalies will be provided.

Tasks:
To work in WP2 to link data from the "Valencia Region Registry" to datasets on mortality/hospital discharge data/prescriptions data and to provide aggregated tables and analysis. To help with the interpretation and provide comments on any papers that subsequently use the data provided and check that any aggregated data on the website is correct. To work in WP7 connecting with Parent Support Groups and becoming part of the e-forum ConnectEpeople. To assist in the consultation and dissemination meetings and the annual EUROCAT Registry Leaders Meeting.

Clara Cavero Carbonell, Researcher. Gender : Female
Clara Cavero Carbonell has long standing experience in the field of rare diseases epidemiology, particularly with surveillance and research on congenital anomalies as researcher of the Valencia Region Registry since 2010. The Registry was established in 2010, with data collected retrospectively from 2007. Clara is Registry Leader for the Valencia Region Registry of Congenital Defects since 2015 and is responsible for the activities of congenital defects coding, management of the database and data analysis for the surveillance of births for the Registry and for the EUROmediCAT project. She is Project manager for the study "Drugs prescription in pregnancy and congenital anomalies: identifying potential risks".

Relevant Previous Publications

1. Gimeno-Martos S, Cavero-Carbonell C, López-Maside A, Bosch-Sánchez S, Martos-Jiménez C, Zurriaga O (2015). Chromosomal anomalies: The experience of the Congenital Anomalies Registry of the Valencia Region. An Pediatr (Barc). pii: S1695-4033(15)00371-9. doi: 10.1016/j.anpedi.2015.09.010.
2. Springett A, Wellesley D, Greenlees R, Loane M, Addor MC, Arriola L, Bergman J, Cavero-Carbonell C, Csaky-Szunyogh M, Draper ES, Garne E, Gatt M, Haeusler M, Khoshnood B, Klungsoyr K, Lynch C, Dias CM, McDonnell R, Nelen V, O'Mahony M, Pierini A, Queisser-Luft A, Rankin J, Rissmann A, Rounding C, Stoianova S, Tuckerz D, Zymak-Zakutnia N, Morris JK (2015). Congenital anomalies associated with trisomy 18 or trisomy 13: A registry-based study in 16 european countries, 2000-2011. Am J Med Genet A. 167: 3062-9. doi: 10.1002/ajmg.a.37355.
3. Páramo-Rodríguez L, Mas Pons R, Cavero-Carbonell C, Martos-Jiménez C, Zurriaga O, Barona Vilar C (2015). An open heart: experiences of the parents of children with congenital heart disease. Gac Sanit. 29: 445-50. doi: 10.1016/j.gaceta.2015.07.009.
4. Cavero-Carbonell C, Gras-Colomer E, Guaita-Calatrava R, López-Briones C, Amorós R, Abaitua I, Posada M, Zurriaga O (2015). Consensus on the Criteria needed for creating a rare diseases patient registry. A Delphy Study. J Public Health (Oxf). pii: fdv099.
5. Cavero Carbonell C, Zurriaga O, Pérez Panadés J, Barona Vilar C, Martos Jiménez C. Temporal variation and geographical distribution: congenital heart defects in the Comunitat Valenciana (2013). An Pediatr (Barc). 79:149-56. doi: 10.1016/j.anpedi.2012.12.007.

Relevant Previous Projects

1. **European Network for Surveillance of Congenital Anomalies** (EUROCAT,http://www.eurocat-network.eu/). Led from Belfast Funded under Health Programme European Union 2008-2014; QMUL led Prenatal Diagnosis WP 2008-2013. EUROCAT now hosted at ISPRA, Milan.
2. **EUROmediCAT**(http://euromedicat.eu/). FP7 funded 2011-2014. The current proposal is adopting much of the methodology of EUROmediCAT which was a successful partnership of congenital anomaly registries which linked their data with hospital discharge data and prescription data to produce innovative research on medication use in pregnancy.
3. “Drugs prescription in pregnancy and congenital anomalies: identifying potential risks". Funded 2013-2014 by the Valencian Medical Institute.
4. “Research to prevent pediatric rare disease: application to congenital heart defects”. Funded 2012-2015 by the Foundation Gent per Gent.
5. “Promoting Implementation of Recommendations on Policy, Information and Data for Rare Diseases — RD-ACTION”. Funded 2015-2018 by Consumers, Health, Agriculture and Food Executive Agency.

Participant No 12: Poznan University of Medical Sciences (PUMS)

PUMS is a leading Polish medical centre with over 80 years of academic experience, well equipped for research in basic medical sciences, clinical investigations, diagnostics and treatment. Teaching and research are mainly based on the co-operation with five Clinical Hospitals as well as with other city hospitals, while advanced research at the University is carried out in virtually every field of modern medicine.The Department of Medical Genetics is involved in scientific projects concerning congenital malformations and mental retardation. Organizer and seat of the Polish Registry of Congenital Malformation (since 1997). The PRCM currently covers the whole Poland (over 400,000 births/year), collaborating with 1,800 medical care units in Poland, and is an associate member of the EUROCAT, while Wielkopolska Registry, a part of the PRCM, is a full member of the EUROCAT.

Tasks
PUMS will be responsible for the dissemination , with a particular responsibility for the final dissemination meeting in Poznan (deputy leader WP8 Dissemination). PUMS is also deputy leader of WP7 - ConnectEpeople.

Prof Anna Latos-Bielenska: clinical geneticist. **Gender : Female**
Prof Anna Latos-Bielenska set up (in 1997) in PUMS the Polish Registry of Congenital Malformations (PRCM) covering currently the entire Poland (information on over 150,000 children with congenital malformations in the data base). Since 2015 notification to the PRCM has been compulsory. PRCM consists of Wielkopolska Registry (EUROCAT full member) and Poland Registry (EUROCAT associate member). She and the PUMS team of clinicians will be particularly active in the dissemination of results at Polish and European level. The PRCM collaborates with over 1500 medical care/institutions in Poland. It makes a unique opportunity to distribute information on the project and to connect with parents groups for WP7. Also current functions (Board member of the Committee on Human Development of the Polish Academy of Sciences; Head of the Section of Clinical Genetics of the Polish Society of Gynaecology; Board member of the Polish Society of Human Genetics; expert of the Polish Ministry of Health for congenital malformations; member of scientific/editorial board of Journal of Applied Genetics, Postępy Neonatologii, Pediatria po Dyplomie) as well as experience in recruiting of large cohorts of patients for research and in education of patients and physicians will be useful for the Project.

Anna Materna-Kiryluk, MD, PhD – paediatrician and clinical geneticist. **Gender : Female**
Anna Materna-Kiryluk is the Organizing Co-ordinator of PRCM.

Anna Jamry-Dziurla, Msc. **Gender : Female**
Anna Jamry-Dziurla is experienced in contacting parents and in organizing conferences

Relevant Previous Publications

1. Hu H, Haas SA, Chelly J, Van Esch H, Raynaud M, de Brouwer AP, Weinert S, Froyen G, Frints SG, Laumonnier F, Zemojtel T, Love MI, Richard H, Emde AK, Bienek M, Jensen C, Hambrock M, Fischer U, Langnick C, Feldkamp M, Wissink-Lindhout W, Lebrun N, Castelnau L, Rucci J, Montjean R, Dorseuil O, Billuart P, Stuhlmann T, Shaw M, Corbett MA, Gardner A, Willis-Owen S, Tan C, Friend KL, Belet S, van Roozendaal KE, Jimenez-Pocquet M, Moizard MP, Ronce N, Sun R, O'Keeffe S, Chenna R, van Bömmel A, Göke J, Hackett A, Field M, Christie L, Boyle J, Haan E, Nelson J, Turner G, Baynam G, Gillessen-Kaesbach G, Müller U, Steinberger D, Budny B, Badura-Stronka M, **Latos-Bieleńska A**, Ousager LB, Wieacker P, Rodríguez Criado G, Bondeson ML, Annerén G, Dufke A, Cohen M, Van Maldergem L, Vincent-Delorme C, Echenne B, Simon-Bouy B, Kleefstra T, Willemsen M, Fryns JP, Devriendt K, Ullmann R, Vingron M, Wrogemann K, Wienker TF, Tzschach A, van Bokhoven H, Gecz J, Jentsch TJ, Chen W, Ropers HH, Kalscheuer VM.: X-exome sequencing of 405 unresolved families identifies seven novel intellectual disability genes. Mol Psychiatry. 2015 Feb 3. doi: 10.1038/mp.2014.193. [Epub ahead of print]
2. Khoshnood B, Loane M, Walle Hd, Arriola L, Addor MC, Barisic I, Beres J, Bianchi F, Dias C, Draper E, Garne E, Gatt M, Haeusler M, Klungsoyr K, **Latos-Bielenska** A, Lynch C, McDonnell B, Nelen V, Neville AJ, O'Mahony MT, Queisser-Luft A, Rankin J, Rissmann A, Ritvanen A, Rounding C, Sipek A, Tucker D, Verellen-Dumoulin C, Wellesley D, Dolk H. Long term trends in prevalence of neural tube defects in Europe: population based study. BMJ. 2015 Nov 24;351:h5949. doi: 10.1136/bmj.h5949.
3. McGivern MR, Best KE, Rankin J, Wellesley D, Greenlees R, Addor MC, Arriola L, de Walle H, Barisic I, Beres J, Bianchi F, Calzolari E, Doray B, Draper ES, Garne E, Gatt M, Haeusler M, Khoshnood B, Klungsoyr K, **Latos-Bielenska** A, O'Mahony M, Braz P, McDonnell B, Mullaney C, Nelen V, Queisser-Luft A, Randrianaivo H, Rissmann A, Rounding C, Sipek A, Thompson R, Tucker D, Wertelecki W, Martos C.: Epidemiology of congenital diaphragmatic hernia in Europe: a register-based study. Arch Dis Child Fetal Neonatal Ed. 2015 Mar;100(2):F137-44.
4. Sanna-Cherchi S, R. V. Sampogna, N. Papeta, K.E. Burgess, S. N. Nees, B.J. Perry, M.Choi, M. Bodria, Y. Liu, P.L. Weng, V.J. Lozanovski, M. Verbitsky, F. Lugani, R. Sterken, N. Paragas, G. Caridi, A. Carrea, M. Dagnino**, A. Materna-Kiryluk**, G.Santamaria, C. Murtas, N.Ristoska-Bojkovska, C. Izzi, N. Kacak, B. Bianco, S. Giberti, M. Gigante, G. Piaggio, L. Gesualdo, D. Kosuljandic Vukic, K. Vukojevic, M. Saraga-Babic, M. Saraga, Z. Gucev, L. Allegri, **A. Latos-Bieleńska**, D. Casu, M.State, F.Scolari, R. Ravazzolo, K.Kiryluk, Q. Al-Awqati, V. D. D'Agati, I. A. Drummond, V. Tasic, R.P. Lifton, G. M. Ghiggeri, A. G. Gharavi. Mutations in *DSTYK* and dominant urinary tract malformations. N. Engl. J. Med. 2013, 369, 621-629. **IF=51.658**
5. **Materna-Kiryluk A**., A.Jamsheer, K. Wiśniewska, B. Więckowska, J.Limon, M. Borszewska-Kornacka, H. Sawulicka-Oleszczuk, E.Szwałkiewicz-Warowicka, **A. Latos-Bieleńska**. Epidemiology of isolated preaxial polydactyly type I: data from the Polish Registry of Congenital Malformations (PRCM). BMC Pediatr. 2013, 13: 26, 1-9.

Relevant Previous Projects

1. **European Network for Surveillance of Congenital Anomalies** (EUROCAT, http://www.eurocat-network.eu/). Led from Belfast Funded under Health Programme European Union 2008-2014; QMUL led Prenatal Diagnosis WP 2008-2013. EUROCAT now hosted at ISPRA, Milan.
2. **EUROmediCAT** (http://euromedicat.eu/). FP7 funded 2011-2014. The current proposal is adopting much of the methodology of EUROmediCAT which was a successful partnership of congenital anomaly registries which linked their data with hospital discharge data and prescription data to produce innovative research on medication use in pregnancy.
3. **PROTECT:** 2011-2014. http://www.imi-protect.eu Pharmacoepidemiological Research on Outcomes of Therapeutics by a European Consortium FP7/2007-2013. Grant agreement no.: 1150004. EU Project.
4. **CHERISH:** 2009-2012. Improving Diagnoses of Mental Retardation in Children in Eastern Europe and Central Asia through Genetic Characterization and Bioinformatics/Statistics HEALTH-F2-2008-223692. Grant agreement no.: 223692. EU Project.

Participant No 13: National Institute for Health and Welfare (THL)

The National Institute for Health and Welfare (THL) is a research and development institute under the Finnish Ministry of Social Affairs and Health. THL seeks to serve the broader society in addition to the scientific community, actors in the field and decision-makers in central government and municipalities. The aim is to promote health and welfare in Finland. The Finnish Register of Congenital Malformations was established in 1963 and is run and financed by THL, the governmental National Institute for Welfare and Health (under the Ministry of Social Affairs and Health). The Finnish Malformation Register became an associate member of EUROCAT in 1998

Tasks
To work in WP2 to link data from the "The Finnish Register of Congenital Malformations" to datasets on mortality/hospital discharge data/prescriptions/education data and to provide aggregated tables and analysis. To help with the interpretation and provide comments on any papers that subsequently use the data provided and check that any aggregated data on the website is correct. To be responsible for a peer reviewed paper in WP4 on morbidity and prenatal diagnosis.

Sonja Kiuru-Kuhlefelt, M.D., Ph.D., Specialist in Clinical Genetics. Gender : Female
Sonja Kiuru-Kuhlefelt has been the Chief Physician of the Finnish Register since 2015. Her expertise includes both clinical and laboratory aspects of congenital malformations and genetic diseases.

Professor Mika Gissler. Gender : Male
Professor Mika Gissler has a Master degree in Economics and Statistics (University of Helsinki) and Doctor of Philosophy degree in Epidemiology (University of Tampere). He holds professorships and faculty appointments at the National Institute for Health and Welfare in Helsinki, Finland, the University of Turku, Finland, the University of Oulu, Finland, and the Karolinska Institute, Stockholm, Sweden. He has been working more than 25 years with the Finnish Reproductive Health Registers, including Medical Birth Register and the Malformation Register. Professor Gissler's main research focus has been in utilization of routinely collected health and welfare registers. He has experience on using registers in all Nordic countries (Finland, Sweden, Norway, Denmark and Iceland), and in several European countries (e.g. Germany and Estonia).

Relevant Previous Publications

1. Räisänen S, Sankilampi U, Gissler M, Kramer MR, Hakulinen-Viitanen T, Saari J, Heinonen S: Smoking cessation in the first trimester reduces most obstetric risks, but not the risks of major congenital anomalies and admission to neonatal care – a population based cohort study of 1,164,953 singleton pregnancies in Finland. Journal of Epidemiology & Community Health 68 (2): 159-164, 2014.
2. Pelkonen S, Hartikainen A-L, Ritvanen A, Koivunen R, Martikainen H, Gissler M, and Tiitinen A: Major congenital anomalies in children born after frozen embryo transfer: a cohort study 1995−2006. Human Reproduction 29 (7): 1552-1557, 2014.
3. Kancherla V, Räisänen S, Gissler M, Kramer MR, Heinonen S: Placenta Previa and Risk of Major Congenital Malformations among Singleton Births in Finland. Birth Defects Research Part A: Clinical and Molecular Teratology 103 (6): 527-535, 2015.
4. Timonen-Soivio L, Sourander A, Malm H, Hinkka-Yli-Salomäki S, Gissler M, Brown A, Vanhala R: The association between autism spectrum disorders and congenital anomalies in organ systems in a Finnish National Birth Cohort. Journal of Autism and Developmental Disorders 45 (10): 3195-3203, 2015.
5. Furu K, Kieler H, Haglund B, Engeland A, Selmer R, Stephansson O, Valdimarsdottir U, Zoega

H, Artama A, Gissler M, Malm H, Nørgaard M: Selective Serotonin-Reuptake Inhibitors and Venlafaxine in early pregnancy and risk of birth defects – a population based cohort study and sibling design. British Medical Journal 350:h1798, 2015.

Relevant Previous Projects

1. **European Network for Surveillance of Congenital Anomalies** (EUROCAT, http://www.eurocat-network.eu/). Led from Belfast Funded under Health Programme European Union 2008-2014; QMUL led Prenatal Diagnosis WP 2008-2013. EUROCAT now hosted at ISPRA, Italy.
2. **EUROmediCAT** (http://euromedicat.eu/). FP7 funded 2011-2014. The current proposal is adopting much of the methodology of EUROmediCAT which was a successful partnership of congenital anomaly registries which linked their data with hospital discharge data and prescription data to produce innovative research on medication use in pregnancy.
3. **International Clearinghouse for Birth Defects Surveillance and Research** (ICBDSR, http://www.icbdsr.org/). The International Clearinghouse Centre, located in Rome - Italy, is the Central Office of the ICBDSR, coordinating the surveillance activities and collaborative research studies of the Organisation. The Finnish Register of Congenital Malformations has been a full member of the ICBDSR since 1974.
4. **Joint Action ECHIM European Community Health Information Monitoring**. (JA ECHIM, http://www.ncbi.nlm.nih.gov/pubmed/23721296). After 14 years of work (1998-2012), the multi-phase action on European Community Health Indicators (ECHI), funded by DG Health and Consumers has created a health monitoring and reporting system. It has generated EU added value by defining the ECHI shortlist with 88 common and comparable key health indicators for Europe. THL was the leader of this joint action until its end 2012.
5. **FoResight and Modelling for European Health Policy and Regulation** (FRESHER, http://www.foresight-fresher.eu//en/). Horizon 2020 –funded 2015-2018. The FRESHER project will produce quantitative estimates of the future global burden of chronic non-communicable diseases in the EU and their impact on health care expenditures and delivery, on population well-being, and on health and socio-economic inequalities, as well as potential changes in these impacts according to alternative health and non-health policy options. THL is one of the partners in this project.

Participant No 14: OMNI-Net Ukraine Birth Defects Program (OMNI-NET)

OMNI-Net is a not-for-profit international organization in Ukraine, and the OMNI-Net Ukraine Birth Defects Program represents three resource OMNI-Centers that provide care for children with birth defects, promote prevention programs, participate in parental organizations and engage in collaborative programs with national and international partners. Population based birth defects surveillance began in 2000 in the framework of the Ukrainian-American Birth Defects Program funded by the United States Agency for International Development (USAID). The program became an associate member of ICBDSR in 2001, and in 2005 the USAID component was completed and the program was assumed by OMNI-Net.

Tasks

To work in WP2 to link data from the OMNI-Net Ukraine Birth Defects Program to datasets on mortality/hospital discharge data and to provide aggregated tables and analysis. To help with the interpretation and provide comments on any papers that subsequently use the data provided and check that any aggregated data on the website is correct.

Wladimir Wertelecki, MD, Professor. Gender : Male.

Prrofessor Wertelecki has experience with medical genetics, teratology and paediatrics. Coordination of population-based monitoring of congenital malformations in regions of Ukraine contaminated by Chornobyl radiation. Facilitation of collaborative investigations in Ukraine coordinated by the University of California, San Diego. Implement in-depth investigations in selected villages of reproductive risks associated with exposures to alcohol, radiation and other teratogens. Development of OMNI-Net international partnerships and collaborative investigations.

Natalya Zymak-Zakutnia, MD, Coordinator. Gender : Female.

Natalya Zymak-Zakutnia has long standing experience in the field of medical genetics, paediatrics, surveillance and research on congenital anomalies, as Regional coordinator of OMNI-Net Ukraine Birth Defects Program in EUROCAT since 2007. Head of Khmelnytsky Medical Genetic Center since 1998. Since 2013 - Deputy Chairman of the Board of Khmelnytsky Regional Organization of All-Ukrainian Medical Association.

Diana Akhmedzhanova, Data Manager. Gender : Female

Diana Akhmedzhanova hase experience with epidemiology, particularly on congenital defects, and with statistical-epidemiological methods for birth defects surveillance. Responsible for the activities of congenital defects coding, management of the database and data analysis for the surveillance of births in OMNI-Net Ukraine Birth Defects Program. Data manager for the EUROmediCAT project and Collaborative Initiative on Fetal Alcohol Spectrum Disorders (CIFASD).

Relevant Previous Publications

1. Wertelecki W, Koerblein A, Ievtushok B, Zymak-Zakutnia N, Komov O, Kuznietsov I, Lapchenko S, Sosyniuk Z (2016). Elevated congenital anomaly rates and incorporated cesium-137 in the Polissia region of Ukraine. Birth Defects Res A Clin Mol Teratol Mar;106(3):194-200. doi: 10.1002/bdra.23476.
2. McGivern MR, Best KE, Rankin J, Wellesley D, Greenlees R, Addor MC, Arriola L, de Walle H, Barisic I, Beres J, Bianchi F, Calzolari E, Doray B, Draper ES, Garne E, Gatt M, Haeusler M, Khoshnood B, Klungsoyr K, Latos-Bielenska A, O'Mahony M, Braz P, McDonnell B, Mullaney C, Nelen V, Queisser-Luft A, Randrianaivo H, Rissmann A, Rounding C, Sipek A, Thompson R, Tucker D, Wertelecki W, Martos C (2014). Epidemiology of congenital diaphragmatic hernia in Europe: a register-based study. Arch Dis Child Fetal Neonatal Ed. Nov 19. pii: fetalneonatal-2014-306174.
3. Yevtushok L, Zymak-Zakutnia N, Kalynka S, Korzhynkyy Y, Sosynyuk Z, Wertelecki W (2012). Population monitoring of congenital malformations according to international standards. Archives of Clinical and Experimental Medicine. 21:153-155 (in Ukrainian).
4. Greenlees R, Neville A, Addor MC, Amar E, Arriola L, Bakker M, Barisic I, Boyd PA, Calzolari E, Doray B, Draper E, Vollset SE, Garne E, Gatt M, Haeusler M, Kallen K, Khoshnood B, Latos-Bielenska A, Martinez-Frias ML, Materna-Kiryluk A, Dias CM, McDonnell B, Mullaney C, Nelen V, O'Mahony M, Pierini A, Queisser-Luft A, Randrianaivo-Ranjatoélina H, Rankin J, Rissmann A, Ritvanen A, Salvador J, Sipek A, Tucker D, Verellen-Dumoulin C, Wellesley D, Wertelecki W (2011). EUROCAT member registries: organization and activities. Birth Defects Res A Clin Mol Teratol Mar;91 Suppl 1:S51-S100.
5. Dancause KN, Yevtushok L, Lapchenko S, Shumlyansky I, Shevchenko G, Wertelecki W, Garruto RM (2010). Chronic radiation exposure in the Rivne-Polissia region of Ukraine: implications for birth defects. Am J Hum Biol Sep-Oct; 22(5):667-74.

Relevant Previous Projects

1. **European Network for Surveillance of Congenital Anomalies** (EUROCAT, http://www.eurocat-network.eu/). Led from Belfast Funded under Health Programme European Union 2008-2014; EUROCAT now hosted at ISPRA, Milan.
2. **EUROmediCAT** (http://euromedicat.eu/). FP7 funded 2011-2014. The current proposal is adopting much of the methodology of EUROmediCAT which was a successful partnership of congenital anomaly registries which linked their data with hospital discharge data and prescription data to produce innovative research on medication use in pregnancy.
3. **International Clearinghouse for Birth Defects Surveillance and Research** (ICBDSR, http://www.icbdsr.org/). The International Clearinghouse Centre, located in Rome - Italy, is the Central Office of the ICBDSR, coordinating the surveillance activities and collaborative research studies of the Organisation.
4. **Ukrainian-American Birth Defects Program (UABDP).** Development of population neonatal registries and establishing the congenital anomalies surveillance system based on international standards. Promoting medical education and scientific research funded by the United States Agency for International Development (USAID) till 2005. After 2005 the program was assumed by OMNI-Net, a not-for-profit international organization incorporated in Ukraine.

5. **Collaborative Initiative on Fetal Alcohol Spectrum Disorders** (CIFASD, http://cifasd.org/). The purpose of this consortium is to inform and develop effective interventions and treatment approaches for Fetal Alcohol Spectrum Disorders (FASD), through multidisciplinary research involving basic, behavioral and clinical investigators and projects.

