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Transfer of the central database and coordinating activities of **EUROCAT** to the **JRC**

EUROCAT: network of population-based registries for the epidemiological surveillance of congenital anomalies in Europe

Simona Martin, Javier de la Cruz,
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Foreword

The history of EUROCAT is inseparably linked to the European Commission (EC) and the EU as a whole.

As the European Economic Community's Committee on Medicinal and Public Health Research convened in 1974 at a Workshop to improve the methodology of population studies throughout the Community, congenital anomalies were chosen to be the first topic for concerted European action.

In line with this decision, in 1979 the EC's Directorate-General XII (Science, Research and Development) established the 'European Concerted Action on Congenital Anomalies and Twins', the original name of EUROCAT. This 'concerted action' was conceived as a prototype for European surveillance, originally planned to assess the feasibility of pooling data across European countries while standardising definitions, diagnoses and terminology.

More than a decade later, funding was provided by the EC's Directorate-General V (Employment, Industrial Relations and Social Affairs, Health and Safety) from 1991 to 1998. Since then, the network functioned as a service for the surveillance of congenital anomalies in Europe. In 2000, European funding was re-established under the Programme of Community Action on Rare Diseases and this continued under the EC's Directorate-General for Health and Consumers (DG SANCO – Public Health Programmes) until December 2014.

Throughout its evolution the EC supported and funded the Central Registry of EUROCAT, considering EU action on congenital anomalies and indeed rare diseases as having undisputed EU added value. The Central Registry, including the central database, was initially located at the Catholic University of Louvain, Belgium, then at the Scientific Institute for Public Health in Brussels, wherefrom it moved briefly to the London School of Hygiene and Tropical Medicine, UK, and finally to the University of Ulster, Northern Ireland, UK. In the meantime, the network evolved to an internationally recognised and highly valued collaboration

of population-based registries that surveys one third of the European births with partners on three continents.

Considering the aforementioned chronology in tandem with the fact that no EU funding was available from 2014, the recent and successful transfer of European-level coordinating activities of EUROCAT back to the EC (Directorate-General Joint Research Centre in collaboration with the Directorate-General for Health and Food Safety) closes the circle. Furthermore, this is a remarkable achievement towards the development of the European Platform on Rare Diseases Registration.

Today, EUROCAT is located on a sustainable foundation which is independent of all national, private and commercial interests. Thus, the excellent work and dedication of those who made EUROCAT what it is today will be continued and further developed.

Elke Anklam

Director

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EXECUTIVE SUMMARY

In the framework of implementing European Commission's strategy in the field of rare diseases, the Directorate-General Joint Research Centre (JRC) and the Directorate-General for Health and Food Safety (DG SANTE) signed in December 2013 the Administrative Arrangement (AA) on the 'Development and Maintenance of the European Platform on Rare Diseases Registration'. One objective of the AA is the transfer of the European-level coordination activities of EUROCAT to the JRC.

EUROCAT is a network of 55 population-based registries in 33 countries acting in the epidemiological surveillance of congenital anomalies. It covers one third of the European birth population which corresponds to more than 1.7 million births/year. The EUROCAT central database contains half a million cases of children with congenital anomalies. This data enables provision of prevalence, prenatal diagnosis and perinatal mortality data, detection of teratogenic exposures among others. It develops recommendations considered for primary prevention in the Rare Diseases National Plans for medicinal drugs, food/nutrition, lifestyle, health services, environmental pollution. These results are highly relevant for European public health and may require public health action.

In order to offer a sustainable solution for the continuation of EUROCAT activities, to secure the results of former work and to keep the system functioning, it was agreed that EUROCAT becomes part of the European Platform on Rare Diseases Registration, since the diseases/conditions the network is dealing with belong to the category 'rare'.

This report presents the preparation phase, the negotiations and the procedures carried out for the effective transfer of the EUROCAT Central Registry including the central database and the coordinating activities to the JRC. The different types of activities and the involvement of different services (legal, IT, information security, procurement) in a concerted action are detailed.