Participant No 15: Saxony-Anhalt Registry (OVGU)

Otto-von-Guericke University Magdeburg
Saxony-Anhalt Registry **is based in the Malformation Monitoring Centre Saxony-Anhalt at the** Otto-von-Guericke University Magdeburg. The Otto-von-Guericke University Magdeburg was founded in 1993 and is one of the youngest universities in Germany. It was formed by a merger of the existing Technical University, the Teacher Training College and the Medical School, and comprises 9 faculties and almost 14000 students.

Tasks
To work in WP2 to link data from the "Saxony-Anhalt Registry" to datasets on mortality/hospital discharge data/prescriptions/education data and to provide aggregated tables and analysis. To help with the interpretation and provide comments on any papers that subsequently use the data provided and check that any aggregated data on the website is correct.

Anke Rissmann,paediatrician **Gender : Female**
Anke Rissmann is a paediatrician, specialised in paediatric nephrology and neonatology and has a long standing experience in the field of surveillance and research on congenital anomalies, as Head of the Malformation Monitoring Center Saxony-Anhalt since 2010.

Dorit Götz , data manager **Gender : Female**
Dorit Götz is registry data manager and statistician and coordinates data transmission to EUROCAT. The Malformation Monitoring Centre Saxony-Anhalt was established in 1980 and has been a full member of EUROCAT since 1992.

Relevant Previous Publications

1. Bergman JEH, Loane M, Vrijheid M, Pierini A, Nijman RJM, Addor M-C, Barisic I, Beres J, Braz P, Budd J, Delany V, Gatt M, Khoshnood B, Klungsoyr K, Martos C, Mullaney C, Nelen V, Neville A, O'Mahony M, Queisser-Luft A, Randrianaivo-Ranjatoelina H, **Rissmann A**, Rounding C, Tucker D, Wellesley D, Zymak-Zakutnya, N, Bakker M and de Walle H (2015). Epidemiology of hypospadias in Europe: a registry-based study. World Journal of Urology.
2. Wemakor, A, Casson K, Garne E, Bakker M, Addor M-C, Arriola L, Gatt M, Khoshnood B, Klungsoyr K, Nelen V, O'Mahony M, Pierini A, **Rissmann A**, Tucker D, Boyle B, de Jong-van den Berg L and Dolk H (2015). Selective serotonin reuptake inhibitor antidepressant use in first trimester pregnancy and risk of specific congenital anomalies: A European register-based study. European Journal of Epidemiology.
3. Barisic I, Boban L, Greenlees R, Garne E, Wellesley D, Calzolari E, Addor M-C, Arriola L, Bergman JEH, Braz P, Budd J, Gatt M, Haeusler M, Khoshnood B, Klungsoyr K, McDonnell R, Nelen V, Pierini A, Queisser-Wahrendorf A, Rankin J, **Rissmann A**, Rounding C, Tucker D, Verellen-Dumoulin C and Dolk H (2014). Holt Oram syndrome: a registry-based study in Europe. Orphanet Journal of Rare Diseases. 9: 156-165.
4. Barisic I, Boban L, Loane M, Garne E, Wellesley D, Calzolari E, Dolk H, Addor M-C, Bergman JEH, Braz P, Draper E, Haeusler M, Khoshnood B, Klungsoyr K, Pierini A, Queisser-Luft A, Rankin J, **Rissmann A** and Verellen-Dumoulin C (2014). Meckel-Gruber syndrome: a population-based study on prevalence, prenatal diagnosis, clinical features, and survival in Europe. European Journal of Human Genetics.
5. Barisic I, Odak, L, Loane M, Garne E, Wellesley D, Calzolari E, Dolk H, Addor M-C, Arriola L, Bergman JEH, Bianca S, Doray B, Khoshnood B, Klungsoyr K, McDonnell R, Pierini A, Rankin J,

Rissmann A, Rounding C, Queisser-Luft A, Scarano G and Tucker D (2014). Prevalence, prenatal diagnosis and clinical features of oculo-auriculo-vertebral spectrum: a registry-based study in Europe. European Journal of Human Genetics.

Relevant Previous Projects

1. **European Network for Surveillance of Congenital Anomalies** (EUROCAT, http://www.eurocat-network.eu/). Led from Belfast Funded under Health Programme European Union 2008-2014; QMUL led Prenatal Diagnosis WP 2008-2013. EUROCAT now hosted at ISPRA, Milan.
2. **EUROmediCAT** (http://euromedicat.eu/). FP7 funded 2011-2014. The current proposal is adopting much of the methodology of EUROmediCAT which was a successful partnership of congenital anomaly registries which linked their data with hospital discharge data and prescription data to produce innovative research on medication use in pregnancy.
3. **International Clearinghouse for Birth Defects Surveillance and Research** (ICBDSR, http://www.icbdsr.org/). The International Clearinghouse Centre, located in Rome - Italy, is the Central Office of the ICBDSR, coordinating the surveillance activities and collaborative research studies of the Organisation.

Participant No 16: National Health Institute Doutor Ricardo Jorge (INSA)

The National Institute of Health Doutor Ricardo Jorge (INSA) develops its activity as the National Health Observatory; State Laboratory for the health sector and National Reference Laboratory. Its mission is to contribute to gains in public health, either on specialized health care or through the laboratory area, to provide the Ministry of Health with adequate data and information for knowledge-based decision-making, essential to support the definition of national health policies, to follow the guidelines defined by the Ministry of Health and to answer questions raised by the scientific community and the society. INSA ensures its mission through epidemiological and laboratory-based research, technological development, epidemiological surveillance health services research, external evaluation of laboratory quality, diffusion of scientific culture, fostering knowledge and skills and capacities of health staff through training programs and by providing specialized services in several domains including screening of genetic diseases. INSA develops several R&D activities on the health sciences domain, with a special focus on epidemiology, environmental health, food and nutrition, genetics, proteomics, health services, infectious diseases, non-communicable diseases and health promotion. The Department of Epidemiology of INSA hosts the National Registry of Congenital Anomalies (RENAC) since 1995 and participates in EUROCAT since 1990 with data from the South of Portugal. Within INSA, the Department of Epidemiology will be committed to this project.

Tasks

To work in WP2 to link data from the South Portugal Registry to datasets on hospital discharge data and to provide aggregated tables and analysis. To help with the interpretation and provide comments on any papers that subsequently use the data provided and check that any aggregated data on the website is correct. To collaborate in WP7 in relation with the connectEpeople platform.

Carlos Matias Dias, Public Health Specialist. Gender : Male

Carlos Matias Dias is a senior medical doctor specialist in Public Health, holds an MSc in Epidemiology from the University of London and a PhD in epidemiology from the New University of Lisboa. He is the head of the Epidemiology department of the Portuguese National Institute of Health since 2007. From 2000 to 2007 he was responsible for the epidemiology unit of the National Health Observatory at INSA. He has an extensive expertise in designing and conducting epidemiological observational studies, health surveys and conducting data analysis using registry data namely in the congenital anomalies area. Since 2006 is the coordinator of the National Registry of Congenital Anomalies (RENAC). RENAC is member of the European Network for Surveillance of Congenital Anomalies-EUROCAT since 1990, contributing with data from the South of Portugal region.

Paula Braz, MSc. Gender : Female

Paula Braz is a Researcher with experience in congenital anomalies and clinical genetics epidemiology, statistical-epidemiological methods for birth defects surveillance. She is responsible for the validation and coding activities of congenital defects, management of the registry database and data analysis for the surveillance of births in RENAC. She also coordinates the data validation and transfer for EUROCAT and has been project leader in national studies for congenital anomalies and participated in EUROCAT data analysis projects.

Ausenda Machado, MSc. Gender : Female

Since 2005 Ausenda Machado has been working at the Epidemiology Department of the Portuguese National Health Institute in planning and preparation of epidemiological, clinical and health services research. She has experience in statistical and epidemiological methods in birth defects surveillance. She collaborates in national studies for congenital anomalies.

Relevant Previous Publications

1. Best KE, Addor M-C, Arriola L, Balku E, Barisic I, Bianchi F, Calzolari E, Curran R, Doray B, Draper E, Garne E, Gatt M, Haeusler M, van Kammen-Bergman, Khoshnood B, Klungsoyr K, Martos C, Materna-Kiryluk A, **Matias Dias C**, McDonnell R, Mullaney C, Nelen V, O'Mahony M, Queisser-Luft A, Randrianaivo-Ranjatoelina H, Rissmann A, Rounding C, Sipek A, Thompson R, Tucker D, Wellesley D, Zymak-Zakutnya, N and Rankin J (2014). Hirschsprung's disease prevalence in Europe: a register based study. *Birth Defects Research Part A Clinical and Molecular Teratology*.
2. Morris J, Garne E, Wellesley D, Addor M-C, Arriola L, Barisic I, Beres J, Bianchi F, Budd J, **Dias C M**, Gatt M, Klungsoyr K, Khoshnood B, Latos- Bielenska A, Mullaney C, Nelen V, Neville A, O'Mahony M, Queisser-Luft A, Randrianaivo-Ranjatoelina H, Rankin J, Rissmann A, Rounding C, Sipek A, Tucker D, de Walle H, Yevtushok L, Loane M, Dolk H and Stoianova S (2014). Major Congenital Anomalies in Babies Born with Down Syndrome: A EUROCAT Population-Based Registry Study. American Journal of Medical Genetics Part A.
3. Wijers CHW, van Rooij IALM, Bakker M, Marcelis CLM, Addor M-C, Barisic I, Beres J, Bianca S, Bianchi F, Calzolari E, Greenlees R, Lelong N, Latos- Bielenska A, **Dias C M**, McDonnell R, Mullaney C, Nelen V, O'Mahony M, Queisser-Luft A, Rankin J, Zymak-Zakutnya, N, I de Blaauw, Roeleveld N and de Walle H (2013). Anorectal malformations and pregnancy-related disorders: a registry-based case-control study in 17 European regions. British Journal of Gynaecology.
4. Best KE, Tennant P, Addor M-C, Bianchi F, Boyd P, Calzolari E, **Dias C M**, Doray B, Draper E, Garne E, Gatt M, Greenlees R, Haeusler M, Khoshnood B, McDonnell R, Mullaney C, Nelen V, Randrianaivo-Ranjatoelina H, Rissmann A, Salvador J, Tucker D, Wellesley D and Rankin J (2012). Epidemiology of small intestinal atresia in Europe: a register-based study. Archives of Disease in Childhood - Fetal and Neonatal Edition. 97: F353-F358.
5. Garne E, Loane M, Dolk H, Barisic I, Addor M-C, Arriola L, Bakker M, Calzolari E, **Dias C M**, Doray B, Gatt M, Klungsoyr K, Nelen V, O'Mahony M, Pierini A, Randrianaivo-Ranjatoelina H, Rankin J, Rissmann A, Tucker D, Verellen-Dumoulin C and Wiesel A (2012). Spectrum of congenital anomalies in pregnancies with pregestational diabetes. *Birth Defects Research (Part A)*. 94: 134-140.

Relevant Previous Projects

1. **European Network for Surveillance of Congenital Anomalies** (EUROCAT, http://www.eurocat-network.eu/). Led from Belfast Funded under Health Programme European Union 2008-2014. EUROCAT now hosted at ISPRA, Milan.
2. **The EUCERD Joint Action: Working for Rare Diseases (EJA**, http://www.eucerd.eu/?page_id=54. Coordinated by Newcastle University, 2012-2015. Funded by the European Commission to contribute among others, to the development and dissemination of knowledge on Rare Diseases, from specialized research, through to the support of the healthcare professionals and the empowerment of patients.
3. **The third, fourth and fifth (1998/1999, 2004/2005, 2014/2015) National Health Interview Surveys (NHIS - INS)** have been prepared and run jointly by the Portuguese National Institute of Health (INSA), through its Department of Epidemiology (DEP) and Statistics Portugal (INE). The NHIS is funded by the Ministry of Health and Statistics Portugal and

produces official statistics and a set of health indicators used to monitor the National Health Plan and priority health programs.
[http://www.insa.pt/sites/INSA/Portugues/AreasCientificas/Epidemiologia/Unidades/UnInstrObser/Paginas/INS.aspx].

4. **National Health Examination Survey (INSEF)** is a cross sectional prevalence study. An interview, a physical examination and laboratory tests performed on biological samples have taken place during 2015 on a representative sample of 4900 portuguese. Results will be presented in 31 may 2016 on the population health status, its determinants and on the use of healthcare services. This information has been gathered according to standard operating procedures adopted by the European Health Examination Survey. INSEF is financed by the EEA Grants financial mechanism and the Portuguese government [http://www.insef.pt/English/Pages/Inicio.aspx].

Participant No 17: Centre Hospitalier Universitaire Réunion (ILDR)

CHU Reunion is a University teaching hospital of the island, with two sites in the South (St Pierre) and in the North (St Denis). The Unit of the registry for congenital malformations is located in the South of Reunion Island. The registry of the congenital malformations records all the cases on the Island.

Tasks
To work in WP2 to link data from the "Ile de la Reunion Registry" to datasets on mortality (WP3), morbidity (WP4 - Tasks 1,2 and 4) and accuracy of anomaly coding in health care databases (WP6)/hospital discharge data and to provide aggregated tables and analysis. To help with the interpretation and provide comments on any papers that subsequently the data provided and check that any aggregated data on the website is correct to be used. For that, there is a collaboration with the INSEE La Réunion, Mayotte (Service of Studies & Diffusion) for example, with a production of all cases of different mortality in each of the 24 communes of the department. The hospital discharge individual data provide for example from the department of medical information of the CHU. The Sickness Insurance Primary Fund (CPAM) maybe a source of collective data of healthcare.

Hanitra Randrianaivo, medical geneticist. **Gender : Female**
Hanitra Randrianaivo has long standing experience in the field of surveillance and research on congenital anomalies, as scientific director of the Ile de la Reunion Registry since 2010. The Ile de la Reunion Registry was established in 2001 and has contributed data to EUROCAT from 2002 onwards. It is a full member of this network for Surveillance of Congenital Anomalies. Hanitra is a medical geneticist at Reunion University Hospital (CHU South Reunion, St Pierre) with predominant activities in the field of perinatal health and prenatal diagnosis & also in oncogenetics.

Bénédicte Bertaut-Nativel, midwife. **Gender : Female**
Bénédicte Bertaut-Nativel is the midwife at the Reunion Island Registry of Congenital Defects
She is a collaborator for the activities of congenital defects coding, responsible of management of the database and data analysis for the surveillance of births in Reunion Island (exhaustivity of our data of congenital malformations, and statistical monitoring with our software EDMP (for local studies), liases with EUROCAT central registry and participates in the EUROmediCAT project for the Registry of Reunion Island Congenital Defects.

Mathilde André, MSc Geostatistician **Gender : Female**
Mathilde André has worked on our recent activities in spatial investigations of congenital malformations. She has experience with reproductive epidemiology, particularly on congenital defects, and with statistical-epidemiological methods for birth defects surveillance, and data analysis of congenital heart defect, cleft lip and palate and spina bifida/anencephaly in La Reunion, spatial investigation, case-control study.

Relevant Previous Publications

1. Mejlachowicz D, Nolent F, Maluenda J, Ranjatoelina-Randrianaivo H, Giuliano F, Gut I, Sternberg D, Laquerrie A, and Melki J. Truncating Mutations of MAGEL2, a Gene within the Prader-Willi Locus, Are Responsible for Severe Arthrogryposis . AJHG, Volume 97, Issue 4, p616–620, 1 October 2015
2. Audrézet MP, Corbiere C, Lebbah S, Morinière V, Broux F, Louillet F, Fischbach M, Zaloszyc A, Cloarec S, Merieau E, Baudouin V, Deschênes G, Roussey G, Maestri S, Visconti C, Boyer O, Abel C, Lahoche A, Randrianaivo H, Bessenay L, Mekahli D, Ouertani I, Decramer S, Ryckenwaert A, Cornec-Le Gall E, Salomon R, Ferec C and Heidet L. Comprehensive PKD1 and PKD2 Mutation Analysis in Prenatal Autosomal Dominant Polycystic Kidney Disease. JASN July 2, 2015
3. Vincent M, Geneviève D, Ostertag A, Marlin S, Lacombe D, Martin-Coignard D, Coubes C, David A, Lyonnet S, Vilain C, Dieux-Coeslier A, Manouvrier S, Isidor B, Jacquemont ML, Julia S, Layet V, Naudion S, Odent S, Pasquier L, Pelras S, Philip N, Pierquin G, Prieur F, Aboussair N, Attie-Bitach T, Baujat G, Blanchet P, Blanchet C, Dollfus H, Doray B, Schaefer, E, Edery P, Giuliano F, Goldenberg A, Goizet C, Guichet A, Herlin C, Lambert L, Leheup B, Martinovic J, Mercier S, Mignot C, Moutard ML, Perez MJ, Pinson L, Puechberty J, Willems M, Randrianaivo H, Szaskon K, Toutain A, Verloes A, Vigneron J, Sanchez E, Sarda P, Laplanche JL, Collet C. Treacher Collins syndrome: a clinical and molecular study based on a large series of patients. Genet Med. 2015 Mar 19.
4. Oger AS , Robillard PY , Barau G , Randrianaivo H , Bonsante F , Iacobelli S , Boukerrou M (2013). Perinatal outcome of monochorionic and dichorionic twin gestations: a study of 775 pregnancies at Reunion Island. Journal de Gynecologie, Obstetrique et Biologie de la Reproduction, 42(7):655-661.
5. Cartault F, Munier P, Jacquemont ML, Vellayoudom J, Doray B, Payet C, Randrianaivo H, Laville JM, Munnich A, Cormier-Daire V. Expanding the clinical spectrum of B4GALT7 deficiency: homozygous p.R270C mutation with founder effect causes Larsen of Reunion Island syndrome. Eur J Hum Genet. 2014 Apr 23. doi: 10.1038/ejhg.2014.60.

Relevant Previous projects

1. **European Network for Surveillance of Congenital Anomalies** (EUROCAT, http://www.eurocat-network.eu/). Led from Belfast Funded under Health Programme European Union 2008-2014; QMUL led Prenatal Diagnosis WP 2008-2013. EUROCAT now hosted at ISPRA, Milan.
2. **EUROmediCAT** (http://euromedicat.eu/). FP7 funded 2011-2014. The current proposal is adopting much of the methodology of EUROmediCAT which was a successful partnership of congenital anomaly registries which linked their data with hospital discharge data and prescription data to produce innovative research on medication use in pregnancy.
3. Recent activities with cartography and spatial analyses of the inequal distribution of the cases of congenital malformations and their prevalence in different spatial unit. The spatial analyses of this inequal distribution are studied in link with different collective factors (socio-economic, environnemental, and data of collective health care…)
4. Report of a Professional Master's Level II on Health, Territory, and Environment Geography at the University of PARIS OUEST Nanterre-La Défense supported by H Randrianaivo on JUNE 25TH, 2015 “Spatial study of distribution inequalities of congenital malformations in

Reunion" with Director: Mr Stéphane RICAN as director and Mr Vincent HERBRETEAU, as supervisor.

Participant No 18: Provincial Institute for Hygiene (PIH)

The provincial Institute for Hygiene is a provincial company, which is part of the government of the province of Antwerp. The PIH, with 115 staff, has an environmental lab and departments of environment and health. The department of health of the PIH works in the field of public health and hosts the Antwerp EUROCAT registry.

Tasks

To work in WP 3 to link data from the Antwerp Registry to datasets on mortality/hospital discharge data and to provide aggregated tables and analysis. To help with the interpretation and provide comments on any papers that subsequently use the data provided and check that any aggregated data on the website is correct.

Dr Vera Nelen, Director of Provincial Institute for Hygiene. Gender : Female

Dr Vera Nelen has worked since 1989 in the Provincial institute for Hygiene (PIH) in Antwerp; as head of the department of public health; since 2011 as director of the institute. She is the registry leader of the Antwerp EUROCAT -registry of congenital anomalies; member of the EUROCAT Project management committee since 2012; scientific assistant in the European randomized study for screening of prostate cancer in Antwerp; responsible for study on lead intake in toddlers and schoolchildren in Hoboken; participant in the Antwerp respiratory health survey; expert in several advisory committees on health and environment. The Antwerp Registry formally started in 1990 and has been a member of EUROCAT since 1990.

Previous Relevant Publications

1. Bergman JEH, Loane M, Vrijheid M, Pierini A, Nijman RJM, Addor M-C, Barisic I, Beres J, Braz P, Budd J, Delany V, Gatt M, Khoshnood B, Klungsoyr K, Martos C, Mullaney C, **Nelen V**, Neville A, O'Mahony M, Queisser-Luft A, Randrianaivo-Ranjatoelina H, Rissmann A, Rounding C, Tucker D, Wellesley D, Zymak-Zakutnya, N, Bakker M and de Walle H (2015). Epidemiology of hypospadias in Europe: a registry-based study. World Journal of Urology.
2. Dolk H, Loane M, Teljeur C, Densem J, Greenlees R, McCullough N, Morris J, **Nelen V**, Bianchi F and Kelly A (2015). Detection and investigation of temporal clusters of congenital anomaly in Europe: seven years of experience of the EUROCAT surveillance system. European Journal of Epidemiology.
3. Taruscio D, Mantovani A, Carbone P, Barisic I, Bianchi F, Garne E, **Nelen V**, Neville A, Wellesley D and Dolk H (2015). Primary Prevention of Congenital Anomalies: Recommendable, Feasible and Achievable. Public Health Genomics.
4. Wemakor, A, Casson K, Garne E, Bakker M, Addor M-C, Arriola L, Gatt M, Khoshnood B, Klungsoyr K, **Nelen V**, O'Mahony M, Pierini A, Rissmann A, Tucker D, Boyle B, de Jong-van den Berg L and Dolk H (2015). Selective serotonin reuptake inhibitor antidepressant use in first trimester pregnancy and risk of specific congenital anomalies: A European register-based study. European Journal of Epidemiology.
5. Barisic I, Boban L, Greenlees R, Garne E, Wellesley D, Calzolari E, Addor M-C, Arriola L, Bergman JEH, Braz P, Budd J, Gatt M, Haeusler M, Khoshnood B, Klungsoyr K, McDonnell R, **Nelen V**, Pierini A, Queisser-Wahrendorf A, Rankin J, Rissmann A, Rounding C, Tucker D, Verellen-Dumoulin C and Dolk H (2014). Holt Oram syndrome: a registry-based study in Europe. Orphanet Journal of Rare Diseases. 9: 156-165.

Previous Relevant Projects

1. **European Network for Surveillance of Congenital Anomalies** (EUROCAT, http://www.eurocat-network.eu/). Led from Belfast Funded under Health Programme European Union 2008-2014; QMUL led Prenatal Diagnosis WP 2008-2013. EUROCAT now hosted at ISPRA, Milan.
2. **EUROmediCAT** (http://euromedicat.eu/). FP7 funded 2011-2014. The current proposal is adopting much of the methodology of EUROmediCAT which was a successful partnership of congenital anomaly registries which linked their data with hospital discharge data and prescription data to produce innovative research on medication use in pregnancy.
3. Membership of the **Flemish working group on population screening**
4. Membership of the **Project Management Committee EUROCAT**
5. Partner and spokesperson in the **Flemish human biomonitoring programs** since 2001

Participant No 19: Asociacion Instituto Biodonostia (BIOEF)

The Health Research Institute –BIODONOSTIA HRI- was established in 2008. It is a national and international centre of reference in the field of health research, giving priority to promoting translational research and firmly backing innovation in medical and health technologies, which lead to improvements in health care while also generating wealth for the country by converting inventions into products. At its heart is the Donostialdea IHO (Integrated Health Organisation), and as is the case with most Health Research Institutes, the University also forms an integrated part, which in our case is the University of the Basque Country (UPV-EHU). Added to this core are the Regional Government of Gipuzkoa (Health Public Area), the Euskampus Foundation and the Ikerbasque Foundation, thanks to which the critical mass of research has been increased by incorporating internationally renowned personnel.

The main research areas are: Neurosciences, Gastrointestinal and Liver Diseases, Infectious Diseases, Oncology, Systemic Diseases, Epidemiology and Public Health and Bioengineering. Our research is arranged in 7 subject areas that bring together around 300 researchers in 24 groups.

One of the research group in the Epidemiology and Public Health Area is Epidemiology of Chronic and Communicable Diseases. They are committed to the promotion of research and innovation in the Basque Health System as a continuous way of developing and improving the general health quality of the Basque population. The project will be carried out by the group formed by Larraitz Arriola.

Tasks

To work in WP2 to link data from the Basque Country Registry to datasets on mortality/hospital discharge data/prescriptions/education data and to provide aggregated tables and analysis. To help with the interpretation and provide comments on any papers that subsequently use the data provided and check that any aggregated data on the website is correct.

Larraitz Arriola, MD **Gender : Female**

Larraitz Arriola has a M.D., a M.Sc. (in Public Health by the London School of Hygiene and Tropical Medicine) and M.Sc. (in Field Applied Epidemiology by Instituto de Salud Carlos III, Spain) and is also a family physician. Larriatz Arriola has a long standing experience in the field of surveillance and research on congenital anomalies, as Registry Leader of the Basque Country Registry since 2010. The Basque Country Registry started in January 1990, and has been a member of EUROCAT since September 1990.

Previous Relevant Publications

1. Gallo V, Vanacore N, Bueno-de-Mesquita HB, Vermeulen R, Brayne C, Pearce N,Wark PA, Ward HA, Ferrari P, Jenab M, Andersen PM, Wennberg P, Wareham N, Katzke V, Kaaks R, Weiderpass E, Peeters PH, Mattiello A, Pala V, Barricante A, Chirlaque MD, Travier N, Travis RC, Sanchez MJ, Pessah-Rasmussen H, Petersson J, Tjønneland A, Tumino R, Quiros JR, Trichopoulou A, Kyrozis A, Oikonomidou D,Masala G, Sacerdote C, Arriola L, Boeing H, Vigl M, Claver-Chapelon F, Middleton L, Riboli E, Vineis P. Physical activity and risk of Amyotrophic Lateral Sclerosis in a prospective cohort study. Eur J Epidemiol. 2016 Mar 11. [Epub ahead of print]
2. Huerta JM, Chirlaque MD, Tormo MJ, Buckland G, Ardanaz E, Arriola L, Gavrila D, Salmerón D, Cirera L, Carpe B, Molina-Montes E, Chamosa S, Travier N, Quirós JR, Barricarte A, Agudo

A, Sánchez MJ, Navarro C. Work, household, and leisure-time physical activity and risk of mortality in the EPIC-Spain cohort. Prev Med. 2016 Apr;85:106-12.

3. Khoshnood B, Loane M, de Walle H, Arriola L, Addor MC, Barisic I, Beres J, Bianchi F, Dias C, Draper E, Garne E, Gatt M, Haeusler M, Klungsoyr K, Latos-Bielenska A, Lynch C, McDonnell B, Nelen V, Neville AJ, O'Mahony MT, Queisser-Luft A, Rankin J, Rissmann A, Ritvanen A, Rounding C, Sipek A, Tucker D, Verellen-Dumoulin C, Wellesley D, Dolk H. Long term trends in prevalence of neural tube defects in Europe: population based study. BMJ. 2015 Nov 24;351:h5949.
4. Springett A, Wellesley D, Greenlees R, Loane M, Addor MC, Arriola L, Bergman J, Cavero-Carbonell C, Csaky-Szunyogh M, Draper ES, Garne E, Gatt M, Haeusler M, Khoshnood B, Klungsoyr K, Lynch C, Dias CM, McDonnell R, Nelen V, O'Mahony M, Pierini A, Queisser-Luft A, Rankin J, Rissmann A, Rounding C, Stoianova S, Tuckerz D, Zymak-Zakutnia N, Morris JK. Congenital anomalies associated with trisomy 18 or trisomy 13: A registry-based study in 16 European countries, 2000-2011. Am J Med Genet A. 2015 Dec;167(12):3062-9.
5. Abete I, Arriola L, Etxezarreta N, Mozo I, Moreno-Iribas C, Amiano P, Egüés N, Goyenechea E, Lopez de Munain A, Martinez M, Travier N, Navarro C, Chirlaque MD, Tormo MJ, Gavrila D, Huerta JM, Sánchez MJ, Molina-Montes E, Requena M, Jiménez-Hernández MD, Ardanaz E, Barricarte A, Quiros JR, Rodriguez L, Dorronsoro M. Association between different obesity measures and the risk of stroke in the EPIC Spanish cohort. Eur J Nutr. 2015 Apr;54(3):365-75. doi:10.1007/s00394-014-0716-x. Epub 2014 Jun 6. PubMed PMID: 24903807.

Relevant Previous projects

1. **European Network for Surveillance of Congenital Anomalies** (EUROCAT, http://www.eurocat-network.eu/). Led from Belfast Funded under Health Programme European Union 2008-2014; QMUL led Prenatal Diagnosis WP 2008-2013. EUROCAT now hosted at ISPRA, Milan.
2. **EUROmediCAT** (http://euromedicat.eu/). FP7 funded 2011-2014. The current proposal is adopting much of the methodology of EUROmediCAT which was a successful partnership of congenital anomaly registries which linked their data with hospital discharge data and prescription data to produce innovative research on medication use in pregnancy.
3. **EPIC.** European Prospective Investigation into Cancer and Nutrition (EPIC) study is one of the largest cohort studies in the world, with more than half a million (521 000) participants recruited across 10 European countries and followed for almost 15 years. EPIC was designed to investigate the relationships between diet, nutritional status, lifestyle and environmental factors, and the incidence of cancer and other chronic diseases. EPIC investigators are active in all fields of epidemiology, and important contributions have been made in nutritional epidemiology using biomarker analysis and questionnaire information, as well as genetic and lifestyle investigations.

Participant No 20: BioMedical Computing Limited (BIOMED)

BioMedical Computing Limited is a private limited company providing bespoke software development and consultancy. The company was established in 1996 and there are currently five full time programmers employed by BioMedical Computing Limited. The three senior members of staff have been in post for a minimum of 14 years. Further details can be found at http://www.bio-medical.co.uk/MeetTheTeam. The principal purpose of the company is to provide bespoke software development for customers in a range of market segments including medical research. BioMedical Computing Limited is a Gold Application Development Microsoft Partner and is fully ISO accredited to BS EN 9001:2001. The company registration number is 3148645 (registered in England) and the VAT registration number is 724664328. BioMedical Computing Limited has provided the software and IT consultancy used for EUROCAT for the past 15 years as well as for the EUROmediCAT project and as such has in depth knowledge and experience of the data requirements for this project. Software provided included data collection and consolidation database applications as well as the websites used for management and interactive dissemination of results.

Tasks

- Deputy leader for work package 2.
- Standardise and map variables across linked databases including development of a database to record variable mapping. Development of data standardisation scripts, rules, syntax and verification.
- Develop central data repository to store, analyse and report summary results. Develop and include data quality indicators (DQI) for consistency validation.
- Develop website to include public information, secure document storage for access by members only, budget and timesheet recording, searchable publications list and interactive dissemination of summarised results.

Dr James Densem, Managing Director of BioMedical Computing Limited. Gender: Male

Dr James Densem has a BSc in Biology (University of London), MSC in Applied Hydrobiology (UWIST) and a PhD in Aquatic Biology (UWIST). He spent 4 years working as a programmer and statistician in the Heart Disease and Diabetes Research Unit, St Mary's Hospital Medical School, London followed by 11 years at the Wolfson Institute of Preventive Medicine as a programmer, computer manager and research assistant prior to establishing BioMedical Computing Limited.

Simon Mumford, Web Application Specialist. Gender: Male

Simon Mumford has an HND in client / server computing (University of Brighton) and has been with BioMedical Computing Limited for 14 years. He has developed the websites for the EUROCAT and EUROmediCat projects (www.eurocat-network.eu and www.euromedicat.eu). With this experience he is ideally suited to develop the website for EUROlinkCAT given the similar requirements for the website for this project.

Relevant Previous Publications

1. Teljeur C, Kelly A, Loane M, Densem J, Dolk H. Using scan statistics for congenital anomalies surveillance – the EUROCAT methodology. European Journal of Epidemiology. 2015; 30(11): 1165-1173.
2. Dolk H, Loane M, Teljeur C, Densem J, Greenlees R, McCullough N, Morris J, Nelen V, Bianchi F, Kelly A. Detection and investigation of temporal clusters of congenital anomaly in Europe: seven years of experience of the EUROCAT surveillance system. European Journal of Epidemiology. 2015; 30(11): 1153-1164.
3. Maria Loane, Helen Dolk, Alan Kelly, Conor Teljeur, Ruth Greenlees, James Densem, and a EUROCAT Working Group. Paper 4: EUROCAT statistical monitoring: Identification and investigation of ten year trends of congenital anomalies in Europe Birth Defects Research Part A: Clinical and Molecular Teratology 91: S31- S43, 2011
4. Ester Garne, Helen Dolk, Maria Loane, Diana Wellesley, Ingeborg Barisic, Elisa Calzolari, James Densem, and a EUROCAT Working Group. Paper 5: Surveillance of multiple congenital anomalies: Implementation of a computer algorithm in European registers for classification of cases. Birth Defects Research Part A: Clinical and Molecular Teratology 91: S44- S50, 2011
5. MRC Vitamin Study Research Group. N Wald, J Sneddon, J Densem, C Frost and R Stone. Prevention of neural tube defects: results of the MRC Vitamin Study. The Lancet, 338:132-137, 1991.

Relevant Previous Projects

1. **EUROCAT** : Led from Belfast Funded under Health Programme European Union 2008-2014; EUROCAT is now hosted at ISPRA, Milan. James Densem developed over the last 14 years the data entry and analysis program (EDMP) used by registries to collect, analyse and transmit case data. He also developed the central database (ECD) used to store and analyse case data from participating registries. He has also been closely involved in the development of algorithms used for case classification and also in the creation of the statistical monitoring and surveillance procedures. Simon Mumford created the EUROCAT website (www.eurocat-network.eu) which also includes interactive analysis and reporting of summary data.
2. **EUROmediCAT** : FP7 funded 2011-2014. The database used by participating registries for the collation and analysis of linked case and prescription data (LDMP) was developed by James Densem. Simon Mumford developed the website (www.euromedicat.eu) which includes interactive analysis of the prevalence of congenital anomalies by medication exposure.
3. **British Isles Network of Congenital Anomaly Registers** (BINOCAR) HUB: funded by Department of Health through Health Quality Improvements Program 2010-2014. Simon Mumford developed a web data portal for the transmission of data from 8 congenital anomaly registries in England and Wales collated to provide national data on the prevalence of anomalies.
4. **WHO** BioMedical computing limited are currently being funded by the WHO to develop a data collection, transfer and collation system for use in developing countries for the epidemiological surveillance of drug safety in pregnancy.

Participant No 21: Redburn Solutions Limited (REDBURN)

Redburn Solutions Ltd is an SME and a Business Integration company based in Titanic Quarter Belfast, UK. We specialise in portals, mobile and Business Intelligence. Our focus is Health and Education, delivering EU research to public and commercial organisations. Currently we are working with 19 Universities in eHealth on midwifery (**Optibirth**), maternity and associated disciplines research from Iceland to Australia. We are also researching the psychological patterns that exist within the English speaking education systems. Our partnerships are fundamental in developing and implementing ICT solutions using Open source/Cloud technologies Redburn has substantial experience leading projects with ICT implementation in health projects. Redburn bring their extensive European wide management capabilities to the project, delivering diplomatic and negotiation skills as well as highly focused project management skills. The key areas of managing through and across pilots, and delivering social media linkages are well within the capabilities of Redburn.

Dr David Elliott, Director. **Gender : Male**

Dr David Elliott has a BSc in Applied Mathematics and Physics, a PhD in Atomic Physics and an MBA (Ulster). He has been director of Redburn Solutions Ltd since March 2012. He has previously worked for Women in Business NI Ltd,North Eastern Education and Library Board, Resolute Public Affairs Partnership, Northern Ireland Library Authority, DSE Engagement, DELL Computers Incorporated and BT.

Hugh Wiseman, Director. **Gender : Male**

Mr Hugh Wiseman is Director responsible for ehealth applications and Europenan funded Projects. He has been director of Redburn Solutions Ltd since 2009. He is currently project managing the technology of two FP7 research project focussed on Midwifery. These projects, iResearch4Birth and Optibirth involve managing the technology for Communities of Practice and Knowledge Transfer Partnership for 36 Universities worldwide utilising web2 open source technologies, From 2007 to 2009 he was a NIDirect Implementation Manager responsible for data migration from Directgov to NIdirect and ensuring the web portal services all public facing content from all Government Departments in Northern Ireland. Implementation of the project within budget and timescale.

Relevant publications, and/or products, services or other achievements

1. New National Library service, with Internet for the public in every Library, designed and implemented, €70M Electronic Libraries Programme as a Private Finance Initiative. Enabled over 900,000 library members to have access to social media.
2. Designed and implemented a New Educational Product – BrightLightOn enabling Software as a Service and linking of database and service users.
3. Under a EuroStars 2015 project designing and building a new right brain psychological test for the 14 Massachusetts Institute of Technology characteristics of an Entrepreneur.
4. Design and implementation of the a €600M Private Finance Initiative Building Schools in the Greater Belfast Area. This included all services within the buildings including assessment of disability needs etc.
5. Design and Implementation of NIDirect in Northern Ireland. A Portal delivering all NI Government services to the Public.

Relevant previous projects

1. European project Eurovet Project Manager 1996- 1999

2. European project Eurovet II Project Manager 1999- 2000
    a. Bulgaria implementation 2001 – 2001
    b. Eurovet Trial in Estonia, Latvia and Lithuania 2001 –2003
    c. Bosnia implementation manager 2003 –2003
    d. Lithuania implementation manager 2004 – 2004
    e. Turkey implementation manager 2005 – leaving e-blana
3. European project FP4 /FP5 Project Management of Bulgarian National Veterinarian Service 650K€
4. European project FP4 /FP5 Lithuanian Veterinarian Service 1.07M€
5. European project FP7 Project Manager for **Optibirth.** Midwifery project ongoing.

Participant No 22: Swansea University (SU)

Swansea University
Swansea University was founded in 1920. Swansea University Medical School is a UK top 10 medical school, ranked 1st in the UK for research environment and 2nd in the UK for overall research quality.

SAIL (Secure Anonymised Information Linkage) is a world-class, anonymous data linkage system that securely brings together the widest possible array of routinely-collected data for research, development and evaluation in Wales. Robust Governance arrangements underpin all areas of their work so that SAIL represents a valuable data resource, whilst complying with data protection legislation and confidentiality guidelines. SAIL was established in 2006 and is part of the Swansea University Medical School. and they work closely with policy-makers, regulatory and statutory bodies, public service professionals, the private sector, and many academic and research groups.

Tasks
To work in WP2 to link data from the "Congenital Anomaly Register and Information Service for Wales" to datasets on mortality/hospital discharge data/prescriptions/education data and to provide aggregated tables and analysis. To help with the interpretation and provide comments on any papers that subsequently use the data provided and check that any aggregated data on the website is correct.

Daniel Thayer, Senior Data Analyst. **Gender : Male**
Mr Daniel Thayer is a senior data analyst working on the SAIL database at Swansea University Medical School. His responsibilities include data quality, documentation, supporting projects and providing guidance on using the SAIL system. He works with researchers to articulate their research requirements of the SAIL Databank and supports the training and development of analysts. He provides the user view to all SAIL system developments. Dan's background as a software engineer drives him to develop better tools for linked data analysis, which includes leading the International Health Data Linkage Network Technical Working Group. He is a member of all of the major SAIL committees and worked on the previously funded EUROmediCAT project. He will be supervising a junior data analyst.

Sue Jordan, Professor . **Gender : Female**
Sue Jordan has long standing experience in medicines' management, adverse drug reactions, adverse events and biosciences in nursing. She is a member of the EUROmediCAT consortium which successfully linked medication exposures in pregnancy to subsequent pregnancy outcomes to evaluate the risk of congenital anomalies in the fetuses. She is experienced in working with the SAIL database and will be advising the analysts in SAIL on aspects of coding and interpretation. Her track record of publications in professional journals will assist in project dissemination. She has recently joined the NICE Panel of Expert Advisers for the NICE Centre for Guidelines and the ENCePP Special Interest Group (SIG) on Measuring the Impact of Pharmacovigilance Activities. She is patient safety lead for the community nursing research strategy, primary and emergency care centre, Wales.

Relevant Previous Publications

1. Sayers A, Thayer D, Harvey JN, Luzio S, Atkinson MD, French R, Warner JT, Dayan CM, Wong SF, Gregory JW (2015). Evidence for a persistent, major excess in all cause admissions to hospital in children with type-1 diabetes: results from a large Welsh national matched community cohort study. *BMJ Open* 5(4), e005644-e005644.
2. de Jonge L, Garne E, Gini R, Jordan SE, Klungsoyr K, Loane M, Neville AJ, Pierini A, Puccini A, Thayer DS, Tucker D, Vinkel Hansen A, Bakker MK (2015). Improving Information on Maternal Medication Use by Linking Prescription Data to Congenital Anomaly Registers: A EUROmediCAT Study. *Drug Safety* 38(11), 1083-1093.
3. Jones KH, Ford DV, Jones C, Dsilva R, Thompson S, Brooks CJ, Heaven ML, Thayer DS, McNerney CL, Lyons RA (2014). A case study of the Secure Anonymous Information Linkage (SAIL) Gateway: A privacy-protecting remote access system for health-related research and evaluation. *Journal of Biomedical Informatics* 50, 196-204.
4. Garne E, Vinkel Hansen A, Morris J, Jordan S, Klungsøyr K, Engeland A, Tucker D, Thayer DS, Davies GI, Nybo Andersen AM, Dolk H. Risk of congenital anomalies after exposure to asthma medication in the first trimester of pregnancy – a cohort linkage study. BJOG. 2016 May 12. doi: 10.1111/1471-0528.14026
5. Jordan S, Watkins A, Storey M, Allen SJ, Brooks CJ, Garaiova I, Heaven ML, Jones R, Plummer SF, Russell IT, Thornton CA, Morgan G. (2013) Volunteer Bias in Recruitment, Retention, and Blood Sample Donation in a Randomised Controlled Trial Involving Mothers and Their Children at Six Months and Two Years: A Longitudinal Analysis. PLoS ONE 8(7): e67912. doi:10.1371/journal.pone.0067912

Relevant Previous Projects

1. EUROmediCAT: Safety of Medication Use in Pregnancy in Relation to Risk of Congential Malformations. 2011 – 2014. FP7-HEALTH-2010-single-stage. Dolk H., de Jong van den Berg L., de Vries C., Bakker M., Garne E., Raducha B., Pierini A., Jordan S., with S. Jordan, M. Morgan, R. Lyons, A. Watkins, D. Tucker, J. Greenacre, G. Morgan
2. Evaluation to identify the health benefits for social care clients attending an integrated Health and Social Care day care unit. 2010 - 2012 Centre for Nursing Innovation Initiative project, fostering links between clinicians and the university. Based in Hywel Dda Health Board., with J. Bowen, F. Murphy, S. Jordan, T. Morrissey, S. Davies, K. Manning,
3. Children and Young People's Research Network, WORD, Research Development Group Pregnancy, childbirth, infant feeding and medicines. 2012 – 2013. S. Jordan, G. Morgan, M. Morgan, S. Emery, A. Watkins, C. Begley, M. Davies, L. Rees, F. Majoko, A. Brown, I. Russell, M. Hyatt, F. Murphy, C. Phillips, M. Storey, R. Davies, J. Hanley, M. Heaven, L. Howard, R. Charlton, C. de Vries.
4. Probiotics in the prevention of childhood atopy: Electronic follow up of a double-blind randomised controlled trial. SME industrial parternes, Cultech Ltd 2012 - 2013 with M. Gravenor, C. Li, S. Plummer, I. Garaiova G. Davies.

4.2 Third parties involved in the project (including use of third party resources)

We declare that selection of subcontractors will conform to competitive selection in compliance with the rules of the beneficiary and H2020 (Article 13 of Grant Agreement), while respecting applicable rules on conflict of interest (Article 35 of the Grant Agreement).

Does the participant plan to subcontract certain tasks	Yes
Aside from those mentioned below, no other participant will subcontract on EUROlinkCAT **Partner 1 (QMUL)** will subcontract access to 4 UK data registries; CAROBB (€97788), EMSYCAR (€113214), WANDA (€128843) and SWCAR (€170158). The costs here pay for staff time to check linked data, confirm any data discrepancies, answer data queries from the researchers in WP3,4,5 and 6 and aid in the interpretation of their data in all papers, as well as travel to project meetings (where relevant). We declare that the selection of subcontractors will follow EU and QMUL procurement policy **Partner 6 (KDB)** will subcontract IT services to link to data sets in Croatia (€35100). **Partner 14 (OMNI-NET)** will subcontract to develop, update and run the software for data input and linkage (€2000). **Partner 16 (INSA)** will subcontract access and linkage between Portuguese congenital anomalies registry data and morbidity data (€50291).	
Does the participant envisage that part of its work is performed by linked third parties[9]	Yes
Aside from those mentioned below, no other participant will have a linked third party working on EUROlinkCAT **Partner 7 (CNR-IFC)** Estimated costs: Direct personnel costs declared as actual costs € 35,885.00; Indirect costs € 8,971.25; Total costs € 44,856.25. Agenzia regionale di sanità della Toscana (ARS) is an agency of the regional government of Tuscany. It performs epidemiological and health services research, and has access to the administrative health care data of the Tuscan population. ARS will provide record linkage between its databases and the CNR-IFC registry, and in particular ensure Data descriptions, Ethics, Standardisation of variables, Creation of linked dataset, Production of short linkage report, Production of output tables for WP3, WP4 hospital and WP4 prescription. CNR-IFC and ARS have a long-standing synergistic partnership. ARS is responsible for the database query and the linkage between data from different sources to integrate data of the Tuscany Registry of Congenital Defects. **Partner 19 (Asociacion Instituto Biodonostia)** Estimated costs: Direct personnel costs declared as actual costs € 12,500; Indirect cost € 3,125; Total costs €15,625 The Basque Government will participate in the project as linked third party of BIOEF. The Department of Health of the Basque Government is the employer of Larraitz Arriola and is responsible for the payment of her salary costs. This relationship by nature is broad and is not limited to the present action. The Principal Investigator's salary will be claimed as an eligible cost under the project's budget as third party's costs and it will be declared by the third party in a separate financial statement (Form C).	
Does the participant envisage the use of contributions in kind provided by third parties (Articles 11 and 12 of the General Model Grant Agreement)	Yes

Aside from those mentioned below, no other participant will have a third party providing resources in kind free of charge or against payment on EUROlinkCAT

Partner 1 (QMUL)
Miriam Gatt from the **Directorate of Health Information and Research** Strategy and Sustainability Division, Ministry for Health, Malta will provide linked data from **Malta**. These resources will be provided as in-kind contribution free of charge to the coordinating beneficiary (QMUL). The work will be carried out at the premises of the Directorate of Health Information and Research. The estimated effort is 0.5 person months of Miriam's time equating to a value provided in-kind, free of charge of €6,563. This will not be a reported cost as the resources are provided free of charge.

5. Ethics and Security

5.1 Ethics

5.1.1 Ethical Issues Overview

This study does not involve carrying out any clinical interventions or procedures, and does not involve biologic material. The study will analyse existing data generated by health services. There will be no contact with patients.

Twenty one EUROCAT congenital anomaly registers from 13 countries will participate in EUROlinkCAT. All these registries already have the correct ethics permission and procedures for data collection and transmission of anonymised data to a central database, according to national guidelines (see appendix 1 for summary details; all ethics permissions will be submitted before starting the project). Local registries follow national legislation as to whether parental consent is needed for registration of babies with anomalies (Busby A, Ritvanen A, Dolk H et al. Survey of informed consent for registration of congenital anomalies in Europe. BMJ 2005; 331:141-1). All registries have demonstrated that they can securely store and protect this data. Each registry will be responsible for applying for and obtaining the additional ethics and other permissions required to link their data to one or more electronic data bases on mortality, e-health records, prescriptions and education to create a linked standardised dataset. Some information on morbidity and mortality for the first year of life is already held by registries, but this project is using new methods of collecting and improving the quality of the information held.