The establishment of the new JRC-EUROCAT Central Registry (CR) located at the JRC, Directorate F–Health, Consumers and Reference Materials–Health in Society Unit (former Institute for Health and Consumer Protection–Public Health Policy Support Unit) since 1st of January 2015 corresponds to the ‘data repository’ function of the Rare Diseases Platform. The CR activities including collection of data from the registries, data management, communication with the registries, production of dissemination materials, management of the website are described. In addition, the role and functioning of the new joint JRC-EUROCAT Management Committee and JRC’s role in supporting also other activities of the network (meetings of Registry Leaders, Coding Committee, Working Groups, etc.) are presented.

The accomplishment of the transfer is a milestone in the development of the European Platform on Rare Diseases Registration.

1. Introduction

European Commission's strategy in the field of rare diseases, as expressed in the Commission Communication (COM (2008) 679 final) [1], focuses on three main areas: i) improving the recognition and visibility of rare diseases; ii) supporting policies on rare diseases in the Member States for a coherent overall strategy, and iii) developing cooperation, coordination and regulation for rare diseases at EU level. Alongside the Communication, the Council Recommendations (2009/C 151/02) [2] emphasise the need for sustainability in the field of rare diseases.

Implementing the EU policies in the field of rare diseases, the Directorate-General Joint Research Centre (JRC) and the Directorate-General for Health and Food Safety (DG SANTE) signed in December 2013 the Administrative Arrangement (AA) on the 'Development and Maintenance of the European Platform on Rare Diseases Registration' [3]. One of the main objectives of the AA is the transfer of the European-level coordination activities of EUROCAT to the JRC.

EUROCAT is a network of population-based registries for the epidemiological surveillance of congenital anomalies covering one third of the European birth population, which corresponds to more than 1.7 million births/year. It consists of 55 registries in 33 countries. Since the establishment in 1979, EUROCAT central activities including the Central Registry with the central database were located successively in Louvain (BE), Brussels (BE), London (UK) and Belfast (UK) and have been funded by the European Commission in the frame of successive projects and health programmes.

The transfer of EUROCAT coordinating activities to the Commission at the JRC fulfilled in close collaboration with DG SANTE is aimed to ensure a sustainable solution for the continuation of EUROCAT activities, in order to secure the results of former work and to keep the network functioning. EUROCAT Central Registry becomes part of the European Platform on Rare Diseases Registration, since the diseases/conditions the network is dealing with belong to the category 'rare' [4]. This is in accordance with the general objective of the Platform to support and coordinate rare diseases registries and networks in view of their sustainability.

The EUROCAT central database contains half a million cases of children with congenital anomalies. This data enables provision of prevalence, prenatal diagnosis and perinatal mortality data. The valuable scientific work done over decades combined with the dedication, competence and passion of the people who built and maintained every single registry has led to EUROCAT becoming an EU-wide and internationally recognised entity with results highly relevant for European public health. EUROCAT performs annual statistical monitoring to detect new or increasing teratogenic exposures which may require public health action [5-8]. It develops recommendations considered for primary prevention in the Rare Diseases National Plans for medicinal products, food/nutrition, lifestyle, health services, environmental pollution [9,10].

The transfer of EUROCAT coordinating activities to the JRC proved to be itself a complex process. This report gives an overview about the experiences of the Directorate F–Health, Consumers and Reference Materials–Health in Society Unit (former Institute for Health and Consumers Protection–Public Health Policy Support Unit) synthesised in the establishment of the new JRC-EUROCAT Central Registry and the new joint coordinating structure, the JRC-EUROCAT Management Committee. These were established by accomplishing a plethora of procedures with the involvement of different services: legal, IT, information security, data protection, intellectual property rights, procurement. A close and very helpful collaboration between JRC and SANTE accompanied the whole process.

The finalisation of the transfer and the establishment of the new, fully operational structures, are a milestone in the Platform. It represents the basis for continuing the monitoring of congenital anomalies in Europe. The output of this activity is highly relevant for European public health and will be open to a wide range of stakeholders including healthcare providers, researchers, patients, pharmaceutical industry, decision makers. The final goal is to provide strong benefit for patient's healthcare and may require public health action.