5.1.2 Independent Ethics and Data Protection Board (EDPB)

An Ethics and Data Protection Board (EDPB) will be appointed led by Professor Allan Hackshaw, Deputy Director of the Cancer Research UK and UCL cancer trials centre and an additional professor (or professional of equivalent standing) who has experience of the issues involved in data linkage projects and is independent from any of the partners. The members of the EDPB will be provided with all documentation concerning ethics or data management. An annual report will be prepared and submitted to the EDPB summarising any existing ethics or data management issues and the EDPB will meet annually face to face with the Management Team to discuss outstanding issues. A report by the EDPB will be submitted with the financial reports. The EDPB will provide advice to ensure that EUROlinkCAT will be compliant with the EU General Data Protection Regulation (Regulation (EU) 2016/679) when it comes into force. A final report suitable for publication will be produced highlighting the different legal and ethics requirements for the data linkage across Europe.

5.1.3 Detailed Ethics Issues

There are four distinct stages for which the ethics and data management issues will be considered separately: the registration of children born with congenital anomalies, the linkage of children with CA with other data , the creation and analysis of a database of aggregated linked data and finally the future uses of such data.

1. Registration of Children born with Congenital Anomalies

All the 21 Congenital Anomaly Registries involved in EUROlinkCAT are established registries and as such already have the correct ethics permission and procedures for data collection and storage of the data. At present only two congenital anomaly registries require informed consent to register the child with a congenital anomaly (Isle de la Reunion and Northern

Netherlands Registry), the remaining registries do not require this and rely on national legislation for permission to collect this information without informed consent. All registries will be required to provide evidence of their existing ethics permission and procedures for data collection to the lead of Work Package 2 before the start of the project. If, during the length of the project, there are any changes in data collection procedures or other procedures (perhaps due to the UK leaving the EU) with potential ethical implications it is the responsibility of each registry to notify the lead of Work Package 2. All evidence will be examined to ensure all registries comply with Horizon 2020 and EU regulations, particularly the non-EU registry in the Ukraine. The EDPB will be provided with all this information and it will be available to the Commission for Ethics Checks or Audits.

2. Linkage of children born with congenital anomalies with information from National Electronic Databases and the storage of this data

An initial scoping exercise involving all the registries to assess the quality and availability of the data to be linked will be performed and a common protocol will be developed for the linkage to ensure that only essential information is collected (Task 1 WP2). The common protocol will specify the analyses that will be performed on the data in order to obtain approval for these analyses to be performed. Another data protection issue is data accuracy. The project will seek to collect data of the highest quality, but where deficiencies in data quality are unavoidable, to make those deficiencies transparent. Each Congenital Anomaly Registry will use the common protocol to apply for permission to link their data to one or more of their national electronic data bases on mortality, e-health records, prescriptions and education and to perform the specified analyses on it (Task 1 WP 2). All such linked data will be anonymised (unless the EDPB considers that there are valid reasons for not doing this) and then stored securely according to local and National guidelines. UU will provide guidance and advice on the applications. However, each registry will ultimately be responsible for obtaining the linkage and storage permission. Evidence of such permissions will need to be submitted to the leader of WP2 and also be available to the EDPB. It is envisaged that such permissions will be obtained nationally for 19 of the registries. For the two congenital anomaly registries requiring informed consent to register the child with a congenital anomaly additional processes may be required to gain permission for the linkage to occur. In these circumstances all additional forms and information sheets will need to be submitted to the leader of WP2 and the EDPB for particular consideration.

3. Analysis of the linked data – Secondary Use

Each registry will create aggregate data and perform specific analyses on each standardised data set. The aggregated data and analytical results will be submitted to the Central Results Repository to enable pan-European analyses to be performed combining the individual aggregated data and analytic results. Although all the data is anonymised, with such rare anomalies aggregated data can be considered disclosive (for example if there was only 1 child with a specific anomaly in a country and if they died before the age of 1, then producing an aggregated table showing deaths before 1 year of age would disclose information about that child to other people). Therefore the aggregated data will also need to be treated as if it contains personal information. Each registry will need to obtain permissions to transfer this data to the Central Results Repository at UU. These permissions will be requested as part of the linkage permissions mentioned in 2 above. In addition ethics permission from the University of Ulster ethics committee in relation to holding the aggregated Central Results Repository and its use for research will be applied for by the leader of WP2. Where extracts are made for the various work packages from the Central Results Repository, only the data necessary to the work package will be extracted, and work package leaders will need to provide evidence of sufficient data security and archiving

procedures specified by the Leader of WP2. All permissions, including those applicable to the Central registry, will be reviewed by the EDPB. Secondary suppression will be applied to all tables of results to prohibit possible identification of any individuals.

4. Future Uses of the Linked Data

Each registry will continue to be responsible for their own linked data and the storage, use and destruction of it must comply with their own local and national legislation. It will not be the responsibility of the EUROlinkCAT project after the completion of the project. The leader of each WP will be responsible for ensuring the destruction of any data they received from the Central Results Repository five years after the completion of the EUROlinkCAT project. The EUROlinkCAT Management Team will be responsible for obtaining the necessary permissions for the storage, use and destruction of the aggregated data in the Central Results Repository. In order to ensure that such a valuable resource will be available for future researchers the model successfully employed by EUROCAT will be adopted: Researchers may apply for the use of this data and a scientific committee will determine if such applications are scientifically sound. If so each individual registry will be approached for permission to use the data they contributed. Once the researcher has obtained the necessary ethics permissions the data will be provided to the researcher. One member from the EUROlinkCAT project must be included as a collaborator in all research using EUROlinkCAT data to ensure that the data is used and interpreted correctly. Destruction of the data will occur after 20 years, as which point it is believed such data will no longer be of use.

The central EUROCAT database on congenital malformations is stored on the JRC platform in Ispra (Italy). This data base holds an anonymised set of congenital anomaly cases from each EUROlinkCAT registry and it will be used to validate some of the results from the anonymised aggregated central repository in this EUROlinkCAT project.

5.1.4 Incidental Findings

Incidental findings are previously undiagnosed medical or psychiatric conditions that are discovered unintentionally. This will not occur in this project as only data on recorded diagnoses will be analysed. There will not be access to any new information that could lead to a different diagnosis.

5.1.5 Data Management Plan

A detailed data management plan will be developed in WP2 (Task 1) to cover data collection, storage, protection, retention and destruction. This plan needs to comply with all national and EU legislation. Each registry will be required to provide confirmation by the competent Institutional Data Protection Officer and/or authorization or notification by the National Data Protection Authority (which ever applies according to the Data Protection Directive (EC Directive 95/46, still applicable till May the 24th 2018 and the national law)

5.1.6 Ethics Documentation

A complete portfolio of copies of Informed Consent Forms and Information Sheets that cover all aspects of the research by all of the partners of the Consortium throughout the lifetime of the project will be compiled and retained by the Consortium (WP 1 Task 8). An ethics management table will be completed for each registry to keep a track of all documentation.

5.1.7 Details of individual ethics and informed consent for all registries in EUROlinkCAT

Belgium:

Antwerp Registry: The registries' procedure was presented to the Belgian privacy committee. In this procedure that was agreed the registry provides information to the parents on aims and methods of registration, data protection and the right to opt out. If the parents don't opt out the data are registered. The registry does not require ethics committee approval in order to operate. No additional ethics committee approval is required for studies that use not- identifiable data.
Information on the registration of CA is given to the parents by medically qualified staff treating the child and other HCPs treating the child.

Croatia:
Zagreb Registry
At present the registry collects data as hospital statistics are needed for public health planning and for this informed consent is not required. In order to collect and store data for specific scientific projects the registry requires ethics committee approval from the Ethics Committee of the Children's University Hospital Zagreb and the Ethics Committee of Medical School University of Zagreb. Ethics committee approval was last obtained in 2007 for a scientific project funded by our Ministry of Health. We will apply for ethics permission for the EUROlinkCAT project as part of the work in WP2.

Denmark:
Odense Registry: registries and database linkages are done with approval from the Danish Data Protection Agency, no ethical approval, and no informed consent. Access to medical records needs permission from National Board of Health. For personal data protection, database linkage will take place inside "Statistics Denmark" and personal ID will be protected. Statistics Denmark is the central authority on Danish statistics. It is a state institution under the Ministry of Social Affairs and the Interior.

Finland:
According to the law on the nationwide person data health registers and the Person Data Act, no informed consent is needed for collection of identifiable case data into the national health care registers (these registers are specified by the law and statute). Thus no informed consent is required in order to register a baby with a congenital anomaly into the Registry. It is not allowed for the Registry to contact the registered persons or their families. Because of the legislation ethics committee approval in order to collect and store data in the national health care registers is neither required. It is obligatory for the health care personnel to notify the malformed cases.
It is possible to use the case data in the national health care registers for scientific studies with a specific permission from the register administrators (governmental authorities like THL). The data protection authority also gives a statement on each study. Studies using only register data from national registers +/- hospital registers do not require ethical approval, but whilst it is not obligatory it is usually highly recommended. Encrypted unidentifiable data are always preferably given out by THL instead of identifiable case data.

France:
Paris Registry and Isle de la Reunion Registry : The registries require ethics committee approval from the French National Committee of Freedom and Informatics (CNIL) in order to collect and store data. Review of procedures regarding confidentiality of data of these registries is overseen by both the French National Committee of Registries and the French National Committee of Informatics and

Freedom. The registries are allowed to register cases without explicit written consent of parents. Information letters are sent to chief of services for them to post in waiting rooms, patient rooms or other areas of the maternity in order to inform parents that anonymous data are recorded for cases of congenital anomalies

Germany:
Saxony Anhalt Registry: The registry has the ethics committee approval from the Medical Faculty, Otto-von-Guericke University, Magdeburg. Because of the data protection law in Germany, since 1992 national legislation requires informed consent in order to register a baby with a congenital anomaly. Parents have to agree to the inclusion of the child on the Register (opt-in).

Italy:
IMER registry and
Tuscany Registry:
Both registries are recognised as part of the Regional Health system information flow and regulated by Regional Laws. They operate in the same way as other pathology registers and mortality registries according to the Italian Law on data protection and privacy. (Decreto legislativo 196 /2003 art 24 punto 1C) and further clarified in Decreto Legge del 18/10/2012 n. 179 page 12
http://www.privacy.it/codiceprivacy.html#art23
Malta: The Superintendant of Public Health, within his legal responsibility, requires that a Malta Congenital Anomalies Register is kept in the interests of Public Health (DH circular 36/09). Ethics approval is needed prior to data being released for individual studies, projects or theses. Malta became an EU member in 2004 and complies with directive EC95/46. There is no national legislation requiring informed consent in order to register a baby with a congenital anomaly.

N Netherlands registry: consent is needed for registration of a congenital anomaly case, at which time consent for access to medical or pharmacy records is asked. Linkage with other databases is done through a trusted third party. Anonymous data from medical records can be used without consent.

Portugal:
South Portugal Registry: Data on cases is transmitted by attending doctors at hospital departments to the central registry and registered centrally without personal information. A specific numeric code permits linking
registry data with clinical data at local level by the attending medical doctor.

Spain:
Basque Registry: No ethics committee approval required to operate registry. No approval needed for studies that require identifiable patient data. The hospitals have an ethics committee if further ethical recommendations are considered necessary.
Legislation complies with EC95/46 Directive with respect to disease registers and surveillance since 1999. There is not national legislation requiring informed consent to register a baby with a congenital anomaly.
Valencia Registry: The registry is allowed to register cases without explicit written consent of parents. Information letters are sent to chief of clinical services for them to post in waiting rooms, patient rooms or other areas of the maternity in order to inform parents that anonymous data are recorded for
cases of congenital anomalies

UK (England):
NorCAS, EMSYCAR, SWCAR, CAROBB, WANDA registries have approval from the Confidentiality Advisory Group (CAG) to be exempted from obtaining informed consent. Ethics approval is being sought to link to the specified databases and generate a linked, de-identified research database to enable research into the health, mortality and educational outcomes of congenital anomalies. The linkage and storage of the combined English registers will occur at QMUL with each register receiving a de-identified research database of the data from their registry. QMUL operates with security measures including passworded computers, passworded backup, and a locked office with security lock, under the responsibility of the Data Protection Officer for QMUL.

UK (Wales): The register (CARIS) is exempted from obtaining informed consent. All data emanate from existing databases. There will be no new data collection for this study. Data will be obtained from the Secure Anonymous Information Linkage (SAIL) databank, linking CARIS and primary care data, using the Blue C supercomputer. Participants' identities will be split from clinical data. Identities will be passed to Health Solutions Wales, where NHS numbers will be verified, anonymised and returned to SAIL to be re-united with clinical data (Ford et al 2009, Lyons et al 2009). *Ford DV, Jones KH, Verplancke JP,Lyons RA, John G, Brown G, Brooks CJ, Thompson S, Bodger O, Couch T, Leake K. The SAIL Databank:building a national architecture for e-health research and evaluation. BMC Health Services Research2009;9:157 doi:10.1186/1472-6963-9-157.* http://www.biomedcentral.com/1472-6963/9/157*. Lyons RA, Jones KH, John G, Brooks CJ, Verplancke JP, Ford DV, Brown G, Leake K. The SAIL databank: linking multiple health and social care datasets. BMC Medical Informatics and Decision* 69 *Making 2009; 9:3.* http://www.biomedcentral.com/1472-6947/9/3 Integrated Research Application System (IRAS) documentation for the study will need to be completed before work can commence.

Ukraine:
Registration of birth defects and follow-up is an integral part of health care protocols. The registry does not require ethics committee approval in order to collect and store data. National legislation does not require informed consent in order to register a baby with a congenital anomaly.

5.2 Security[1]

Please indicate if your project will involve:

☐ activities or results raising security issues: (NO)

[1] Article 37.1 of the Model Grant Agreement: *Before disclosing results of activities raising security issues to a third party (including affiliated entities), a beneficiary must inform the coordinator — which must request written approval from the Commission/Agency.* Article 37.2: *Activities related to 'classified deliverables' must comply with the 'security requirements' until they are declassified. Action tasks related to classified deliverables may not be subcontracted without prior explicit written approval from the Commission/Agency. The beneficiaries must inform the coordinator — which must immediately inform the Commission/Agency — of any changes in the security context and — if necessary —request for Annex 1 to be amended (see Article 55*

- 'EU-classified information' as background or results: (NO)

6. References

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ESTIMATED BUDGET FOR THE ACTION (page 1 of 2)

	Estimated eligible[1] costs (per budget category)									EU contribution			Additional information		
	A. Direct personnel costs				B. Direct costs of subcontracting	C. Direct costs of fin. support	D. Other direct costs	E. Indirect costs[2]	Total costs	Reimbursement rate %	Maximum EU contribution[3]	Maximum grant amount[4]	Information for indirect costs	Information for auditors	Other information:
	A.1 Employees (or equivalent) A.2 Natural persons under direct contract A.3 Seconded persons [A.6 Personnel for providing access to research infrastructure]		A.4 SME owners without salary A.5 Beneficiaries that are natural persons without salary				D.1 Travel D.2 Equipment D.3 Other goods and services D.4 Costs of large research infrastructure						Estimated costs of in-kind contributions not used on premises	Declaration of costs under Point D.4	Estimated costs of beneficiaries/ linked third parties not receiving EU funding
Form of costs[6]	Actual	Unit[7]	Unit[8]		Actual	Actual	Actual	Flat-rate[9] 25%							
	(a)	Total (b)	No hours	Total (c)	(d)	(e)	(f)	(g)=0,25x ((a)+(b)+ (c)+(f) +[(h1)+(h2)]- (m))	(i)= (a)+(b)+(c)+ (d)+(e)+(f)+ (g)+(h1)+(h2)+(h3)	(j)	(k)	(l)	(m)	Yes/No	
1. QMUL	1262596.00	0.00	0	0.00	510003.00	0.00	198741.00	365334.25	2336674.25	100.00	2336674.25	2336674.25	0.00	No	
2. UU	1051008.00	0.00	0	0.00	0.00	0.00	71027.00	280508.75	1402543.75	100.00	1402543.75	1402543.75	0.00	No	
3. RSD	445750.00	0.00	0	0.00	0.00	0.00	68552.00	128575.50	642877.50	100.00	642877.50	642877.50	0.00	No	
4. UNEW	403835.00	0.00	0	0.00	0.00	0.00	43265.00	111775.00	558875.00	100.00	558875.00	558875.00	0.00	No	
5. UNIFE	222314.00	0.00	0	0.00	0.00	0.00	52260.00	68643.50	343217.50	100.00	343217.50	343217.50	0.00	No	
6. KDB	55040.00	0.00	0	0.00	35100.00	0.00	32160.00	21800.00	144100.00	100.00	144100.00	144100.00	0.00	No	
7. CNR-IFC	104119.00	0.00	0	0.00	0.00	0.00	20366.00	31121.25	155606.25	100.00	155606.25	155606.25	0.00	No	
- ARS[14]	35885.00	0.00	0	0.00	0.00	0.00	0.00	8971.25	44856.25	100.00	44856.25	44856.25	0.00	No	
Total beneficiary 7	140004.00	0.00			0.00	0.00	20366.00	40092.50	200462.50		200462.50	200462.50	0.00		
8. UMCG	222845.00	0.00	0	0.00	0.00	0.00	32366.00	63802.75	319013.75	100.00	319013.75	319013.75	0.00	No	
9. PHW NHS	16000.00	0.00	0	0.00	0.00	0.00	2126.00	4531.50	22657.50	100.00	22657.50	22657.50	0.00	No	
10. INSERM	18900.00	0.00	0	0.00	0.00	0.00	2126.00	5256.50	26282.50	100.00	26282.50	26282.50	0.00	No	
11. FISABIO	91344.00	0.00	0	0.00	0.00	0.00	2126.00	23367.50	116837.50	100.00	116837.50	116837.50	0.00	No	
12. PUMS	65000.00	0.00	0	0.00	0.00	0.00	46020.00	27755.00	138775.00	100.00	138775.00	138775.00	0.00	No	
13. THL	203530.00	0.00	0	0.00	0.00	0.00	68626.00	68039.00	340195.00	100.00	340195.00	340195.00	0.00	No	
14. OMNI NET	26344.00	0.00	0	0.00	2000.00	0.00	6052.00	8099.00	42495.00	100.00	42495.00	42495.00	0.00	No	
15. OVGU	24120.00	0.00	0	0.00	0.00	0.00	18109.00	10557.25	52786.25	100.00	52786.25	52786.25	0.00	No	
16. INSA	36304.00	0.00	0	0.00	50291.00	0.00	2126.00	9607.50	98328.50	100.00	98328.50	98328.50	0.00	No	
17. CHURéunion	50004.00	0.00	0	0.00	0.00	0.00	4926.00	13732.50	68662.50	100.00	68662.50	68662.50	0.00	No	
18. PIH	38340.00	0.00	0	0.00	0.00	0.00	2126.00	10116.50	50582.50	100.00	50582.50	50582.50	0.00	No	
19. BIOEF	56500.00	0.00	0	0.00	0.00	0.00	2126.00	14656.50	73282.50	100.00	73282.50	73282.50	0.00	No	
- BasqueGov[14]	12500.00	0.00	0	0.00	0.00	0.00	0.00	3125.00	15625.00	100.00	15625.00	15625.00	0.00	No	
Total beneficiary 19	69000.00	0.00			0.00	0.00	2126.00	17781.50	88907.50		88907.50	88907.50	0.00		
20. BIOMED	88548.00	0.00	0	0.00	0.00	0.00	21910.00	27614.50	138072.50	100.00	138072.50	138072.50	0.00	No	
21. Redburn	51840.00	0.00	0	0.00	0.00	0.00	14070.00	16477.50	82387.50	100.00	82387.50	82387.50	0.00	No	
22. SU	104545.00	0.00	0	0.00	0.00	0.00	2126.00	26667.75	133338.75	100.00	133338.75	133338.75	0.00	No	
Total consortium	4687211.00	0.00		0.00	597394.00	0.00	713332.00	1350135.75	7348072.75		7348072.75	7348072.75	0.00		0.00

ESTIMATED BUDGET FOR THE ACTION (page 2 of 2)

(1) See Article 6 for the eligibility conditions
(2) The indirect costs covered by the operating grant (received under any EU or Euratom funding programme; see Article 6.5.(b)) are ineligible under the GA. Therefore, a beneficiary that receives an operating grant during the action's duration cannot declare indirect costs for the year(s)/reporting period(s) covered by the operating grant (see Article 6.2.E).
(3) This is the theoretical amount of EU contribution that the system calculates automatically (by multiplying all the budgeted costs by the reimbursement rate). This theoretical amount is capped by the 'maximum grant amount' (that the Commission/Agency decided to grant for the action) (see Article 5.1).
(4) The 'maximum grant amount' is the maximum grant amount decided by the Commission/Agency. It normally corresponds to the requested grant, but may be lower.
(5) Depending on its type, this specific cost category will or will not cover indirect costs. Specific unit costs that include indirect costs are: costs for energy efficiency measures in buildings, access costs for providing trans-national access to research infrastructure and costs for clinical studies.
(6) See Article 5 for the forms of costs
(7) Unit : hours worked on the action; costs per unit (hourly rate) : calculated according to beneficiary's usual accounting practice
(8) See Annex 2a 'Additional information on the estimated budget' for the details (costs per hour (hourly rate)).
(9) Flat rate : 25% of eligible direct costs, from which are excluded: direct costs of subcontracting, costs of in-kind contributions not used on premises, direct costs of financial support, and unit costs declared under budget category F if they include indirect costs
(10) See Annex 2a 'Additional information on the estimated budget' for the details (units, costs per unit).
(11) See Annex 2a 'Additional information on the estimated budget' for the details (units, costs per unit, estimated number of units, etc)
(12) Only specific unit costs that do not include indirect costs
(13) See Article 9 for beneficiaries not receiving EU funding
(14) Only for linked third parties that receive EU funding

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

UNIVERSITY OF ULSTER (UU) GB22, RC000726, established in CROMORE ROAD, COLERAINE BT52 1SA, United Kingdom, VAT number GB672390524, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('2')

in Grant Agreement No 733001 ('the Agreement')

between QUEEN MARY UNIVERSITY OF LONDON **and** the European Union ('the EU'), represented by the European Commission ('the Commission'),

for the action entitled 'EUROlinkCAT: Establishing a linked European Cohort of Children with Congenital Anomalies (EUROlinkCAT)'.

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement the grant in accordance with the Agreement, with all the obligations and conditions it sets out ('accession date') — if the Commission agrees with the request for amendment.

SIGNATURE

For the beneficiary

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

REGION SYDDANMARK (RSD), 29190909, established in DAMHAVEN 12, VEJLE 7100, Denmark, VAT number DK29190909, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('3')

in Grant Agreement No 733001 ('the Agreement')

between QUEEN MARY UNIVERSITY OF LONDON **and** the European Union ('the EU'), represented by the European Commission ('the Commission'),

for the action entitled 'EUROlinkCAT: Establishing a linked European Cohort of Children with Congenital Anomalies (EUROlinkCAT)'.

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement the grant in accordance with the Agreement, with all the obligations and conditions it sets out ('accession date') — if the Commission agrees with the request for amendment.

SIGNATURE

For the beneficiary

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

UNIVERSITY OF NEWCASTLE UPON TYNE (UNEW), established in KINGS GATE, NEWCASTLE UPON TYNE NE1 7RU, United Kingdom, VAT number GB499672470, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('4')

in Grant Agreement No 733001 ('the Agreement')

between QUEEN MARY UNIVERSITY OF LONDON **and** the European Union ('the EU'), represented by the European Commission ('the Commission'),

for the action entitled 'EUROlinkCAT: Establishing a linked European Cohort of Children with Congenital Anomalies (EUROlinkCAT)'.

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement the grant in accordance with the Agreement, with all the obligations and conditions it sets out ('accession date') — if the Commission agrees with the request for amendment.

SIGNATURE

For the beneficiary

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

UNIVERSITA DEGLI STUDI DI FERRARA (UNIFE), established in VIA ARIOSTO 35, FERRARA 44121, Italy, VAT number IT00434690384, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('5')

in Grant Agreement No 733001 ('the Agreement')

between QUEEN MARY UNIVERSITY OF LONDON **and** the European Union ('the EU'), represented by the European Commission ('the Commission'),

for the action entitled 'EUROlinkCAT: Establishing a linked European Cohort of Children with Congenital Anomalies (EUROlinkCAT)'.

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement the grant in accordance with the Agreement, with all the obligations and conditions it sets out ('accession date') — if the Commission agrees with the request for amendment.

SIGNATURE

For the beneficiary

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

KLINIKA ZA DJECJE BOLESTI ZAGREB (KDB) HR6, 080797139, established in KLAICEVA 16, ZAGREB HR-10000, Croatia, VAT number HR70641763756, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('6')

in Grant Agreement No 733001 ('the Agreement')

between QUEEN MARY UNIVERSITY OF LONDON **and** the European Union ('the EU'), represented by the European Commission ('the Commission'),

for the action entitled 'EUROlinkCAT: Establishing a linked European Cohort of Children with Congenital Anomalies (EUROlinkCAT)'.

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement the grant in accordance with the Agreement, with all the obligations and conditions it sets out ('accession date') — if the Commission agrees with the request for amendment.

SIGNATURE

For the beneficiary

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

CONSIGLIO NAZIONALE DELLE RICERCHE (CNR-IFC), 80054330586, established in PIAZZALE ALDO MORO 7, ROMA 00185, Italy, VAT number IT02118311006, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('7')

in Grant Agreement No 733001 ('the Agreement')

between QUEEN MARY UNIVERSITY OF LONDON **and** the European Union ('the EU'), represented by the European Commission ('the Commission'),

for the action entitled 'EUROlinkCAT: Establishing a linked European Cohort of Children with Congenital Anomalies (EUROlinkCAT)'.

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement the grant in accordance with the Agreement, with all the obligations and conditions it sets out ('accession date') — if the Commission agrees with the request for amendment.

SIGNATURE

For the beneficiary

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

ACADEMISCH ZIEKENHUIS GRONINGEN (UMCG), 01169570, established in HANZEPLEIN 1, GRONINGEN 9713 GZ, Netherlands, VAT number NL800866393B01, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('8')

in Grant Agreement No 733001 ('the Agreement')

between QUEEN MARY UNIVERSITY OF LONDON **and** the European Union ('the EU'), represented by the European Commission ('the Commission'),

for the action entitled 'EUROlinkCAT: Establishing a linked European Cohort of Children with Congenital Anomalies (EUROlinkCAT)'.

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement the grant in accordance with the Agreement, with all the obligations and conditions it sets out ('accession date') — if the Commission agrees with the request for amendment.

SIGNATURE

For the beneficiary

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

PUBLIC HEALTH WALES NATIONAL HEALTH SERVICE TRUST (PHW NHS), -, established in CHARNWOOD COURT UNIT 1 PARC, CARDIFF CF11 9LJ, United Kingdom, VAT number GB654439854, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('9')

in Grant Agreement No 733001 ('the Agreement')

between QUEEN MARY UNIVERSITY OF LONDON **and** the European Union ('the EU'), represented by the European Commission ('the Commission'),

for the action entitled 'EUROlinkCAT: Establishing a linked European Cohort of Children with Congenital Anomalies (EUROlinkCAT)'.

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement the grant in accordance with the Agreement, with all the obligations and conditions it sets out ('accession date') — if the Commission agrees with the request for amendment.

SIGNATURE

For the beneficiary

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MEDICALE (INSERM), 180036048, established in RUE DE TOLBIAC 101, PARIS 75654, France, VAT number FR31180036048, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('10')

in Grant Agreement No 733001 ('the Agreement')

between QUEEN MARY UNIVERSITY OF LONDON **and** the European Union ('the EU'), represented by the European Commission ('the Commission'),

for the action entitled 'EUROlinkCAT: Establishing a linked European Cohort of Children with Congenital Anomalies (EUROlinkCAT)'.

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement the grant in accordance with the Agreement, with all the obligations and conditions it sets out ('accession date') — if the Commission agrees with the request for amendment.

SIGNATURE

For the beneficiary

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

FUNDACION PARA EL FOMENTO DE LA INVESTIGACION SANITARIA Y BIOMEDICA DELA COMUNITAT VALENCIANA (FISABIO) ES3, 501V, established in CALLE MICER MASCO 31, VALENCIA 46010, Spain, VAT number ESG98073760, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('11')

in Grant Agreement No 733001 ('the Agreement')

between QUEEN MARY UNIVERSITY OF LONDON **and** the European Union ('the EU'), represented by the European Commission ('the Commission'),

for the action entitled 'EUROlinkCAT: Establishing a linked European Cohort of Children with Congenital Anomalies (EUROlinkCAT)'.

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement the grant in accordance with the Agreement, with all the obligations and conditions it sets out ('accession date') — if the Commission agrees with the request for amendment.

SIGNATURE

For the beneficiary

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

UNIWERSYTET MEDYCZNY IM KAROLA MARCINKOWSKIEGO W POZNANIU (PUMS), established in UL. FREDRY 10, POZNAN 61 701, Poland, VAT number PL7770003104, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('12')

in Grant Agreement No 733001 ('the Agreement')

between QUEEN MARY UNIVERSITY OF LONDON **and** the European Union ('the EU'), represented by the European Commission ('the Commission'),

for the action entitled 'EUROlinkCAT: Establishing a linked European Cohort of Children with Congenital Anomalies (EUROlinkCAT)'.

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement the grant in accordance with the Agreement, with all the obligations and conditions it sets out ('accession date') — if the Commission agrees with the request for amendment.

SIGNATURE

For the beneficiary

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

TERVEYDEN JA HYVINVOINNIN LAITOS (THL), 22295006, established in MANNERHEIMINTIE 166, HELSINKI 00271, Finland, VAT number FI22295006, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('13')

in Grant Agreement No 733001 ('the Agreement')

between QUEEN MARY UNIVERSITY OF LONDON **and** the European Union ('the EU'), represented by the European Commission ('the Commission'),

for the action entitled 'EUROlinkCAT: Establishing a linked European Cohort of Children with Congenital Anomalies (EUROlinkCAT)'.

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement the grant in accordance with the Agreement, with all the obligations and conditions it sets out ('accession date') — if the Commission agrees with the request for amendment.

SIGNATURE

For the beneficiary

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

INTERNATIONAL CHARITABLE FUND OMNI-NET FOR CHILDREN (OMNI NET) UA5, 33334985, established in 16 LYPNYA ST 36, RIVNE 33028, Ukraine, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('14')

in Grant Agreement No 733001 ('the Agreement')

between QUEEN MARY UNIVERSITY OF LONDON **and** the European Union ('the EU'), represented by the European Commission ('the Commission'),

for the action entitled 'EUROlinkCAT: Establishing a linked European Cohort of Children with Congenital Anomalies (EUROlinkCAT)'.

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement the grant in accordance with the Agreement, with all the obligations and conditions it sets out ('accession date') — if the Commission agrees with the request for amendment.

SIGNATURE

For the beneficiary

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

OTTO-VON-GUERICKE-UNIVERSITAET MAGDEBURG (OVGU), GESETZ 07/10/1993, established in UNIVERSITAETSPLATZ 2, MAGDEBURG 39106, Germany, VAT number DE139238413, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('15')

in Grant Agreement No 733001 ('the Agreement')

between QUEEN MARY UNIVERSITY OF LONDON **and** the European Union ('the EU'), represented by the European Commission ('the Commission'),

for the action entitled 'EUROlinkCAT: Establishing a linked European Cohort of Children with Congenital Anomalies (EUROlinkCAT)'.

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement the grant in accordance with the Agreement, with all the obligations and conditions it sets out ('accession date') — if the Commission agrees with the request for amendment.

SIGNATURE

For the beneficiary

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

INSTITUTO NACIONAL DE SAUDE DR. RICARDO JORGE (INSA), 271, established in AVENIDA PADRE CRUZ, LISBOA 1600 560, Portugal, VAT number PT501427511, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('16')

in Grant Agreement No 733001 ('the Agreement')

between QUEEN MARY UNIVERSITY OF LONDON **and** the European Union ('the EU'), represented by the European Commission ('the Commission'),

for the action entitled 'EUROlinkCAT: Establishing a linked European Cohort of Children with Congenital Anomalies (EUROlinkCAT)'.

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement the grant in accordance with the Agreement, with all the obligations and conditions it sets out ('accession date') — if the Commission agrees with the request for amendment.

SIGNATURE

For the beneficiary

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

CENTRE HOSPITALIER UNIVERSITAIRE DE LA REUNION (CHURéunion), 200030013, established in BELLEPIERRE, ALL DES TOPAZES, SAINT-DENIS 97400, France, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('17')

in Grant Agreement No 733001 ('the Agreement')

between QUEEN MARY UNIVERSITY OF LONDON **and** the European Union ('the EU'), represented by the European Commission ('the Commission'),

for the action entitled 'EUROlinkCAT: Establishing a linked European Cohort of Children with Congenital Anomalies (EUROlinkCAT)'.

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement the grant in accordance with the Agreement, with all the obligations and conditions it sets out ('accession date') — if the Commission agrees with the request for amendment.

SIGNATURE

For the beneficiary

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

PROVINCIAAL INSTITUUT VOOR HYGIENE (PIH), established in KRONENBURGSTRAAT 45, ANTWERPEN 2000, Belgium, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('18')

in Grant Agreement No 733001 ('the Agreement')

between QUEEN MARY UNIVERSITY OF LONDON **and** the European Union ('the EU'), represented by the European Commission ('the Commission'),

for the action entitled 'EUROlinkCAT: Establishing a linked European Cohort of Children with Congenital Anomalies (EUROlinkCAT)'.

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement the grant in accordance with the Agreement, with all the obligations and conditions it sets out ('accession date') — if the Commission agrees with the request for amendment.

SIGNATURE

For the beneficiary

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

ASOCIACION INSTITUTO BIODONOSTIA (BIOEF) ES5, AS/G/15251/2010, established in Paseo Dr. Beguiristain s/n, DONOSTIA-SAN SEBASTIAN 20014, Spain, VAT number ES G-75020313, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('19')

in Grant Agreement No 733001 ('the Agreement')

between QUEEN MARY UNIVERSITY OF LONDON **and** the European Union ('the EU'), represented by the European Commission ('the Commission'),

for the action entitled 'EUROlinkCAT: Establishing a linked European Cohort of Children with Congenital Anomalies (EUROlinkCAT)'.

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement the grant in accordance with the Agreement, with all the obligations and conditions it sets out ('accession date') — if the Commission agrees with the request for amendment.

SIGNATURE

For the beneficiary

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

BIOMEDICAL COMPUTING LIMITED (BIOMED) LTD, 03148645, established in INNOVATION CENTRE HIGHFIELD DRIVE CHURCHFIELDS, ST LEONARDS ON SEA EAST SUSSEX TN38 9UH, United Kingdom, VAT number GB724664328, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('20')

in Grant Agreement No 733001 ('the Agreement')

between QUEEN MARY UNIVERSITY OF LONDON **and** the European Union ('the EU'), represented by the European Commission ('the Commission'),

for the action entitled 'EUROlinkCAT: Establishing a linked European Cohort of Children with Congenital Anomalies (EUROlinkCAT)'.

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement the grant in accordance with the Agreement, with all the obligations and conditions it sets out ('accession date') — if the Commission agrees with the request for amendment.

SIGNATURE

For the beneficiary

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

REDBURN SOLUTIONS LIMITED (Redburn) LTD, NI611699, established in INNOVATION CENTRE NOTHERN IRELAND SCIENCE PARK, BELFAST BT3 9DT, United Kingdom, VAT number GB136893870, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('21')

in Grant Agreement No 733001 ('the Agreement')

between QUEEN MARY UNIVERSITY OF LONDON **and** the European Union ('the EU'), represented by the European Commission ('the Commission'),

for the action entitled 'EUROlinkCAT: Establishing a linked European Cohort of Children with Congenital Anomalies (EUROlinkCAT)'.

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement the grant in accordance with the Agreement, with all the obligations and conditions it sets out ('accession date') — if the Commission agrees with the request for amendment.

SIGNATURE

For the beneficiary

ANNEX 3

ACCESSION FORM FOR BENEFICIARIES

SWANSEA UNIVERSITY (SU) GB22, established in SINGLETON PARK, SWANSEA SA2 8PP, United Kingdom, VAT number GB123853477, ('the beneficiary'), represented for the purpose of signing this Accession Form by the undersigned,

hereby agrees

to become beneficiary No ('22')

in Grant Agreement No 733001 ('the Agreement')

between QUEEN MARY UNIVERSITY OF LONDON **and** the European Union ('the EU'), represented by the European Commission ('the Commission'),

for the action entitled 'EUROlinkCAT: Establishing a linked European Cohort of Children with Congenital Anomalies (EUROlinkCAT)'.

and mandates

the coordinator to submit and sign in its name and on its behalf any **amendments** to the Agreement, in accordance with Article 55.

By signing this Accession Form, the beneficiary accepts the grant and agrees to implement the grant in accordance with the Agreement, with all the obligations and conditions it sets out ('accession date') — if the Commission agrees with the request for amendment.

SIGNATURE

For the beneficiary

ⓘ print format A4 landscape

MODEL ANNEX 4 FOR H2020 GENERAL MGA — MULTI

FINANCIAL STATEMENT FOR *[BENEFICIARY [name]/ LINKED THIRD PARTY [name]]* FOR REPORTING PERIOD [reporting period]

	Eligible[1] costs (per budget category)										Receipts	EU contribution			Additional information
	A. Direct personnel costs				B. Direct costs of subcontracting	*[C. Direct costs of fin. support]*	D. Other direct costs		E. Indirect costs[2]	*[F. Costs of …]*	Total costs	Receipts	Reimbursement rate %	Maximum EU contribution[3]	Requested EU contribution	Information for indirect costs :
	A.1 Employees (or equivalent) A.2 Natural persons under direct contract A.3 Seconded persons *[A.6 Personnel for providing access to research infrastructure]*		A.4 SME owners without salary A.5 Beneficiaries that are natural persons without salary				D.1 Travel D.2 Equipment D.3 Other goods and services	*[D.4 Costs of large research infrastructure]*		*[F.1 Costs of …]*		Receipts of the action, to be reported in the last reporting period, according to Article 5.3.3				Costs of in-kind contributions not used on premises
Form of costs[4]	Actual	Unit	Unit		Actual	Actual	Actual	Actual	Flat-rate[5] 25%	Unit	Unit					
	a	Total b	No hours	Total c	d	*[e]*	f	*[g]*	h=0,25 x (a+b+ c+f+*[g]* + *[i1]*[6] +*[i2]*[6] - o)	No units	Total *[i1]*	Total *[i2]*	j = a+b+c+d+*[e]* +f +*[g]* +h+*[i1]* +*[i2]*	k	l	m	n	o
[short name beneficiary/linked third party]																

The beneficiary/linked third party hereby confirms that:
The information provided is complete, reliable and true.
The costs declared are eligible (see Article 6).
The costs can be substantiated by adequate records and supporting documentation that will be produced upon request or in the context of checks, reviews, audits and investigations (see Articles 17, 18 and 22).
For the last reporting period: that all the receipts have been declared (see Article 5.3.3).

ⓘ Please declare all eligible costs, even if they exceed the amounts indicated in the estimated budget (see Annex 2). Only amounts that were declared in your individual financial statements can be taken into account lateron, in order to replace other costs that are found to be ineligible.

[1] See Article 6 for the eligibility conditions

[2] The indirect costs claimed must be free of any amounts covered by an operating grant (received under any EU or Euratom funding programme; see Article 6.2.E). If you have received an operating grant during this reporting period, you cannot claim any indirect costs.

[3] This is the *theoretical* amount of EU contribution that the system calculates automatically (by multiplying the reimbursement rate by the total costs declared). The amount you request (in the column 'requested EU contribution') may have to be less (e.g. if you and the other beneficiaries are above budget, if the 90% limit (see Article 21) is reached, etc).

[4] See Article 5 for the form of costs

[5] Flat rate : 25% of eligible direct costs, from which are excluded: direct costs of subcontracting, costs of in-kind contributions not used on premises, direct costs of financial support, and unit costs declared under budget category F if they include indirect costs (see Article 6.2.E)

[6] Only specific unit costs that do not include indirect costs

ANNEX 5

MODEL FOR THE CERTIFICATE ON THE FINANCIAL STATEMENTS

- **For options [*in italics in square brackets*]: choose the applicable option. Options not chosen should be deleted.**
- **For fields in [grey in square brackets]: enter the appropriate data**

TABLE OF CONTENTS

Terms of Reference for an Independent Report of Factual Findings on costs declared under a Grant Agreement financed under the Horizon 2020 Research and Innovation Framework Programme

This document sets out the '**Terms of Reference (ToR)**' under which

[OPTION 1: [insert name of the beneficiary] ('the Beneficiary')] [OPTION 2: [insert name of the linked third party] ('the Linked Third Party'), third party linked to the Beneficiary [insert name of the beneficiary] ('the Beneficiary')]

agrees to engage

[**insert legal name of the auditor**] ('the Auditor')

to produce an independent report of factual findings ('the Report') concerning the Financial Statement(s)[1] drawn up by the *[Beneficiary] [Linked Third Party]* for the Horizon 2020 grant agreement [insert number of the grant agreement, title of the action, acronym and duration from/to] ('the Agreement'), and

to issue a Certificate on the Financial Statements' ('CFS') referred to in Article 20.4 of the Agreement based on the compulsory reporting template stipulated by the Commission.

The Agreement has been concluded under the Horizon 2020 Research and Innovation Framework Programme (H2020) between the Beneficiary and *[OPTION 1: the European Union, represented by the European Commission ('the Commission')][OPTION 2: the European Atomic Energy Community (Euratom,) represented by the European Commission ('the Commission')][OPTION 3: the [Research Executive Agency (REA)] [European Research Council Executive Agency (ERCEA)] [Innovation and Networks Executive Agency (INEA)] [Executive Agency for Small and Medium-sized Enterprises (EASME)] ('the Agency'), under the powers delegated by the European Commission ('the Commission').]*

[1] By which costs under the Agreement are declared (see template 'Model Financial Statements' in Annex 4 to the Grant Agreement).

The *[Commission] [Agency]* is mentioned as a signatory of the Agreement with the Beneficiary only. The *[European Union][Euratom][Agency]* is not a party to this engagement.

1.1 Subject of the engagement

The coordinator must submit to the *[Commission][Agency]* the final report within 60 days following the end of the last reporting period which should include, amongst other documents, a CFS for each beneficiary and for each linked third party that requests a total contribution of EUR 325 000 or more, as reimbursement of actual costs and unit costs calculated on the basis of its usual cost accounting practices (see Article 20.4 of the Agreement). The CFS must cover all reporting periods of the beneficiary or linked third party indicated above.

The Beneficiary must submit to the coordinator the CFS for itself and for its linked third party(ies), if the CFS must be included in the final report according to Article 20.4 of the Agreement..

The CFS is composed of two separate documents:

- The Terms of Reference ('the ToR') to be signed by the *[Beneficiary] [Linked Third Party]* and the Auditor;
- The Auditor's Independent Report of Factual Findings ('the Report') to be issued on the Auditor's letterhead, dated, stamped and signed by the Auditor (or the competent public officer) which includes the agreed-upon procedures ('the Procedures') to be performed by the Auditor, and the standard factual findings ('the Findings') to be confirmed by the Auditor.

If the CFS must be included in the final report according to Article 20.4 of the Agreement, the request for payment of the balance relating to the Agreement cannot be made without the CFS. However, the payment for reimbursement of costs covered by the CFS does not preclude the *[Commission,][Agency,]* the European Anti-Fraud Office and the European Court of Auditors from carrying out checks, reviews, audits and investigations in accordance with Article 22 of the Agreement.

1.2 Responsibilities

The *[Beneficiary] [Linked Third Party]:*

- must draw up the Financial Statement(s) for the action financed by the Agreement in compliance with the obligations under the Agreement. The Financial Statement(s) must be drawn up according to the *[Beneficiary's] [Linked Third Party's]* accounting and book-keeping system and the underlying accounts and records;
- must send the Financial Statement(s) to the Auditor;
- is responsible and liable for the accuracy of the Financial Statement(s);
- is responsible for the completeness and accuracy of the information provided to enable the Auditor to carry out the Procedures. It must provide the Auditor with a written representation letter supporting these statements. The written representation letter must state the period covered by the statements and must be dated;
- accepts that the Auditor cannot carry out the Procedures unless it is given full access to the *[Beneficiary's] [Linked Third Party's]* staff and accounting as well as any other relevant records and documentation.

The Auditor:

- *[Option 1 by default:* is qualified to carry out statutory audits of accounting documents in accordance with Directive 2006/43/EC of the European Parliament and of the Council of 17 May 2006 on statutory audits of annual accounts and consolidated accounts, amending Council Directives 78/660/EEC and 83/349/EEC and repealing Council Directive 84/253/EEC or similar national regulations*]*.
- *[Option 2 if the Beneficiary or Linked Third Party has an independent Public Officer:* is a competent and independent Public Officer for which the relevant national authorities have established the legal capacity to audit the Beneficiary*].*
- *[Option 3 if the Beneficiary or Linked Third Party is an international organisation:* is an [internal] [external] auditor in accordance with the internal financial regulations and procedures of the international organisation*].*

The Auditor:

- must be independent from the Beneficiary *[and the Linked Third Party]*, in particular, it must not have been involved in preparing the *[Beneficiary's] [Linked Third Party's]* Financial Statement(s);
- must plan work so that the Procedures may be carried out and the Findings may be assessed;
- must adhere to the Procedures laid down and the compulsory report format;
- must carry out the engagement in accordance with this ToR;
- must document matters which are important to support the Report;
- must base its Report on the evidence gathered;
- must submit the Report to the *[Beneficiary] [Linked Third Party]*.

The Commission sets out the Procedures to be carried out by the Auditor. The Auditor is not responsible for their suitability or pertinence. As this engagement is not an assurance engagement, the Auditor does not provide an audit opinion or a statement of assurance.

1.3 Applicable Standards

The Auditor must comply with these Terms of Reference and with[2]:

- the International Standard on Related Services ('ISRS') 4400 *Engagements to perform Agreed-upon Procedures regarding Financial Information* as issued by the International Auditing and Assurance Standards Board (IAASB);
- the *Code of Ethics for Professional Accountants* issued by the International Ethics Standards Board for Accountants (IESBA). Although ISRS 4400 states that independence is not a requirement for engagements to carry out agreed-upon procedures, the *[Commission][Agency]* requires that the Auditor also complies with the Code's independence requirements.

The Auditor's Report must state that there is no conflict of interests in establishing this Report between the Auditor and the Beneficiary *[and the Linked Third Party]*, and must specify - if the service is invoiced - the total fee paid to the Auditor for providing the Report.

1.4 Reporting

The Report must be written in the language of the Agreement (see Article 20.7).

Under Article 22 of the Agreement, the [*Commission*] [*Agency*], the European Anti-Fraud Office and the Court of Auditors have the right to audit any work that is carried out under the action and for which costs are declared from [*the European Union*] [*Euratom*] budget. This includes work related to this engagement. The Auditor must provide access to all working papers (e.g. recalculation of hourly rates, verification of the time declared for the action) related to this assignment if the *[Commission] [Agency]*, the European Anti-Fraud Office or the European Court of Auditors requests them.

1.5 Timing

The Report must be provided by *[*dd Month yyyy*]*.

[2] Supreme Audit Institutions applying INTOSAI-standards may carry out the Procedures according to the corresponding International Standards of Supreme Audit Institutions and code of ethics issued by INTOSAI instead of the International Standard on Related Services ('ISRS') 4400 and the Code of Ethics for Professional Accountants issued by the IAASB and the IESBA.