2 Description of the EUROCAT network (status 2014). Identification of the structures and activities to be transferred

2.1. History

- Conceived in 1974, at a Workshop convened by the European Economic Community's Committee on Medicinal and Public Health Research to improve 'the methodology of population studies throughout the Community'. Congenital anomalies chosen as first topic for concerted action.
- EUROCAT (acronym derived from its original name 'European Concerted Action on Congenital Anomalies and Twins') established in 1979 by Directorate General XII (Science, Research and Development) as a prototype for European surveillance aiming to assess the feasibility of pooling data across national boundaries, in terms of standardization of definitions, diagnosis, terminology and confidentiality. Central Registry in the Department of Epidemiology, Catholic University of Louvain, Belgium.
- Funding transferred in 1991 to Directorate General V (Employment, Industrial Relations and Social Affairs, Health and Safety), to function as a service for the surveillance of congenital anomalies in Europe. Central Registry at Scientific Institute for Public Health, Brussels.
- Maintained by registry subscriptions 1998-2000. Central Registry moved briefly to London School of Hygiene and Tropical Medicine, UK 1999-2000.
- European funding re-established under the Programme of Community Action on Rare Diseases in 2000. Central Registry at the University of Ulster, Northern Ireland, UK where it remained until 2014.
- Funded under DG Health and Consumers (DG SANCO)–Public Health Programmes 2004-2013.
- Funded by DG SANCO – Consumers, Health, Agriculture and Food Executive Agency (CHAFEA)–Operating Grant 2014.

2.2. Structure of the network

EUROCAT network is a collaboration of population-based registries of congenital anomalies (CA) which is active since 1979. It surveys more than 1.7 million births/year—about one third of the European births.

The structure of the EUROCAT Network includes (*Figures 1 and 2*):

- EUROCAT Registries.
- EUROCAT Central Registry.
- EUROCAT Committees.

In addition, an IT company closely accompanied and supported the functioning of the network.

2.2.1. EUROCAT Registries

The network is composed of five types of active registry members and the non-active past members [11].

1) **Full members:** 32 registries in 18 countries (*Table 1*):

- EU Member States, n=15
Austria, Belgium (2), Croatia, Denmark, France (4), Germany (2), Hungary, Ireland (3), Italy (2), Malta, Netherlands, Poland, Portugal, Spain (2), United Kingdom (6).
- EFTA Countries, n=2
Norway, Switzerland.
- Non EU/EFTA, n=1
Ukraine.

Full member registries transmit *case data* on all congenital anomaly cases in their region, yearly, by the first or second data deadline. Full members are population-based CA registries which should cover a recommended population of at least 10000 annual births and data will not be published on the website unless it refers to at least 25000 births over one or more years. They register the full range

of CA, with high ascertainment and very good data quality (measured by Data Quality Indicators), including all neonatally and antenatally diagnosed cases and preferably all diagnoses made up to one year of age, including all affected live-births, stillbirths and terminations of pregnancy with CA.

Table 1. *EUROCAT Full member registries by Member State.*

EU/EFTA Member states, others		Code and Registry Name		Count
1	Austria	16	Styria	1
2	Belgium	02	Antwerp	2
2	Belgium	29	Hainaut	3
3	Croatia	21	Zagreb	4
4	Denmark	03	Odense	5
5	France	60	Auvergne	6
5	France	81	F West Indies	7
5	France	66	I Réunion	8
5	France	05	Paris	9
6	Germany	34	Mainz	10
6	Germany	39	Saxony-Anhalt	11
7	Hungary	75	Hungary	12
8	Ireland	49	Cork and Kerry	13
8	Ireland	10	Dublin	14
8	Ireland	79	SE Ireland	15
9	Italy	18	Emilia Romagna	16
9	Italy	04	Tuscany	17
10	Malta	23	Malta	18
11	Netherlands	13	N Netherlands	19

Table 1. (cont.)

EU/EFTA Member States, other		Code and Registry Name		Count
12	Norway	59	Norway	20
13	Poland	67	Wielkopolska	21
14	Portugal	28	S Portugal	22
15	Spain	30	Basque Country	23
15	Spain	86	Valencia Region	24
16	Switzerland	20	Vaud	25
17	Ukraine	62	Ukraine	26
18	United Kingdom	72	East Midlands & S Yorkshire	27
18	United Kingdom	73	Northern England	28
18	United Kingdom	84	South West England	29
18	United Kingdom	68	Thames Valley	30
18	United Kingdom	57	Wales	31
18	United Kingdom	70	Wessex	32

2) **Associate members:** 6 registries in 6 countries (*Table 2*):

- EU Member States, n=6
Czech Republic, Finland, France, Poland, Spain, Sweden.

Associate member registries transmit an *aggregate file* containing the total number of cases in each congenital anomaly subgroup by type of birth. Preferably must not overlap geographically with a full member register, preferably population-based register, registering a wide range of CA, livebirths, stillbirths and terminations of pregnancy with CA.

Table 2. EUROCAT Associate member registries by Member State.

EU Member States		Code and Registry Name		Count
19	Czech Republic	83	Czech Republic	1
20	Finland	38	Finland	2
5	France	80	Rhone-Alps	3
13	Poland	76	Rest of Poland	4
15	Spain	55	S Hospital Network	5
21	Sweden	71	Sweden	6

3) **Affiliate members:** 9 registries in 9 countries (*Table 3*):

- EU Member States, n=7
Bulgaria, France, Italy (2), Latvia, Slovenia, United Kingdom.
- Non EU/EFTA, n=2
Greenland, Moldova.

Table 3. EUROCAT Affiliate member registries by Member State.

EU Member States, others		Registry Name	Count
22	Bulgaria	Pleven	1
5	France	Brittany	2
23	Greenland	Greenland	3
9	Italy	Campania	4
9	Italy	Sicily	5
24	Latvia	Latvia-CDPC	6
25	Moldova	Moldova	7
26	Slovenia	Slovenia	8
18	United Kingdom	NDSCR	9

Affiliate member registries *do not transmit data* to EUROCAT but participate in meetings and projects. They are registries with an active interest in CA surveillance which do not conform to requirements for full or associate members but are still working toward the requirements.

4) **Applicant registries:** 4 registries in 4 countries (*Table 4*):

- EU Member States, n=3
Latvia, Lithuania, Slovakia.
- EFTA Countries, n=1
Iceland.

Table 4. *EUROCAT Applicant registries by Member State.*

EU/EFTA Member States		Registry Name	Count
27	Iceland	Iceland	1
24	Latvia	Latvia	2
28	Lithuania	Lithuania	3
29	Slovakia	Slovakia	4

Applicant Registries are those who are *in the process* of applying for membership.

5) **World affiliates:** 4 registries in 4 countries (*Table 5*):

- Non EU/EFTA, n=4
Argentina, Iran, New Zealand, Saudi Arabia.

Table 5. *EUROCAT World Affiliate registries by country.*

World Affiliate countries		Registry Name	Count
30	Argentina	RENAC	1
31	Iran	TRoCA	2
32	New Zealand	NZBDR	3
33	Saudi Arabia	MSD-BDR	4

World Affiliate Registries are non-European registries that benefit from close liaison with the EUROCAT Network (*e.g.* guidance on setting up a registry and on coding and classification). World Affiliates do not transmit data to EUROCAT, but do participate in meetings and may be asked to participate in specific projects.

6) Past member registries (*Table 6*)

Table 6. EUROCAT Past member registries by Member State.

EU Member States		Code and Registry Name		Count
1	Bulgaria	41	Sofia	1
2	France	54	Central East France	2
2	France	19	Strasbourg	3
3	Ireland	11	Galway	4
4	Italy	51	Campania	5
5	Italy	25	North East Italy	6
5	Italy	50	Sicily	7
5	Spain	32	Asturias	8
5	Spain	35	Barcelona	9
6	United Kingdom	14	Glasgow	10
6	United Kingdom	52	Merseyside & Cheshire	11
7	United Kingdom	54	North West Thames	12

Past Members Registries are those who have closed their activities or have made such fundamental organisational changes that a new membership application is required.