1.6 Other terms

[*The [Beneficiary] [Linked Third Party] and the Auditor can use this section to agree other specific terms, such as the Auditor's fees, liability, applicable law, etc. Those specific terms must not contradict the terms specified above.*]

[legal name of the Auditor]	[legal name of the *[Beneficiary][Linked Third Party]*]
[name & function of authorised representative]	[name & function of authorised representative]
[dd Month yyyy]	[dd Month yyyy]
Signature of the Auditor	Signature of the *[Beneficiary][Linked Third Party]*

Independent Report of Factual Findings on costs declared under Horizon 2020 Research and Innovation Framework Programme

(To be printed on the Auditor's letterhead)

To

[name of contact person(s)], [Position]

[[*Beneficiary's*] [*Linked Third Party's*] name]

[Address]

[dd Month yyyy]

Dear [Name of contact person(s)],

As agreed under the terms of reference dated [dd Month yyyy]

with *[OPTION 1: [insert name of the beneficiary] ('the Beneficiary')] [OPTION 2: [insert name of the linked third party] ('the Linked Third Party'), third party linked to the Beneficiary [insert name of the beneficiary] ('the Beneficiary')],*

we

[name of the auditor] ('the Auditor'),

established at

[full address/city/state/province/country],

represented by

[name and function of an authorised representative],

have carried out the procedures agreed with you regarding the costs declared in the Financial Statement(s)[3] of the *[Beneficiary] [Linked Third Party]* concerning the grant agreement

[insert grant agreement reference: number, title of the action and acronym] ('the Agreement'),

with a total cost declared of

[total amount] EUR,

and a total of actual costs and 'direct personnel costs declared as unit costs calculated in accordance with the [*Beneficiary's*] [*Linked Third Party's*] usual cost accounting practices' declared of

[sum of total actual costs and total direct personnel costs declared as unit costs calculated in accordance with the *[Beneficiary's] [Linked Third Party's]* usual cost accounting practices] EUR

and **hereby provide our Independent Report of Factual Findings ('the Report')** using the compulsory report format agreed with you.

The Report

Our engagement was carried out in accordance with the terms of reference ('the ToR') appended to this Report. The Report includes the agreed-upon procedures ('the Procedures') carried out and the standard factual findings ('the Findings') examined.

The Procedures were carried out solely to assist the [*Commission*] [*Agency*] in evaluating whether the [*Beneficiary's*] [*Linked Third Party's*] costs in the accompanying Financial Statement(s) were declared in accordance with the Agreement. The *[Commission] [Agency]* draws its own conclusions from the Report and any additional information it may require.

[3] By which the Beneficiary declares costs under the Agreement (see template 'Model Financial Statement' in Annex 4 to the Agreement).

The scope of the Procedures was defined by the Commission. Therefore, the Auditor is not responsible for their suitability or pertinence. Since the Procedures carried out constitute neither an audit nor a review made in accordance with International Standards on Auditing or International Standards on Review Engagements, the Auditor does not give a statement of assurance on the Financial Statements.

Had the Auditor carried out additional procedures or an audit of the *[Beneficiary's] [Linked Third Party's]* Financial Statements in accordance with International Standards on Auditing or International Standards on Review Engagements, other matters might have come to its attention and would have been included in the Report.

Not applicable Findings

We examined the Financial Statement(s) stated above and considered the following Findings not applicable:

Explanation (to be removed from the Report):

*If a Finding was not applicable, it must be marked as '**N.A**.' ('Not applicable') in the corresponding row on the right-hand column of the table and means that the Finding did not have to be corroborated by the Auditor and the related Procedure(s) did not have to be carried out.*

The reasons of the non-application of a certain Finding must be obvious i.e.

i) if no cost was declared under a certain category then the related Finding(s) and Procedure(s) are not applicable;

ii) if the condition set to apply certain Procedure(s) are not met the related Finding(s) and those Procedure(s) are not applicable. For instance, for 'beneficiaries with accounts established in a currency other than euro' the Procedure and Finding related to 'beneficiaries with accounts established in euro' are not applicable. Similarly, if no additional remuneration is paid, the related Finding(s) and Procedure(s) for additional remuneration are not applicable.

List here all Findings considered not applicable for the present engagement and explain the reasons of the non-applicability.

….

Exceptions

Apart from the exceptions listed below, the *[Beneficiary] [Linked Third Party]* provided the Auditor all the documentation and accounting information needed by the Auditor to carry out the requested Procedures and evaluate the Findings.

Explanation (to be removed from the Report):

- *If the Auditor was not able to successfully complete a procedure requested, it must be marked as '**E**' ('Exception') in the corresponding row on the right-hand column of the table. The reason such as the inability to reconcile key information or the unavailability of data that prevents the Auditor from carrying out the Procedure must be indicated below.*
- *If the Auditor cannot corroborate a standard finding after having carried out the corresponding procedure, it must also be marked as '**E**' ('Exception') and, where possible, the reasons why the Finding was not fulfilled and its possible impact must be explained here below.*

List here any exceptions and add any information on the cause and possible consequences of each exception, if known. If the exception is quantifiable, include the corresponding amount.

….

Example (to be removed from the Report):

1. *The Beneficiary was unable to substantiate the Finding number 1 on … because ….*
2. *Finding number 30 was not fulfilled because the methodology used by the Beneficiary to calculate unit costs was different from the one approved by the Commission. The differences were as follows: …*
3. *After carrying out the agreed procedures to confirm the Finding number 31, the Auditor found a difference of _____ EUR. The difference can be explained by …*

Further Remarks

In addition to reporting on the results of the specific procedures carried out, the Auditor would like to make the following general remarks:

Example (to be removed from the Report):

1. *Regarding Finding number 8 the conditions for additional remuneration were considered as fulfilled because …*
2. *In order to be able to confirm the Finding number 15 we carried out the following additional procedures: ….*

Use of this Report

This Report may be used only for the purpose described in the above objective. It was prepared solely for the confidential use of the *[Beneficiary] [Linked Third Party]* and the [*Commission*] [*Agency*], and only to be submitted to the [*Commission*] [*Agency*] in connection with the requirements set out in Article 20.4 of the Agreement. The Report may not be used by the *[Beneficiary] [Linked Third Party]* or by the [*Commission*] [*Agency*] for any other purpose, nor may it

be distributed to any other parties. The [*Commission*] [*Agency*] may only disclose the Report to authorised parties, in particular to the European Anti-Fraud Office (OLAF) and the European Court of Auditors.

This Report relates only to the Financial Statement(s) submitted to the *[Commission] [Agency]* by the *[Beneficiary] [Linked Third Party]* for the Agreement. Therefore, it does not extend to any other of the [*Beneficiary's*] [*Linked Third Party's*] Financial Statement(s).

There was no conflict of interest[4] between the Auditor and the Beneficiary *[and Linked Third Party]* in establishing this Report. The total fee paid to the Auditor for providing the Report was EUR _____ (including EUR_____ of deductible VAT).

We look forward to discussing our Report with you and would be pleased to provide any further information or assistance.

[legal name of the Auditor]

[name and function of an authorised representative]

[dd Month yyyy]

Signature of the Auditor

[4] A conflict of interest arises when the Auditor's objectivity to establish the certificate is compromised in fact or in appearance when the Auditor for instance:
- was involved in the preparation of the Financial Statements;
- stands to benefit directly should the certificate be accepted;
- has a close relationship with any person representing the beneficiary;
- is a director, trustee or partner of the beneficiary; or
- is in any other situation that compromises his or her independence or ability to establish the certificate impartially.

Agreed-upon procedures to be performed and standard factual findings to be confirmed by the Auditor

The European Commission reserves the right to i) provide the auditor with additional guidance regarding the procedures to be followed or the facts to be ascertained and the way in which to present them (this may include sample coverage and findings) or to ii) change the procedures, by notifying the Beneficiary in writing. The procedures carried out by the auditor to confirm the standard factual finding are listed in the table below.

If this certificate relates to a Linked Third Party, any reference here below to 'the Beneficiary' is to be considered as a reference to 'the Linked Third Party'.

The 'result' column has three different options: 'C', 'E' and 'N.A.':

- 'C' stands for 'confirmed' and means that the auditor can confirm the 'standard factual finding' and, therefore, there is no exception to be reported.
- 'E' stands for 'exception' and means that the Auditor carried out the procedures but cannot confirm the 'standard factual finding', or that the Auditor was not able to carry out a specific procedure (e.g. because it was impossible to reconcile key information or data were unavailable),
- 'N.A.' stands for 'not applicable' and means that the Finding did not have to be examined by the Auditor and the related Procedure(s) did not have to be carried out. The reasons of the non-application of a certain Finding must be obvious i.e. i) if no cost was declared under a certain category then the related Finding(s) and Procedure(s) are not applicable; ii) if the condition set to apply certain Procedure(s) are not met then the related Finding(s) and Procedure(s) are not applicable. For instance, for 'beneficiaries with accounts established in a currency other than the euro' the Procedure related to 'beneficiaries with accounts established in euro' is not applicable. Similarly, if no additional remuneration is paid, the related Finding(s) and Procedure(s) for additional remuneration are not applicable.

Ref	Procedures	Standard factual finding	Result (C / E / N.A.)
A	**ACTUAL PERSONNEL COSTS AND UNIT COSTS CALCULATED BY THE BENEFICIARY IN ACCORDANCE WITH ITS USUAL COST ACCOUNTING PRACTICE**		

Ref	Procedures	Standard factual finding	Result (C / E / N.A.)
	The Auditor draws a sample of persons whose costs were declared in the Financial Statement(s) to carry out the procedures indicated in the consecutive points of this section A. (*The sample should be selected randomly so that it is representative. Full coverage is required if there are fewer than 10 people (including employees, natural persons working under a direct contract and personnel seconded by a third party), otherwise the sample should have a minimum of 10 people, or 10% of the total, whichever number is the highest)* The Auditor sampled _____ people out of the total of _____ people.		
A.1	**PERSONNEL COSTS** <u>For the persons included in the sample and working under an employment contract or equivalent act (general procedures for individual actual personnel costs and personnel costs declared as unit costs)</u> To confirm standard factual findings 1-5 listed in the next column, the Auditor reviewed following information/documents provided by the Beneficiary: ○ a list of the persons included in the sample indicating the period(s) during which they worked for the action, their position (classification or category) and type of contract; ○ the payslips of the employees included in the sample; ○ reconciliation of the personnel costs declared in the Financial Statement(s) with the accounting system (project accounting and general ledger) and payroll system; ○ information concerning the employment status and employment conditions of personnel included in the sample, in particular their employment contracts or equivalent;	1) The employees were i) directly hired by the Beneficiary in accordance with its national legislation, ii) under the Beneficiary's sole technical supervision and responsibility and iii) remunerated in accordance with the Beneficiary's usual practices.	
		2) Personnel costs were recorded in the Beneficiary's accounts/payroll system.	
		3) Costs were adequately supported and reconciled with the accounts and payroll	

Ref	Procedures	Standard factual finding	Result (C / E / N.A.)
	○ the Beneficiary's usual policy regarding payroll matters (e.g. salary policy, overtime policy, variable pay); ○ applicable national law on taxes, labour and social security and ○ any other document that supports the personnel costs declared. The Auditor also verified the eligibility of all components of the retribution (see Article 6 GA) and recalculated the personnel costs for employees included in the sample.	records.	
		4) Personnel costs did not contain any ineligible elements.	
		5) There were no discrepancies between the personnel costs charged to the action and the costs recalculated by the Auditor.	
	Further procedures if 'additional remuneration' is paid To confirm standard factual findings 6-9 listed in the next column, the Auditor: ○ reviewed relevant documents provided by the Beneficiary (legal form, legal/statutory obligations, the Beneficiary's usual policy on additional remuneration, criteria used for its calculation…); ○ recalculated the amount of additional remuneration eligible for the action based on the supporting documents received (full-time or part-time work, exclusive or non-exclusive dedication to the action, etc.) to arrive at the applicable FTE/year and pro-rata rate (see data collected in the course of carrying out the procedures under A.2 'Productive hours' and A.4 'Time recording system').	6) The Beneficiary paying "additional remuneration" was a non-profit legal entity.	
		7) The amount of additional remuneration paid corresponded to the Beneficiary's usual remuneration practices and was consistently paid whenever the same kind of work or expertise was required.	

Ref	Procedures	Standard factual finding	Result (C / E / N.A.)
	IF ANY PART OF THE REMUNERATION PAID TO THE EMPLOYEE IS NOT MANDATORY ACCORDING TO THE NATIONAL LAW OR THE EMPLOYMENT CONTRACT ("ADDITIONAL REMUNERATION") AND IS ELIGIBLE UNDER THE PROVISIONS OF ARTICLE 6.2.A.1, THIS CAN BE CHARGED AS ELIGIBLE COST TO THE ACTION UP TO THE FOLLOWING AMOUNT: *(A) IF THE PERSON WORKS FULL TIME AND EXCLUSIVELY ON THE ACTION DURING THE FULL YEAR: UP TO EUR 8 000/YEAR;* *(B) IF THE PERSON WORKS EXCLUSIVELY ON THE ACTION BUT NOT FULL-TIME OR NOT FOR THE FULL YEAR: UP TO THE CORRESPONDING PRO-RATA AMOUNT OF EUR 8 000, OR* *(C) IF THE PERSON DOES NOT WORK EXCLUSIVELY ON THE ACTION: UP TO A PRO-RATA AMOUNT CALCULATED IN ACCORDANCE TO ARTICLE 6.2.A.1.*	8) The criteria used to calculate the additional remuneration were objective and generally applied by the Beneficiary regardless of the source of funding used.	
		9) The amount of additional remuneration included in the personnel costs charged to the action was capped at EUR 8,000 per FTE/year (up to the equivalent pro-rata amount if the person did not work on the action full-time during the year or did not work exclusively on the action).	
	Additional procedures in case "unit costs calculated by the Beneficiary in accordance with its usual cost accounting practices" is applied: Apart from carrying out the procedures indicated above to confirm standard factual findings 1-5 and, if applicable, also 6-9, the Auditor carried out following procedures to confirm standard factual findings 10-13 listed in the next column:	10) The personnel costs included in the Financial Statement were calculated in accordance with the Beneficiary's usual cost accounting practice. This methodology was consistently used in all H2020 actions.	

Ref	Procedures	Standard factual finding	Result (C / E / N.A.)
	○ obtained a description of the Beneficiary's usual cost accounting practice to calculate unit costs;. ○ reviewed whether the Beneficiary's usual cost accounting practice was applied for the Financial Statements subject of the present CFS; ○ verified the employees included in the sample were charged under the correct category (in accordance with the criteria used by the Beneficiary to establish personnel categories) by reviewing the contract/HR-record or analytical accounting records; ○ verified that there is no difference between the total amount of personnel costs used in calculating the cost per unit and the total amount of personnel costs recorded in the statutory accounts; ○ verified whether actual personnel costs were adjusted on the basis of budgeted or estimated elements and, if so, verified whether those elements used are actually relevant for the calculation, objective and supported by documents.	11) The employees were charged under the correct category.	
		12) Total personnel costs used in calculating the unit costs were consistent with the expenses recorded in the statutory accounts.	
		13) Any estimated or budgeted element used by the Beneficiary in its unit-cost calculation were relevant for calculating personnel costs and corresponded to objective and verifiable information.	
	<u>For natural persons included in the sample and working with the Beneficiary under a direct contract other than an employment contract, such as consultants (no subcontractors).</u> To confirm standard factual findings 14-18 listed in the next column the Auditor reviewed following information/documents provided by the Beneficiary: ○ the contracts, especially the cost, contract duration, work description, place of work, ownership of the results and reporting obligations to the Beneficiary;	14) The natural persons reported to the Beneficiary (worked under the Beneficiary's instructions).	
		15) They worked on the Beneficiary's premises (unless otherwise agreed with the Beneficiary).	

Ref	Procedures	Standard factual finding	Result (C / E / N.A.)
	○ the employment conditions of staff in the same category to compare costs and; ○ any other document that supports the costs declared and its registration (e.g. invoices, accounting records, etc.).	16) The results of work carried out belong to the Beneficiary.	
		17) Their costs were not significantly different from those for staff who performed similar tasks under an employment contract with the Beneficiary.	
		18) The costs were supported by audit evidence and registered in the accounts.	
	<u>For personnel seconded by a third party and included in the sample (not subcontractors)</u> To confirm standard factual findings 19-22 listed in the next column, the Auditor reviewed following information/documents provided by the Beneficiary: ○ their secondment contract(s) notably regarding costs, duration, work description, place of work and ownership of the results; ○ if there is reimbursement by the Beneficiary to the third party for the resource made available (in-kind contribution against payment): any documentation that supports the costs declared (e.g. contract, invoice, bank payment, and proof of registration in its accounting/payroll, etc.) and reconciliation of the Financial Statement(s) with the accounting system (project accounting and general ledger) as well as any proof that the amount invoiced by the third party did not include any profit;	19) Seconded personnel reported to the Beneficiary and worked on the Beneficiary's premises (unless otherwise agreed with the Beneficiary).	
		20) The results of work carried out belong to the Beneficiary.	
		If personnel is seconded against payment: 21) The costs declared were supported with documentation and recorded in the	

Ref	Procedures	Standard factual finding	Result (C / E / N.A.)
	○ if there is no reimbursement by the Beneficiary to the third party for the resource made available (in-kind contribution free of charge): a proof of the actual cost borne by the Third Party for the resource made available free of charge to the Beneficiary such as a statement of costs incurred by the Third Party and proof of the registration in the Third Party's accounting/payroll; ○ any other document that supports the costs declared (e.g. invoices, etc.).	Beneficiary's accounts. The third party did not include any profit.	
		If personnel is seconded free of charge: 22) The costs declared did not exceed the third party's cost as recorded in the accounts of the third party and were supported with documentation.	
A.2	**PRODUCTIVE HOURS** To confirm standard factual findings 23-28 listed in the next column, the Auditor reviewed relevant documents, especially national legislation, labour agreements and contracts and time records of the persons included in the sample, to verify that: ○ the annual productive hours applied were calculated in accordance with one of the methods described below, ○ the full-time equivalent (FTEs) ratios for employees not working full-time were correctly calculated.	23) The Beneficiary applied method [*choose one option and delete the others*] [**A**: 1720 hours] [**B**: the 'total number of hours worked'] [**C**: 'annual productive hours' used correspond to usual accounting practices]	

Ref	Procedures	Standard factual finding	Result (C / E / N.A.)
	If the Beneficiary applied method B, the auditor verified that the correctness in which the total number of hours worked was calculated and that the contracts specified the annual workable hours. If the Beneficiary applied method C, the auditor verified that the 'annual productive hours' applied when calculating the hourly rate were equivalent to at least 90 % of the 'standard annual workable hours'. The Auditor can only do this if the calculation of the standard annual workable hours can be supported by records, such as national legislation, labour agreements, and contracts. *BENEFICIARY'S PRODUCTIVE HOURS' FOR PERSONS WORKING FULL TIME SHALL BE ONE OF THE FOLLOWING METHODS:* ***A.*** *1720 ANNUAL PRODUCTIVE HOURS (PRO-RATA FOR PERSONS NOT WORKING FULL-TIME)* ***B.*** *THE TOTAL NUMBER OF HOURS WORKED BY THE PERSON FOR THE BENEFICIARY IN THE YEAR (THIS METHOD IS ALSO REFERRED TO AS 'TOTAL NUMBER OF HOURS WORKED' IN THE NEXT COLUMN). THE CALCULATION OF THE TOTAL NUMBER OF HOURS WORKED WAS DONE AS FOLLOWS: ANNUAL WORKABLE HOURS OF THE PERSON ACCORDING TO THE EMPLOYMENT CONTRACT, APPLICABLE LABOUR AGREEMENT OR NATIONAL LAW PLUS OVERTIME WORKED MINUS ABSENCES (SUCH AS SICK LEAVE OR SPECIAL LEAVE).*	24) Productive hours were calculated annually.	
		25) For employees not working full-time the full-time equivalent (FTE) ratio was correctly applied.	
		If the Beneficiary applied method B. 26) The calculation of the number of 'annual workable hours', overtime and absences was verifiable based on the documents provided by the Beneficiary.	
		If the Beneficiary applied method C. 27) The calculation of the number of 'standard annual workable hours' was verifiable based on the documents provided by the Beneficiary.	

Ref	Procedures	Standard factual finding	Result (C / E / N.A.)
	C. THE STANDARD NUMBER OF ANNUAL HOURS GENERALLY APPLIED BY THE BENEFICIARY FOR ITS PERSONNEL IN ACCORDANCE WITH ITS USUAL COST ACCOUNTING PRACTICES (THIS METHOD IS ALSO REFERRED TO AS 'TOTAL ANNUAL PRODUCTIVE HOURS' IN THE NEXT COLUMN). THIS NUMBER MUST BE AT LEAST 90% OF THE STANDARD ANNUAL WORKABLE HOURS. *'ANNUAL WORKABLE HOURS' MEANS THE PERIOD DURING WHICH THE PERSONNEL MUST BE WORKING, AT THE EMPLOYER'S DISPOSAL AND CARRYING OUT HIS/HER ACTIVITY OR DUTIES UNDER THE EMPLOYMENT CONTRACT, APPLICABLE COLLECTIVE LABOUR AGREEMENT OR NATIONAL WORKING TIME LEGISLATION.*	28) The 'annual productive hours' used for calculating the hourly rate were consistent with the usual cost accounting practices of the Beneficiary and were equivalent to at least 90 % of the 'annual workable hours'.	
A.3	**HOURLY PERSONNEL RATES** <u>I) For unit costs calculated in accordance to the Beneficiary's usual cost accounting practice (unit costs):</u> If the Beneficiary has a "Certificate on Methodology to calculate unit costs " (CoMUC) approved by the Commission, the Beneficiary provides the Auditor with a description of the approved methodology and the Commission's letter of acceptance. The Auditor verified that the Beneficiary has indeed used the methodology approved. If so, no further verification is necessary. If the Beneficiary does not have a "Certificate on Methodology" (CoMUC) approved by the	29) The Beneficiary applied [*choose one option and delete the other*]: [Option I: "Unit costs (hourly rates) were calculated in accordance with the Beneficiary's usual cost accounting practices"] [Option II: Individual hourly rates were applied]	

Ref	Procedures	Standard factual finding	Result (C / E / N.A.)
	Commission, or if the methodology approved was not applied, then the Auditor: o reviewed the documentation provided by the Beneficiary, including manuals and internal guidelines that explain how to calculate hourly rates; o recalculated the unit costs (hourly rates) of staff included in the sample following the results of the procedures carried out in A.1 and A.2. II) For individual hourly rates: The Auditor: o reviewed the documentation provided by the Beneficiary, including manuals and internal guidelines that explain how to calculate hourly rates; o recalculated the hourly rates of staff included in the sample following the results of the procedures carried out in A.1 and A.2. *"UNIT COSTS CALCULATED BY THE BENEFICIARY IN ACCORDANCE WITH ITS USUAL COST ACCOUNTING PRACTICES":* *IT IS CALCULATED BY DIVIDING THE TOTAL AMOUNT OF PERSONNEL COSTS OF THE CATEGORY TO WHICH THE EMPLOYEE BELONGS VERIFIED IN LINE WITH PROCEDURE A.1 BY THE NUMBER OF FTE AND THE ANNUAL TOTAL PRODUCTIVE HOURS OF THE SAME CATEGORY CALCULATED BY THE BENEFICIARY IN ACCORDANCE WITH PROCEDURE A.2.* *HOURLY RATE FOR INDIVIDUAL ACTUAL PERSONAL COSTS:* *IT IS CALCULATED BY DIVIDING THE TOTAL AMOUNT OF PERSONNEL COSTS OF AN EMPLOYEE VERIFIED IN LINE WITH*	*For option I concerning unit costs and if the Beneficiary applies the methodology approved by the Commission (CoMUC):* 30) The Beneficiary used the Commission-approved methodology to calculate hourly rates. It corresponded to the organisation's usual cost accounting practices and was applied consistently for all activities irrespective of the source of funding.	
		For option I concerning unit costs and if the Beneficiary applies a methodology not approved by the Commission: 31) The unit costs re-calculated by the Auditor were the same as the rates applied by the Beneficiary.	
		For option II concerning individual hourly rates:	

Ref	Procedures	Standard factual finding	Result (C / E / N.A.)
	PROCEDURE A.1 BY THE NUMBER OF ANNUAL PRODUCTIVE HOURS VERIFIED IN LINE WITH PROCEDURE A.2.	32) The individual rates re-calculated by the Auditor were the same as the rates applied by the Beneficiary.	
A.4	**TIME RECORDING SYSTEM** To verify that the time recording system ensures the fulfilment of all minimum requirements and that the hours declared for the action were correct, accurate and properly authorised and supported by documentation, the Auditor made the following checks for the persons included in the sample that declare time as worked for the action on the basis of time records: o description of the time recording system provided by the Beneficiary (registration, authorisation, processing in the HR-system); o its actual implementation; o time records were signed at least monthly by the employees (on paper or electronically) and authorised by the project manager or another manager; o the hours declared were worked within the project period; o there were no hours declared as worked for the action if HR-records showed absence due to holidays or sickness (further cross-checks with travels are carried out in B.1 below) ;	33) All persons recorded their time dedicated to the action on a **daily/ weekly/ monthly** basis using a **paper/computer-based** system. (*delete the answers that are not applicable)*	
		34) Their time-records were authorised at least monthly by the project manager or other superior.	
		35) Hours declared were worked within the project period and were consistent with the presences/absences recorded in HR-records.	

Ref	Procedures	Standard factual finding	Result (C / E / N.A.)
	○ the hours charged to the action matched those in the time recording system. *ONLY THE HOURS WORKED ON THE ACTION CAN BE CHARGED. ALL WORKING TIME TO BE CHARGED SHOULD BE RECORDED THROUGHOUT THE DURATION OF THE PROJECT, ADEQUATELY SUPPORTED BY EVIDENCE OF THEIR REALITY AND RELIABILITY (SEE SPECIFIC PROVISIONS BELOW FOR PERSONS WORKING EXCLUSIVELY FOR THE ACTION WITHOUT TIME RECORDS).*	36) There were no discrepancies between the number of hours charged to the action and the number of hours recorded.	
	<u>If the persons are working exclusively for the action and without time records</u> For the persons selected that worked exclusively for the action without time records, the Auditor verified evidence available demonstrating that they were in reality exclusively dedicated to the action and that the Beneficiary signed a declaration confirming that they have worked exclusively for the action.	37) The exclusive dedication is supported by a declaration signed by the Beneficiary's and by any other evidence gathered.	
B	**COSTS OF SUBCONTRACTING**		
B.1	**The Auditor obtained the detail/breakdown of subcontracting costs and sampled _____ cost items selected randomly** (*full coverage is required if there are fewer than 10 items, otherwise the sample should have a minimum of 10 item, or 10% of the total, whichever number is highest*). To confirm standard factual findings 38-42 listed in the next column, the Auditor reviewed the	38) The use of claimed subcontracting costs was foreseen in Annex 1 and costs were declared in the Financial Statements under the subcontracting category.	

Ref	Procedures	Standard factual finding	Result (C / E / N.A.)
	following for the items included in the sample: o the use of subcontractors was foreseen in Annex 1; o subcontracting costs were declared in the subcontracting category of the Financial Statement; o supporting documents on the selection and award procedure were followed; o the Beneficiary ensured best value for money (key elements to appreciate the respect of this principle are the award of the subcontract to the bid offering best price-quality ratio, under conditions of transparency and equal treatment. In case an existing framework contract was used the Beneficiary ensured it was established on the basis of the principle of best value for money under conditions of transparency and equal treatment). In particular, i. if the Beneficiary acted as a contracting authority within the meaning of Directive 2004/18/EC or of Directive 2004/17/EC, the Auditor verified that the applicable national law on public procurement was followed and that the subcontracting complied with the Terms and Conditions of the Agreement. ii. if the Beneficiary did not fall under the above-mentioned category the Auditor verified that the Beneficiary followed their usual procurement rules and respected the Terms and Conditions of the Agreement.. For the items included in the sample the Auditor also verified that: o the subcontracts were not awarded to other Beneficiaries in the consortium;	39) There were documents of requests to different providers, different offers and assessment of the offers before selection of the provider in line with internal procedures and procurement rules. Subcontracts were awarded in accordance with the principle of best value for money. *(When different offers were not collected the Auditor explains the reasons provided by the Beneficiary under the caption "Exceptions" of the Report. The Commission will analyse this information to evaluate whether these costs might be accepted as eligible)*	
		40) The subcontracts were not awarded to other Beneficiaries of the consortium.	

Ref	Procedures	Standard factual finding	Result (C / E / N.A.)
	○ there were signed agreements between the Beneficiary and the subcontractor; ○ there was evidence that the services were provided by subcontractor;	41) All subcontracts were supported by signed agreements between the Beneficiary and the subcontractor.	
		42) There was evidence that the services were provided by the subcontractors.	
C	**COSTS OF PROVIDING FINANCIAL SUPPORT TO THIRD PARTIES**		
C.1	**The Auditor obtained the detail/breakdown of the costs of providing financial support to third parties and sampled _____ cost items selected randomly** (*full coverage is required if there are fewer than 10 items, otherwise the sample should have a minimum of 10 item, or 10% of the total, whichever number is highest*). The Auditor verified that the following minimum conditions were met: a) the maximum amount of financial support for each third party did not exceed EUR 60 000, unless explicitly mentioned in Annex 1; b) the financial support to third parties was agreed in Annex 1 of the Agreement and the other provisions on financial support to third parties included in Annex 1 were	43) All minimum conditions were met	

Ref	Procedures	Standard factual finding	Result (C / E / N.A.)
	respected.		

D	**OTHER ACTUAL DIRECT COSTS**		
D.1	**COSTS OF TRAVEL AND RELATED SUBSISTENCE ALLOWANCES** **The Auditor sampled _____ cost items selected randomly** (*full coverage is required if there are fewer than 10 items, otherwise the sample should have a minimum of 10 item, or 10% of the total, whichever number is the highest*). The Auditor inspected the sample and verified that: o travel and subsistence costs were consistent with the Beneficiary's usual policy for travel. In this context, the Beneficiary provided evidence of its normal policy for travel costs (e.g. use of first class tickets, reimbursement by the Beneficiary on the basis of actual costs, a lump sum or per diem) to enable the Auditor to compare the travel costs charged with this policy; o travel costs are correctly identified and allocated to the action (e.g. trips are directly linked to the action) by reviewing relevant supporting documents such as minutes of meetings, workshops or conferences, their registration in the correct project account, their consistency with time records or with the dates/duration of the workshop/conference; o no ineligible costs or excessive or reckless expenditure was declared.	44) Costs were incurred, approved and reimbursed in line with the Beneficiary's usual policy for travels.	
		45) There was a link between the trip and the action.	
		46) The supporting documents were consistent with each other regarding subject of the trip, dates, duration and reconciled with time records and accounting.	
		47) No ineligible costs or excessive or reckless expenditure was declared.	
D.2	**DEPRECIATION COSTS FOR EQUIPMENT, INFRASTRUCTURE OR OTHER ASSETS** **The Auditor sampled _____ cost items selected randomly** (*full coverage is required if there are fewer than 10 items, otherwise the sample should have a minimum of 10 item, or 10% of the total, whichever number is the highest*). For "equipment, infrastructure or other assets" [from now on called "asset(s)"] selected in the	48) Procurement rules, principles and guides were followed.	
		49) There was a link between the grant agreement and the asset charged to the action.	

	sample the Auditor verified that: ○ the assets were acquired in conformity with the Beneficiary's internal guidelines and procedures; ○ they were correctly allocated to the action (with supporting documents such as delivery note invoice or any other proof demonstrating the link to the action) ○ they were entered in the accounting system; ○ the extent to which the assets were used for the action (as a percentage) was supported by reliable documentation (e.g. usage overview table); The Auditor recalculated the depreciation costs and verified that they were in line with the applicable rules in the Beneficiary's country and with the Beneficiary's usual accounting policy (e.g. depreciation calculated on the acquisition value). The Auditor verified that no ineligible costs such as deductible VAT, exchange rate losses, excessive or reckless expenditure were declared (see Article 6.5 GA).	50) The asset charged to the action was traceable to the accounting records and the underlying documents. 51) The depreciation method used to charge the asset to the action was in line with the applicable rules of the Beneficiary's country and the Beneficiary's usual accounting policy. 52) The amount charged corresponded to the actual usage for the action. 53) No ineligible costs or excessive or reckless expenditure were declared.	
D.3	**COSTS OF OTHER GOODS AND SERVICES** **The Auditor sampled _____ cost items selected randomly** (*full coverage is required if there are fewer than 10 items, otherwise the sample should have a minimum of 10 item, or 10% of the total, whichever number is highest*). For the purchase of goods, works or services included in the sample the Auditor verified that: ○ the contracts did not cover tasks described in Annex 1;	54) Contracts for works or services did not cover tasks described in Annex 1. 55) Costs were allocated to the correct action and the goods were not placed in the inventory of durable equipment.	

	○ they were correctly identified, allocated to the proper action, entered in the accounting system (traceable to underlying documents such as purchase orders, invoices and accounting); ○ the goods were not placed in the inventory of durable equipment; ○ the costs charged to the action were accounted in line with the Beneficiary's usual accounting practices; ○ no ineligible costs or excessive or reckless expenditure were declared (see Article 6 GA). In addition, the Auditor verified that these goods and services were acquired in conformity with the Beneficiary's internal guidelines and procedures, in particular: ○ if Beneficiary acted as a contracting authority within the meaning of Directive 2004/18/EC or of Directive 2004/17/EC, the Auditor verified that the applicable national law on public procurement was followed and that the procurement contract complied with the Terms and Conditions of the Agreement. ○ if the Beneficiary did not fall into the category above, the Auditor verified that the Beneficiary followed their usual procurement rules and respected the Terms and Conditions of the Agreement. For the items included in the sample the Auditor also verified that: ○ the Beneficiary ensured best value for money (key elements to appreciate the respect of this principle are the award of the contract to the bid offering best price-quality ratio, under conditions of transparency and equal treatment. In case an existing framework contract was used the Auditor also verified that the Beneficiary ensured it was established on the basis of the principle of best value for money under conditions of transparency and equal treatment); *SUCH GOODS AND SERVICES INCLUDE, FOR INSTANCE, CONSUMABLES AND SUPPLIES, DISSEMINATION (INCLUDING OPEN ACCESS), PROTECTION OF RESULTS, SPECIFIC EVALUATION OF THE ACTION IF IT IS REQUIRED BY THE*	56) The costs were charged in line with the Beneficiary's accounting policy and were adequately supported. 57) No ineligible costs or excessive or reckless expenditure were declared. For internal invoices/charges only the cost element was charged, without any mark-ups. 58) Procurement rules, principles and guides were followed. There were documents of requests to different providers, different offers and assessment of the offers before selection of the provider in line with internal procedures and procurement rules. The purchases were made in accordance with the principle of best value for money. *(When different offers were not collected the Auditor explains the reasons provided by the Beneficiary under the*	

	AGREEMENT, CERTIFICATES ON THE FINANCIAL STATEMENTS IF THEY ARE REQUIRED BY THE AGREEMENT AND CERTIFICATES ON THE METHODOLOGY, TRANSLATIONS, REPRODUCTION.	*caption "Exceptions" of the Report. The Commission will analyse this information to evaluate whether these costs might be accepted as eligible)*	
D.4	**AGGREGATED CAPITALISED AND OPERATING COSTS OF RESEARCH INFRASTRUCTURE** The Auditor ensured the existence of a positive ex-ante assessment (issued by the EC Services) of the cost accounting methodology of the Beneficiary allowing it to apply the guidelines on direct costing for large research infrastructures in Horizon 2020. ***In the cases that a positive ex-ante assessment has been issued*** *(see the standard factual findings 59-60 on the next column)****,*** The Auditor ensured that the beneficiary has applied consistently the methodology that is explained and approved in the positive ex ante assessment;	59) The costs declared as direct costs for Large Research Infrastructures (in the appropriate line of the Financial Statement) comply with the methodology described in the positive ex-ante assessment report.	
		60) Any difference between the methodology applied and the one positively assessed was extensively described and adjusted accordingly.	
	In the cases that a positive ex-ante assessment has NOT been issued *(see the standard factual findings 61 on the next column),* The Auditor verified that no costs of Large Research Infrastructure have been charged as direct costs in any costs category;	61) The direct costs declared were free from any indirect costs items related to the Large Research Infrastructure.	

	In the cases that a draft ex-ante assessment report has been issued with recommendation for further changes *(see the standard factual findings 61 on the next column),* • The Auditor followed the same procedure as above (when a positive ex-ante assessment has NOT yet been issued) and paid particular attention (testing reinforced) to the cost items for which the draft ex-ante assessment either rejected the inclusion as direct costs for Large Research Infrastructures or issued recommendations.		
E	**USE OF EXCHANGE RATES**		
E.1	a) For Beneficiaries with accounts established in a currency other than euros **The Auditor sampled _____ cost items selected randomly and verified that the exchange rates used for converting other currencies into euros were in accordance with the following rules established in the Agreement** (*full coverage is required if there are fewer than 10 items, otherwise the sample should have a minimum of 10 item, or 10% of the total, whichever number is highest)*: *COSTS INCURRED IN ANOTHER CURRENCY SHALL BE CONVERTED INTO EURO AT THE AVERAGE OF THE DAILY EXCHANGE RATES PUBLISHED IN THE C SERIES OF OFFICIAL JOURNAL OF THE EUROPEAN UNION (https://www.ecb.int/stats/exchange/eurofxref/html/index.en.html), DETERMINED OVER THE CORRESPONDING REPORTING PERIOD.* *IF NO DAILY EURO EXCHANGE RATE IS PUBLISHED IN THE OFFICIAL JOURNAL OF THE EUROPEAN UNION FOR THE CURRENCY IN QUESTION, CONVERSION SHALL BE MADE AT THE AVERAGE OF THE MONTHLY ACCOUNTING RATES ESTABLISHED BY THE COMMISSION AND PUBLISHED ON ITS WEBSITE (http://ec.europa.eu/budget/contracts_grants/info_contracts/inforeuro/inforeuro_en.cfm),*	62) The exchange rates used to convert other currencies into Euros were in accordance with the rules established of the Grant Agreement and there was no difference in the final figures.	

	DETERMINED OVER THE CORRESPONDING REPORTING PERIOD.		
	b) For Beneficiaries with accounts established in euros **The Auditor sampled _____ cost items selected randomly and verified that the exchange rates used for converting other currencies into euros were in accordance with the following rules established in the Agreement** (*full coverage is required if there are fewer than 10 items, otherwise the sample should have a minimum of 10 item, or 10% of the total, whichever number is highest)*: *COSTS INCURRED IN ANOTHER CURRENCY SHALL BE CONVERTED INTO EURO BY APPLYING THE BENEFICIARY'S USUAL ACCOUNTING PRACTICES.*	63) The Beneficiary applied its usual accounting practices.	

[legal name of the audit firm]

[name and function of an authorised representative]

[dd Month yyyy]

<Signature of the Auditor>

ANNEX 6

MODEL FOR THE CERTIFICATE ON THE METHODOLOGY

- **For options [*in italics in square brackets*]: choose the applicable option. Options not chosen should be deleted.**
- **For fields in [grey in square brackets]: enter the appropriate data.**

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Terms of reference for an audit engagement for a methodology certificate in connection with one or more grant agreements financed under the Horizon 2020 Research and Innovation Framework Programme

This document sets out the '**Terms of Reference (ToR)**' under which

[OPTION 1: [insert name of the beneficiary] ('the Beneficiary')] [OPTION 2: [insert name of the linked third party] ('the Linked Third Party'), third party linked to the Beneficiary [insert name of the beneficiary] ('the Beneficiary')]

agrees to engage

[**insert legal name of the auditor**] ('the Auditor')

to produce an independent report of factual findings ('the Report') concerning the *[Beneficiary's] [Linked Third Party's]* usual accounting practices for calculating and claiming direct personnel costs declared as unit costs ('the Methodology') in connection with grant agreements financed under the Horizon 2020 Research and Innovation Framework Programme.

The procedures to be carried out for the assessment of the methodology will be based on the grant agreement(s) detailed below:

[title and number of the grant agreement(s)] ('the Agreement(s)')

The Agreement(s) has(have) been concluded between the Beneficiary and *[OPTION 1: the European Union, represented by the European Commission ('the Commission')][OPTION 2: the European Atomic Energy Community (Euratom,) represented by the European Commission ('the Commission')][OPTION 3: the [Research Executive Agency (REA)] [European Research Council Executive Agency (ERCEA)] [Innovation and Networks Executive Agency (INEA)] [Executive Agency for Small and Medium-sized Enterprises (EASME)] ('the Agency'), under the powers delegated by the European Commission ('the Commission').]*.

The *[Commission] [Agency]* is mentioned as a signatory of the Agreement with the Beneficiary only. The *[European Union] [Euratom] [Agency]* is not a party to this engagement.

1.1 Subject of the engagement

According to Article 18.1.2 of the Agreement, beneficiaries *[and linked third parties]* that declare direct personnel costs as unit costs calculated in accordance with their usual cost accounting practices may submit to the *[Commission] [Agency]*, for approval, a certificate on the methodology ('CoMUC') stating that there are adequate records and documentation to prove that their cost accounting practices used comply with the conditions set out in Point A of Article 6.2.

The subject of this engagement is the CoMUC which is composed of two separate documents:

- the Terms of Reference ('the ToR') to be signed by the *[Beneficiary] [Linked Third Party]* and the Auditor;

- the Auditor's Independent Report of Factual Findings ('the Report') issued on the Auditor's letterhead, dated, stamped and signed by the Auditor which includes; the standard statements ('the Statements') evaluated and signed by the *[Beneficiary] [Linked Third Party]*, the agreed-upon procedures ('the Procedures') performed by the Auditor and the standard factual findings ('the Findings') assessed by the Auditor. The Statements, Procedures and Findings are summarised in the table that forms part of the Report.

The information provided through the Statements, the Procedures and the Findings will enable the Commission to draw conclusions regarding the existence of the *[Beneficiary's] [Linked Third Party's]* usual cost accounting practice and its suitability to ensure that direct personnel costs claimed on that basis comply with the provisions of the Agreement. The Commission draws its own conclusions from the Report and any additional information it may require.

1.2 Responsibilities

The parties to this agreement are the *[Beneficiary] [Linked Third Party]* and the Auditor.

The *[Beneficiary] [Linked Third Party]:*

- is responsible for preparing financial statements for the Agreement(s) ('the Financial Statements') in compliance with those Agreements;
- is responsible for providing the Financial Statement(s) to the Auditor and enabling the Auditor to reconcile them with the *[Beneficiary's] [Linked Third Party's]* accounting and bookkeeping system and the underlying accounts and records. The Financial Statement(s) will be used as a basis for the procedures which the Auditor will carry out under this ToR;
- is responsible for its Methodology and liable for the accuracy of the Financial Statement(s);
- is responsible for endorsing or refuting the Statements indicated under the heading 'Statements to be made by the Beneficiary/ Linked Third Party' in the first column of the table that forms part of the Report;
- must provide the Auditor with a signed and dated representation letter;
- accepts that the ability of the Auditor to carry out the Procedures effectively depends upon the *[Beneficiary] [Linked Third Party]* providing full and free access to the *[Beneficiary's] [Linked Third Party's]* staff and to its accounting and other relevant records.

The Auditor:

- *[Option 1 by default: is qualified to carry out statutory audits of accounting documents in accordance with Directive 2006/43/EC of the European Parliament and of the Council of 17 May 2006 on statutory audits of annual accounts and consolidated accounts, amending Council Directives 78/660/EEC and 83/349/EEC and repealing Council Directive 84/253/EEC or similar national regulations]*.
- *[Option 2 if the Beneficiary or Linked Third Party has an independent Public Officer: is a competent and independent Public Officer for which the relevant national authorities have established the legal capacity to audit the Beneficiary]*.
- *[Option 3 if the Beneficiary or Linked Third Party is an international organisation: is an [internal] [external] auditor in accordance with the internal financial regulations and procedures of the international organisation]*.

The Auditor:

- must be independent from the Beneficiary *[and the Linked Third Party]*, in particular, it must not have been involved in preparing the Beneficiary's *[and Linked Third Party's]* Financial Statement(s);
- must plan work so that the Procedures may be carried out and the Findings may be assessed;
- must adhere to the Procedures laid down and the compulsory report format;
- must carry out the engagement in accordance with these ToR;
- must document matters which are important to support the Report;
- must base its Report on the evidence gathered;
- must submit the Report to the *[Beneficiary] [Linked Third Party]*.

The Commission sets out the Procedures to be carried out and the Findings to be endorsed by the Auditor. The Auditor is not responsible for their suitability or pertinence. As this engagement is not an assurance engagement the Auditor does not provide an audit opinion or a statement of assurance.

1.3 Applicable Standards

The Auditor must comply with these Terms of Reference and with[1]:

- the International Standard on Related Services ('ISRS') 4400 *Engagements to perform Agreed-upon Procedures regarding Financial Information* as issued by the International Auditing and Assurance Standards Board (IAASB);
- the *Code of Ethics for Professional Accountants* issued by the International Ethics Standards Board for Accountants (IESBA). Although ISRS 4400 states that independence is not a requirement for engagements to carry out agreed-upon procedures, the Commission requires that the Auditor also complies with the Code's independence requirements.

The Auditor's Report must state that there was no conflict of interests in establishing this Report between the Auditor and the Beneficiary *[and the Linked Third Party]* that could have a bearing on the Report, and must specify – if the service is invoiced - the total fee paid to the Auditor for providing the Report.

1.4 Reporting

The Report must be written in the language of the Agreement (see Article 20.7 of the Agreement).

Under Article 22 of the Agreement, the Commission, *[the Agency]*, the European Anti-Fraud Office and the Court of Auditors have the right to audit any work that is carried out under the action and for which costs are claimed from [*the European Union*] [*Euratom*] budget. This includes work related to this engagement. The Auditor must provide access to all working papers related to this assignment if the Commission*, [the Agency]*, the European Anti-Fraud Office or the European Court of Auditors requests them.

1.5 Timing

The Report must be provided by [dd Month yyyy].

[1] Supreme Audit Institutions applying INTOSAI-standards may carry out the Procedures according to the corresponding International Standards of Supreme Audit Institutions and code of ethics issued by INTOSAI instead of the International Standard on Related Services ('ISRS') 4400 and the Code of Ethics for Professional Accountants issued by the IAASB and the IESBA.

1.6 Other Terms

[The [Beneficiary] [Linked Third Party] and the Auditor can use this section to agree other specific terms, such as the Auditor's fees, liability, applicable law, etc. Those specific terms must not contradict the terms specified above.]

[legal name of the Auditor]	[legal name of the [Beneficiary] [Linked Third Party]]
[name & title of authorised representative]	[name & title of authorised representative]
[dd Month yyyy]	[dd Month yyyy]
Signature of the Auditor Signature	Signature of the *[Beneficiary] [Linked Third Party]*

Independent report of factual findings on the methodology concerning grant agreements financed under the Horizon 2020 Research and Innovation Framework Programme

(To be printed on letterhead paper of the auditor)

To

[name of contact person(s)], [Position]

[[Beneficiary's] [Linked Third Party's] name]

[Address]

[dd Month yyyy]

Dear [Name of contact person(s)],

As agreed under the terms of reference dated [dd Month yyyy]

with *[OPTION 1: [insert name of the beneficiary] ('the Beneficiary')] [OPTION 2: [insert name of the linked third party] ('the Linked Third Party'), third party linked to the Beneficiary [insert name of the beneficiary] ('the Beneficiary')]*,

we

[name of the auditor] ('the Auditor'),

established at

[full address/city/state/province/country],

represented by

[name and function of an authorised representative],

have carried out the agreed-upon procedures ('the Procedures') and provide hereby our Independent Report of Factual Findings ('the Report'), concerning the *[Beneficiary's] [Linked Third Party's]* usual accounting practices for calculating and declaring direct personnel costs declared as unit costs ('the Methodology').