In summary, the network is composed of 55 active member registries in 33 countries. Out of them, 38 registries transmit data to the Central Registry. In addition, data from 12 past member registries are used for surveillance purposes.

EUROCAT Registries are members of the EUROCAT Association. EUROCAT Association is a voluntary, non-profit and non-official organisation legally constituted as the Association of European Registries of Congenital Anomalies. Membership to EUROCAT Association is open to any European Congenital Anomalies Registry. Registries are represented by Registry Leaders. President of the EUROCAT Association was until June 2016 Prof. Ingeborg Barisic, when Dr. Amanda Julie Neville was elected as the new President.

2.2.2. EUROCAT Central Registry (status before the transfer)

Function and activities

The Central Registry was responsible for:

- maintaining the Central Database
- data collection and management for routine surveillance and for research projects
- securing data transmission and storage
- quality assurance and control
- statistical monitoring
- reports
- maintenance of the EUROCAT Website.

The activities of the EUROCAT Central Registry belong to two categories: (1) basically scientific and (2) basically administrative.

(1) The basically scientific activities are:

- registration and management/operation of the Central Database
- coding and classification
- surveillance prevalence
- surveillance clusters and trends
- pharmacovigilance.

A detailed description of the tasks corresponding to each activity is given in *Table 7*.

Table 7. EUROCAT Central Registry: basically scientific activities, list of tasks.

Activity	Description of activities and tasks	Are Member registries actively involved?	Is there a Committee actively involved?	Is staff from Central Registry actively involved? What skills?						Tools / training	Periodicity	
				DM	RS	IT	SM	Ad	PM			PL
Registration and Central Database	Data collection	M								EDMP	--	
	Data validation	M								EDMP	--	
	Local data monitoring	M								EDMP	--	
	Data transmission to ECR	M								ECMP	Feb/Oct	
	Basic data quality checks				DM	RS	IT				ECMP	Feb/Oct
	Data import to ECD				DM	RS	IT				EDMP, ECD	Feb-M/O-Nov
	Update descriptions of registries				DM	RS						--
	Monitor implementation of Guide	M			DM	RS	IT				Guide 1.4	--
	Provide support to registers for EDMP	M			DM	RS	IT				EDMP, ECD	--
	Training on EDMP				DM	RS	IT				EDMP, ECD	--
	Provide data tables/extracts on request				DM	RS	IT					--
	Conduct literature review					RS						--
	Data cleaning, analysis, interpretation				DM	RS						--
	Publish report/paper on requested					RS						--
Obtain approval for use of registry data				DM	RS						--	
Maintain documentation system				DM	RS	IT					--	
Coding & Classification	G&C into subgroups and categories		CCC	DM		IT					EDMP	Feb / Oct
	Upload potential-multiple-malformed-cases			DM							EDMP	Feb / Oct
	Review potential-multiple-malformed-cases		CCC									Mar / Nov
	Download of reviewed cases to ECD		CCC	DM								Mar / Nov
	Reviewing and refining classifications		CCC			RS						Jan-Dec
	Review quality / advise on surveillance		CCC			RS						Jan-Dec
Review information on genetic syndromes		CCC			RS						Jan-Dec	
Surveillance prevalence	Data uploaded to test website		SUC		RS		SM				EDMP	Mar / Nov
	Data confirmed by registries	M									EDMP	Mar / Nov
	Data uploaded to live website tables		SUC		RS		SM				EDMP	Apr / Dec
	Provide data quality indicators		SUC		RS		SM				EDMP	Jun
	Production tables (monogenic syndromes)		SUC		RS		SM				SMM	--
Central analysis to feed Annual Report		SUC		RS		SM				SMM	Jun-Nov	
Surveillance clusters and trends	Data confirmation	M	SUC		RS		SM				SMM	Apr
	Analysis-Monitoring and report of clusters		SUC		RS		SM				SMM	May
	Analysis, feed-back to RIM, and send report	M									SMM	Jun
	Surveillance session at Annual RLM	M	SUC		RS		SM				SMM	Jun
	Investigations / prevention-related issues		SUC		RS		SM				SMM	Jun-Nov
	Compile and publish annual surveillance report		SUC		RS		SM				SMM	Dec
Pharmaco-vigilance	Coding and maintain resource for external queries			DM	RS					PL		Jan-Dec
	Signal detection on confirmed data		Statistic adv	DM	RS					PL		May
	Signal evaluation studies		Statistic adv	DM	RS					PL		Jun-Nov
	Report in collaboration with EUROmedCAT			DM	RS					PL		Dec