You requested certain procedures to be carried out in connection with the grant(s)

[title and number of the grant agreement(s)] ('the Agreement(s)').

The Report

Our engagement was carried out in accordance with the terms of reference ('the ToR') appended to this Report. The Report includes: the standard statements ('the Statements') made by the *[Beneficiary] [Linked Third Party]*, the agreed-upon procedures ('the Procedures') carried out and the standard factual findings ('the Findings') confirmed by us.

The engagement involved carrying out the Procedures and assessing the Findings and the documentation requested appended to this Report, the results of which the Commission uses to draw conclusions regarding the acceptability of the Methodology applied by the *[Beneficiary] [Linked Third Party]*.

The Report covers the methodology used from [dd Month yyyy]. In the event that the *[Beneficiary] [Linked Third Party]* changes this methodology, the Report will not be applicable to any Financial Statement[2] submitted thereafter.

The scope of the Procedures and the definition of the standard statements and findings were determined solely by the Commission. Therefore, the Auditor is not responsible for their suitability or pertinence.

Since the Procedures carried out constitute neither an audit nor a review made in accordance with International Standards on Auditing or International Standards on Review Engagements, we do not

[2] Financial Statement in this context refers solely to Annex 4 of the Agreement by which the Beneficiary declares costs under the Agreement.

give a statement of assurance on the costs declared on the basis of the *[Beneficiary's] [Linked Third Party's]* Methodology. Had we carried out additional procedures or had we performed an audit or review in accordance with these standards, other matters might have come to its attention and would have been included in the Report.

Exceptions

Apart from the exceptions listed below, the *[Beneficiary] [Linked Third Party]* agreed with the standard Statements and provided the Auditor all the documentation and accounting information needed by the Auditor to carry out the requested Procedures and corroborate the standard Findings.

List here any exception and add any information on the cause and possible consequences of each exception, if known. If the exception is quantifiable, also indicate the corresponding amount.

…..

Explanation of possible exceptions in the form of examples (to be removed from the Report):

i. the [Beneficiary] [Linked Third Party] did not agree with the standard Statement number … because…;

ii. the Auditor could not carry out the procedure … established because …. (e.g. due to the inability to reconcile key information or the unavailability or inconsistency of data);

iii. the Auditor could not confirm or corroborate the standard Finding number … because ….

Remarks

We would like to add the following remarks relevant for the proper understanding of the Methodology applied by the [Beneficiary] [Linked Third Party] or the results reported:

Example (to be removed from the Report):

Regarding the methodology applied to calculate hourly rates …

Regarding standard Finding 15 it has to be noted that …

The [Beneficiary] [Linked Third Party] explained the deviation from the benchmark statement XXIV concerning time recording for personnel with no exclusive dedication to the action in the following manner: …

Annexes

Please provide the following documents to the auditor and annex them to the report when submitting this CoMUC to the Commission:

1. Brief description of the methodology for calculating personnel costs, productive hours and hourly rates;
2. Brief description of the time recording system in place;
3. An example of the time records used by the [*Beneficiary] [Linked Third Party*];
4. Description of any budgeted or estimated elements applied, together with an explanation as to why they are relevant for calculating the personnel costs and how they are based on objective and verifiable information;
5. A summary sheet with the hourly rate for direct personnel declared by the [*Beneficiary*] [*Linked Third Party*] and recalculated by the Auditor for each staff member included in the sample (the names do not need to be reported);
6. A comparative table summarising for each person selected in the sample a) the time claimed by the [*Beneficiary*] [*Linked Third Party*] in the Financial Statement(s) and b) the time according to the time record verified by the Auditor;
7. A copy of the letter of representation provided to the Auditor.

Use of this Report

This Report has been drawn up solely for the purpose given under Point 1.1 Reasons for the engagement.

The Report:

- is confidential and is intended to be submitted to the Commission by the [*Beneficiary*] [*Linked Third Party*] in connection with Article 18.1.2 of the Agreement;
- may not be used by the [*Beneficiary*] [*Linked Third Party*] or by the Commission for any other purpose, nor distributed to any other parties;
- may be disclosed by the Commission only to authorised parties, in particular the European Anti-Fraud Office (OLAF) and the European Court of Auditors.
- relates only to the usual cost accounting practices specified above and does not constitute a report on the Financial Statements of the [*Beneficiary*] [*Linked Third Party*].

No conflict of interest[3] exists between the Auditor and the Beneficiary *[and the Linked Third Party*] that could have a bearing on the Report. The total fee paid to the Auditor for producing the Report was EUR _____ (including EUR _____ of deductible VAT).

[3] A conflict of interest arises when the Auditor's objectivity to establish the certificate is compromised in fact or in appearance when the Auditor for instance:

- was involved in the preparation of the Financial Statements;

We look forward to discussing our Report with you and would be pleased to provide any further information or assistance which may be required.

Yours sincerely

[legal name of the Auditor]

[name and title of the authorised representative]

[dd Month yyyy]

Signature of the Auditor

- stands to benefit directly should the certificate be accepted;

- has a close relationship with any person representing the beneficiary;

- is a director, trustee or partner of the beneficiary; or

- is in any other situation that compromises his or her independence or ability to establish the certificate impartially.

Statements to be made by the Beneficiary/Linked Third Party ('the Statements') and Procedures to be carried out by the Auditor ('the Procedures') and standard factual findings ('the Findings') to be confirmed by the Auditor

The Commission reserves the right to provide the auditor with guidance regarding the Statements to be made, the Procedures to be carried out or the Findings to be ascertained and the way in which to present them. The Commission reserves the right to vary the Statements, Procedures or Findings by written notification to the Beneficiary/Linked Third Party to adapt the procedures to changes in the grant agreement(s) or to any other circumstances.

If this methodology certificate relates to the Linked Third Party's usual accounting practices for calculating and claiming direct personnel costs declared as unit costs any reference here below to 'the Beneficiary' is to be considered as a reference to 'the Linked Third Party'.

Please explain any discrepancies in the body of the Report.	
Statements to be made by Beneficiary	**Procedures to be carried out and Findings to be confirmed by the Auditor**
A. Use of the Methodology I. The cost accounting practice described below has been in use since *[*dd Month yyyy*]*. II. The next planned alteration to the methodology used by the Beneficiary will be from [dd Month yyyy*]*.	**Procedure:** ✓ The Auditor checked these dates against the documentation the Beneficiary has provided. **Factual finding:** 1. The dates provided by the Beneficiary were consistent with the documentation.
B. Description of the Methodology III. The methodology to calculate unit costs is being used in a consistent manner and is reflected in the relevant procedures. *[Please describe the methodology your entity uses to calculate personnel costs, productive hours and hourly rates, present your description to the Auditor and annex it to this certificate]* *[If the statement of section "B. Description of the methodology" cannot be endorsed by the Beneficiary or there is no written methodology to calculate unit costs it should be listed here below and reported as exception by the Auditor in the main Report of*	**Procedure:** ✓ The Auditor reviewed the description, the relevant manuals and/or internal guidance documents describing the methodology. **Factual finding:** 2. The brief description was consistent with the relevant manuals, internal guidance and/or other documentary evidence the Auditor has reviewed. 3. The methodology was generally applied by the Beneficiary as part of its usual costs accounting practices.

Please explain any discrepancies in the body of the Report.	
Statements to be made by Beneficiary	**Procedures to be carried out and Findings to be confirmed by the Auditor**
Factual Findings: - *…]*	
C. **Personnel costs** <u>General</u> IV. The unit costs (hourly rates) are limited to salaries including during parental leave, social security contributions, taxes and other costs included in the remuneration required under national law and the employment contract or equivalent appointing act; V. Employees are hired directly by the Beneficiary in accordance with national law, and work under its sole supervision and responsibility; VI. The Beneficiary remunerates its employees in accordance with its usual practices. This means that personnel costs are charged in line with the Beneficiary's usual payroll policy (e.g. salary policy, overtime policy, variable pay) and no special conditions exist for employees assigned to tasks relating to the European Union or Euratom, unless explicitly provided for in the grant agreement(s); VII. The Beneficiary allocates its employees to the relevant group/category/cost centre for the purpose of the unit cost calculation in line with the usual cost accounting practice; VIII. Personnel costs are based on the payroll system and accounting system. IX. Any exceptional adjustments of actual personnel costs resulted from relevant budgeted or estimated elements and were based on objective and verifiable information. *[Please describe the 'budgeted or estimated elements' and their relevance to personnel costs, and explain how they were reasonable and based on objective and verifiable information, present your explanation to the Auditor and annex it to this certificate].* X. Personnel costs claimed do not contain any of the following ineligible costs: costs related to return on capital; debt and debt service charges; provisions for future losses	**Procedure:** *The Auditor draws a sample of employees to carry out the procedures indicated in this section C and the following sections D to F.* *[The Auditor has drawn a random sample of 10 full-time equivalents made up of employees assigned to the action(s). If fewer than 10 full-time equivalents are assigned to the action(s), the Auditor has selected a sample of 10 full-time equivalents consisting of all employees assigned to the action(s), complemented by other employees irrespective of their assignments.].* For this sample: ✓ the Auditor reviewed all documents relating to personnel costs such as employment contracts, payslips, payroll policy (e.g. salary policy, overtime policy, variable pay policy), accounting and payroll records, applicable national tax , labour and social security law and any other documents corroborating the personnel costs claimed; ✓ in particular, the Auditor reviewed the employment contracts of the employees in the sample to verify that: i. they were employed directly by the Beneficiary in accordance with applicable national legislation; ii. they were working under the sole technical supervision and responsibility of the latter; iii. they were remunerated in accordance with the Beneficiary's usual practices; iv. they were allocated to the correct group/category/cost centre for the purposes of calculating the unit cost in line with the Beneficiary's usual cost accounting practices; ✓ the Auditor verified that any ineligible items or any costs claimed under other costs categories or costs covered by other types of grant or by other grants financed from the European Union budget have not been taken

Please explain any discrepancies in the body of the Report.	
Statements to be made by Beneficiary	**Procedures to be carried out and Findings to be confirmed by the Auditor**
or debts; interest owed; doubtful debts; currency exchange losses; bank costs charged by the Beneficiary's bank for transfers from the Commission/Agency; excessive or reckless expenditure; deductible VAT or costs incurred during suspension of the implementation of the action. XI. Personnel costs were not declared under another EU or Euratom grant (including grants awarded by a Member State and financed by the EU budget and grants awarded by bodies other than the Commission/Agency for the purpose of implementing the EU budget). <u>If additional remuneration as referred to in the grant agreement(s) is paid</u> XII. The Beneficiary is a non-profit legal entity; XIII. The additional remuneration is part of the beneficiary's usual remuneration practices and paid consistently whenever the relevant work or expertise is required; XIV. The criteria used to calculate the additional remuneration are objective and generally applied regardless of the source of funding; XV. The additional remuneration included in the personnel costs used to calculate the hourly rates for the grant agreement(s) is capped at EUR 8 000 per full-time equivalent (reduced proportionately if the employee is not assigned exclusively to the action). *[If certain statement(s) of section "C. Personnel costs" cannot be endorsed by the Beneficiary they should be listed here below and reported as exception by the Auditor in the main Report of*	into account when calculating the personnel costs; ✓ the Auditor numerically reconciled the total amount of personnel costs used to calculate the unit cost with the total amount of personnel costs recorded in the statutory accounts and the payroll system. ✓ to the extent that actual personnel costs were adjusted on the basis of budgeted or estimated elements, the Auditor carefully examined those elements and checked the information source to confirm that they correspond to objective and verifiable information; ✓ if additional remuneration has been claimed, the Auditor verified that the Beneficiary was a non-profit legal entity, that the amount was capped at EUR 8 000 per full-time equivalent and that it was reduced proportionately for employees not assigned exclusively to the action(s). ✓ the Auditor recalculated the personnel costs for the employees in the sample. **Factual finding:** 4. All the components of the remuneration that have been claimed as personnel costs are supported by underlying documentation. 5. The employees in the sample were employed directly by the Beneficiary in accordance with applicable national law and were working under its sole supervision and responsibility. 6. Their employment contracts were in line with the Beneficiary's usual policy; 7. Personnel costs were duly documented and consisted solely of salaries, social security contributions (pension contributions, health insurance, unemployment fund contributions, etc.), taxes and other statutory costs included in the remuneration (holiday pay, thirteenth month's pay, etc.); 8. The totals used to calculate the personnel unit costs are consistent with those registered in the payroll and accounting records; 9. To the extent that actual personnel costs were adjusted on the basis of budgeted or estimated elements, those elements were

Please explain any discrepancies in the body of the Report.	
Statements to be made by Beneficiary	**Procedures to be carried out and Findings to be confirmed by the Auditor**
Factual Findings: - *…]*	relevant for calculating the personnel costs and correspond to objective and verifiable information. The budgeted or estimated elements used are: — (indicate the elements and their values). 10. Personnel costs contained no ineligible elements; 11. Specific conditions for eligibility were fulfilled when additional remuneration was paid: a) the Beneficiary is registered in the grant agreements as a non-profit legal entity; b) it was paid according to objective criteria generally applied regardless of the source of funding used and c) remuneration was capped at EUR 8000 per full-time equivalent (or up to up to the equivalent pro-rata amount if the person did not work on the action full-time during the year or did not work exclusively on the action).
D. Productive hours XVI. The number of productive hours per full-time employee applied is *[delete as appropriate]*: A. 1720 productive hours per year for a person working full-time (corresponding pro-rata for persons not working full time). B. the total number of hours worked in the year by a person for the Beneficiary C. the standard number of annual hours generally applied by the beneficiary for its personnel in accordance with its usual cost accounting practices. This number must be at least 90% of the standard annual workable hours. <u>If method B is applied</u> XVII. The calculation of the total number of hours worked was done as follows: annual workable hours of the person according to the employment contract, applicable labour agreement or national law plus overtime worked minus absences (such as sick leave and special leave). XVIII. 'Annual workable hours' are hours	**Procedure (same sample basis as for Section C: Personnel costs):** ✓ The Auditor verified that the number of productive hours applied is in accordance with method A, B or C. ✓ The Auditor checked that the number of productive hours per full-time employee is correct and that it is reduced proportionately for employees not exclusively assigned to the action(s). ✓ If method B is applied the Auditor verified i) the manner in which the total number of hours worked was done and ii) that the contract specified the annual workable hours by inspecting all the relevant documents, national legislation, labour agreements and contracts. ✓ If method C is applied the Auditor reviewed the manner in which the standard number of working hours per year has been calculated by inspecting all the relevant documents, national legislation, labour agreements and contracts and verified that the number of productive hours per year used for these calculations was at least 90% of the standard number of working hours per year.

Please explain any discrepancies in the body of the Report.	
Statements to be made by Beneficiary	**Procedures to be carried out and Findings to be confirmed by the Auditor**
during which the personnel must be working, at the employer's disposal and carrying out his/her activity or duties under the employment contract, applicable collective labour agreement or national working time legislation. XIX. The contract (applicable collective labour agreement or national working time legislation) do specify the working time enabling to calculate the annual workable hours. <u>If method C is applied</u> XX. The standard number of productive hours per year is that of a full-time equivalent; for employees not assigned exclusively to the action(s) this number is reduced proportionately. XXI. The number of productive hours per year on which the hourly rate is based i) corresponds to the Beneficiary's usual accounting practices; ii) is at least 90% of the standard number of workable (working) hours per year. XXII. Standard workable (working) hours are hours during which personnel are at the Beneficiary's disposal preforming the duties described in the relevant employment contract, collective labour agreement or national labour legislation. The number of standard annual workable (working) hours that the Beneficiary claims is supported by labour contracts, national legislation and other documentary evidence. *[If certain statement(s) of section "D. Productive hours" cannot be endorsed by the Beneficiary they should be listed here below and reported as exception by the Auditor:* - *…]*	**Factual finding:** <u>General</u> 12. The Beneficiary applied a number of productive hours consistent with method A, B or C detailed in the left-hand column. 13. The number of productive hours per year per full-time employee was accurate and was proportionately reduced for employees not working full-time or exclusively for the action. <u>If method B is applied</u> 14. The number of 'annual workable hours', overtime and absences was verifiable based on the documents provided by the Beneficiary and the calculation of the total number of hours worked was accurate. 15. The contract specified the working time enabling to calculate the annual workable hours. <u>If method C is applied</u> 16. The calculation of the number of productive hours per year corresponded to the usual costs accounting practice of the Beneficiary. 17. The calculation of the standard number of workable (working) hours per year was corroborated by the documents presented by the Beneficiary. 18. The number of productive hours per year used for the calculation of the hourly rate was at least 90% of the number of workable (working) hours per year.
E. Hourly rates The hourly rates are correct because: XXIII. Hourly rates are correctly calculated since they result from dividing annual personnel	**Procedure** ✓ The Auditor has obtained a list of all personnel rates calculated by the Beneficiary in accordance with the methodology used. ✓ The Auditor has obtained a list of all the relevant employees, based on which the

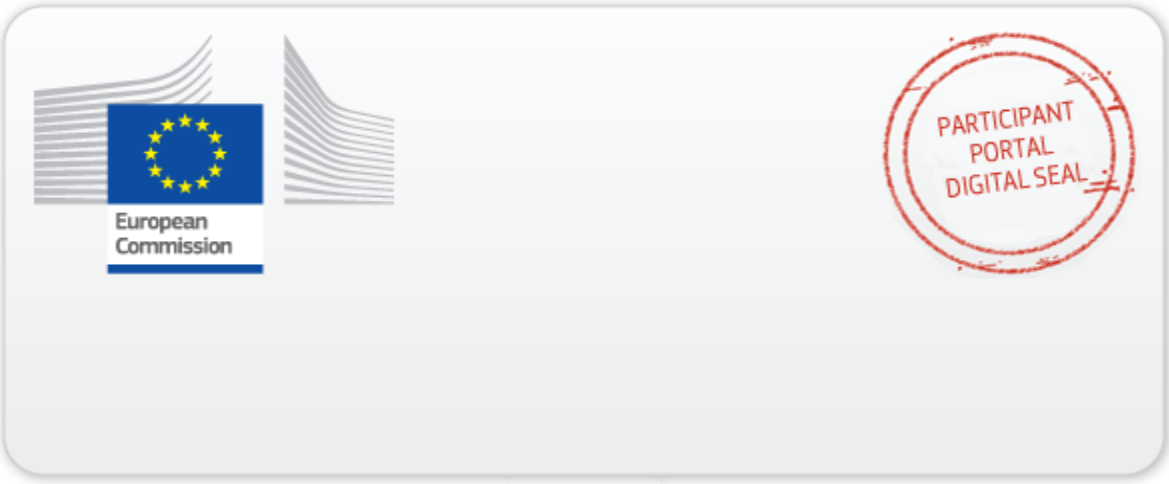
Please explain any discrepancies in the body of the Report.	
Statements to be made by Beneficiary	**Procedures to be carried out and Findings to be confirmed by the Auditor**
costs by the productive hours of a given year and group (e.g. staff category or department or cost centre depending on the methodology applied) and they are in line with the statements made in section C. and D. above. *[If the statement of section 'E. Hourly rates' cannot be endorsed by the Beneficiary they should be listed here below and reported as exception by the Auditor:* - *…]*	personnel rate(s) are calculated. For 10 full-time equivalent employees selected at random (same sample basis as Section C: Personnel costs): ✓ The Auditor recalculated the hourly rates. ✓ The Auditor verified that the methodology applied corresponds to the usual accounting practices of the organisation and is applied consistently for all activities of the organisation on the basis of objective criteria irrespective of the source of funding. **Factual finding:** 19. No differences arose from the recalculation of the hourly rate for the employees included in the sample.
F. Time recording XXIV. Time recording is in place for all persons with no exclusive dedication to one Horizon 2020 action. At least all hours worked in connection with the grant agreement(s) are registered on a **daily/weekly/monthly** basis *[delete as appropriate]* using a **paper/computer-based system** *[delete as appropriate]*; XXV. For persons exclusively assigned to one Horizon 2020 activity the Beneficiary has either signed a declaration to that effect or has put arrangements in place to record their working time; XXVI. Records of time worked have been signed by the person concerned (on paper or electronically) and approved by the action manager or line manager at least monthly; XXVII. Measures are in place to prevent staff from: i. recording the same hours twice, ii. recording working hours during absence periods (e.g. holidays, sick leave), iii. recording more than the number of productive hours per year used to calculate the hourly rates, and	**Procedure** ✓ The Auditor reviewed the brief description, all relevant manuals and/or internal guidance describing the methodology used to record time. The Auditor reviewed the time records of the random sample of 10 full-time equivalents referred to under Section C: Personnel costs, and verified in particular: ✓ that time records were available for all persons with not exclusive assignment to the action; ✓ that time records were available for persons working exclusively for a Horizon 2020 action, or, alternatively, that a declaration signed by the Beneficiary was available for them certifying that they were working exclusively for a Horizon 2020 action; ✓ that time records were signed and approved in due time and that all minimum requirements were fulfilled; ✓ that the persons worked for the action in the periods claimed; ✓ that no more hours were claimed than the productive hours used to calculate the hourly

Please explain any discrepancies in the body of the Report.	
Statements to be made by Beneficiary	**Procedures to be carried out and Findings to be confirmed by the Auditor**
iv. recording hours worked outside the action period. XXVIII. No working time was recorded outside the action period; XXIX. No more hours were claimed than the productive hours used to calculate the hourly personnel rates. *[Please provide a brief description of the time recording system in place together with the measures applied to ensure its reliability to the Auditor and annex it to the present certificate[4]].* *[If certain statement(s) of section "F. Time recording" cannot be endorsed by the Beneficiary they should be listed here below and reported as exception by the Auditor:* *- …]*	personnel rates; ✓ that internal controls were in place to prevent that time is recorded twice, during absences for holidays or sick leave; that more hours are claimed per person per year for Horizon 2020 actions than the number of productive hours per year used to calculate the hourly rates; that working time is recorded outside the action period; ✓ the Auditor cross-checked the information with human-resources records to verify consistency and to ensure that the internal controls have been effective. In addition, the Auditor has verified that no more hours were charged to Horizon 2020 actions per person per year than the number of productive hours per year used to calculate the hourly rates, and verified that no time worked outside the action period was charged to the action. **Factual finding:** 20. The brief description, manuals and/or internal guidance on time recording provided by the Beneficiary were consistent with management reports/records and other documents reviewed and were generally applied by the Beneficiary to produce the financial statements. 21. For the random sample time was recorded or, in the case of employees working exclusively for the action, either a signed declaration or time records were available; 22. For the random sample the time records were signed by the employee and the action manager/line manager, at least monthly. 23. Working time claimed for the action occurred in the periods claimed; 24. No more hours were claimed than the number productive hours used to calculate the hourly

[4] The description of the time recording system must state among others information on the content of the time records, its coverage (full or action time-recording, for all personnel or only for personnel involved in H2020 actions), its degree of detail (whether there is a reference to the particular tasks accomplished), its form, periodicity of the time registration and authorisation (paper or a computer-based system; on a daily, weekly or monthly basis; signed and countersigned by whom), controls applied to prevent double-charging of time or ensure consistency with HR-records such as absences and travels as well as it information flow up to its use for the preparation of the Financial Statements.

Please explain any discrepancies in the body of the Report.	
Statements to be made by Beneficiary	**Procedures to be carried out and Findings to be confirmed by the Auditor**
	personnel rates; 25. There is proof that the Beneficiary has checked that working time has not been claimed twice, that it is consistent with absence records and the number of productive hours per year, and that no working time has been claimed outside the action period. 26. Working time claimed is consistent with that on record at the human-resources department.

[official name of the** [Beneficiary] [Linked Third Party]**]	***[official name of the Auditor]***
[name and title of authorised representative]	***[name and title of authorised representative]***
[dd Month yyyy]	***[dd Month yyyy]***
<Signature of the** [Beneficiary] [Linked Third Party]**>	***<Signature** of the Auditor**>***



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