M: Member; CCC: Coding and classification committee; SUC: Surveillance committee; DM: Data manager; RS: Research; IT: Information technology; SM: Surveillance manager; Ad: Administrative; PM: Project manager; PL: Project leader; EDMP: EUROCAT Database management programme; ECD: EUROCAT Central registry programme; SMM: Statistical monitoring.

(2) The basically administrative activities are:

- network coordination
- dissemination
- registry advisory service
- annual Registry Leaders' Meeting.

A detailed description of the tasks corresponding to each activity is given in *Table 8*.

Table 8. EUROCAT Central Registry: basically administrative activities, list of tasks.

Activity	Description of activities and tasks	Are Member registries actively involved?	Is there a Committee actively involved?	Is staff from Central Registry actively involved? What skills?						Tools / training	Periodicity	
				DM	RS	IT	SM	Adm	PM			PL
Network coordination	Management of EUROCAT Central Registry							Adm	PM	PL		
	Liaison with relevant stakeholders											
	Financial management							Adm	PM	PL		
	Organisation of the STC meetings		STC					Adm	PM	PL		
	Project management							Adm	PM	PL		
	Admin support to ECR and STC							Adm				
	Active information-exchange infrastructure					RS		Adm	PM	PL	W@C	
	Archiving							Adm	PM			
Dissemination	E-mailing database of stakeholders							Adm	PM			
	Website maintenance and update		DSC, STC		RS			adm	PM			
	Leaflet, newsletter, mailing list, press, news		STC ch		RS			Adm	PM			
	Conference / meetings: participation / org		STC ch		RS			Adm	PM			
	Maintain bibliography of E publications		STC ch		RS			Adm	PM			
	Promote national committees, liaise		STC ch					Adm	PM			
	New registries: membership application	ECR	STC, CCC ch					Adm	PM			
Registry advisory service	Registration methodology, training	ECR	STC, CCC ch	DM	RS			Adm			EDMP, Guide	
	Feedback on first datasets	ECR	STC, CCC ch	DM	RS						EDMP, Guide	
	Provide Workshop at RLM	ECR	STC, CCC ch	DM	RS						EDMP, Guide	
Annual Registry Leaders Meeting	Scientific organisation	ECR	STC					Adm	PM	PL		1 / Y
	Operational organisation	ECR	STC					Adm	PM	PL		1 / Y

ECR: EUROCAT Central registry; CCC: Coding and classification committee; STC: Steering committee; ch: Chair; DSC: Dissemination committee; DM: Data manager; RS: Research; Adm: Administrative; PM: Project manager; PL: Project leader; EDMP: EUROCAT Database management programme; W@C: Email EUROCAT communications.

Members and tasks

Until the end of 2014, the EUROCAT Central Registry was located at the University of Ulster, Faculty of Life and Health Sciences, School of Nursing and Health Research – Centre for Maternal, Foetal and Infant Research. It was composed of following members:

Prof Helen Dolk

Professor in Epidemiology and Health Services Research
 EUROCAT Project Leader
 EUROCAT Project Management Committee, Chair
 EUROMediCAT Project Leader

Main tasks:

- Coordination of all EUROCAT grants and projects
- Responsible for EUROCAT Central Registry activities

Dr Maria Loane

Lecturer in Public Health

Senior Researcher – Epidemiology
Project Management Committee, member
EUROCAT Joint Action Work package on Surveillance, Leader
EUROCAT Surveillance Monitoring and Reporting
EUROCAT Epidemiologic Research

Main tasks:

- Responsible of the data campaign from data call to production of prevalence tables and tabulated results
- Responsible for Statistical Monitoring of Trends and Clusters: analysis and preliminary results
- Discussion of results with registries
- Annual report and Executive summary
- Supervision of data management
- Responsible for data quality assurance and control
- Epidemiologic research advisor

Mrs Ruth Greenlees

Research Associate
EUROCAT Database manager

Main tasks:

- Data management: reception of data files, data checking and editing
- Running automated analysis routines
- Contact with registries for data-related issues

Dr Rhonda Curran

Research Associate – Epidemiology
EUROCAT Project Manager

Main tasks:

- Monitoring that all EUROCAT activities run according to schedule
- Planning of activities – meetings, data requests, publications – and
- relation with EUROCAT partners

Dr Breidge Boyle

Research Associate – Epidemiology
EUROCAT Surveillance Monitoring and Reporting

Main tasks:

- Follow-up of statistical monitoring for clusters and trends
- Epidemiologic research

Dr Nichola McCullough

Research Fellow – Epidemiology

EUROCAT Surveillance Monitoring and Reporting

Main tasks:

- Follow-up of statistical monitoring for clusters and trends
- Epidemiologic research

Mrs Barbara Norton

EUROCAT Project Co-ordinator – Administrative

EUROCAT Website Content Management System Administrator

Main tasks:

- Support to Project coordination and management – Administrative and financial
- Responsible for website uploads and updates

Dr Ester Garne

EUROCAT Coding and Classification Committee, Chair

Attached to EUROCAT Central Registry

EUROCAT Subcontractor

Main tasks:

- Development and update of standards for coding and classification of subgroups and cases; review of potential multiple anomalies; review of monogenic syndromes; review coding issues in statistical monitoring
- Coordination of the Coding Committee
- Review of local registries malformation codes and text description; validation routines to be implemented in ECD/EDMP software
- Feed-back and communication with local registries and investigators, and liaise with Central Registry data management
- Production of dissemination and training material on coding

2.2.3. EUROCAT committees

Steering Committee (SC)

The SC members (five) are elected by the Board of members of EUROCAT Association. In addition, two or three permanent (non-elected) members seat in the SC.

Between 2014 and June 2016, the elected SC members were: Ingeborg Barisic, Fabrizio Bianchi, Amanda Neville, Vera Nelen, Diana Wellesley; non-elected: Ester Garne, Maria Loane, Joan Morris. Since June 2016, the elected SC members are: Fabrizio Bianchi, Ester Garne, Amanda Neville, Judith Rankin, David Tucker; non-elected: Maria Loane, Joan Morris.

The functions of the SC, before the transfer, included:

- decisions on EUROCAT policy
- regulation of all affairs concerning registry members and the Central Registry
- decisions on membership
- appointment the Central Registry and its Director
- decisions on additional working groups and meetings
- supervising security and confidentiality of data transmission
- organising the Annual Registry Leaders' Meeting.

The SC met three times/year and held three teleconferences/year.

Coding and Classification Committee (CCC)

The activity of the CCC is critical to the functioning of EUROCAT Surveillance system. Among other tasks, the CCC

- reviews annually multiply malformed cases
- updates coding and classification tools as required to improve malformation coding
- reviews epidemiological information on genetic syndromes for publication in website, tables or papers.

The Chair of CCC is a permanent member of the SC. Currently the Chair is Dr Ester Garne. Members (2014-2015): Ingeborg Barisic, Elisa Calzolari, Berenice Doray, David Tucker, Diana Wellesley; from 2015: Ingeborg Barisic, Norieke van Kammen, David Tucker, Diana Wellesley.

The CCC meets annually and holds teleconferences.

Other working groups active before the transfer:

Surveillance committee

Responsible for supervising the monitoring for trends and clusters in time and support to the Central Registry for the discussion of preliminary results and compilation of the Annual Surveillance Report.

EUROCAT Programme Management Committee (EPMC)

In charge of managing all EUROCAT funding contracts (EU funding, other contracts concluded and all other public or private financial support). The Central Registry was the treasurer. Members of EPMC included the Project leader/Director as chair of the Committee, the Project manager of the Central Registry, leaders of working groups or work packages linked to specific funding contracts, observers and invited consultants.

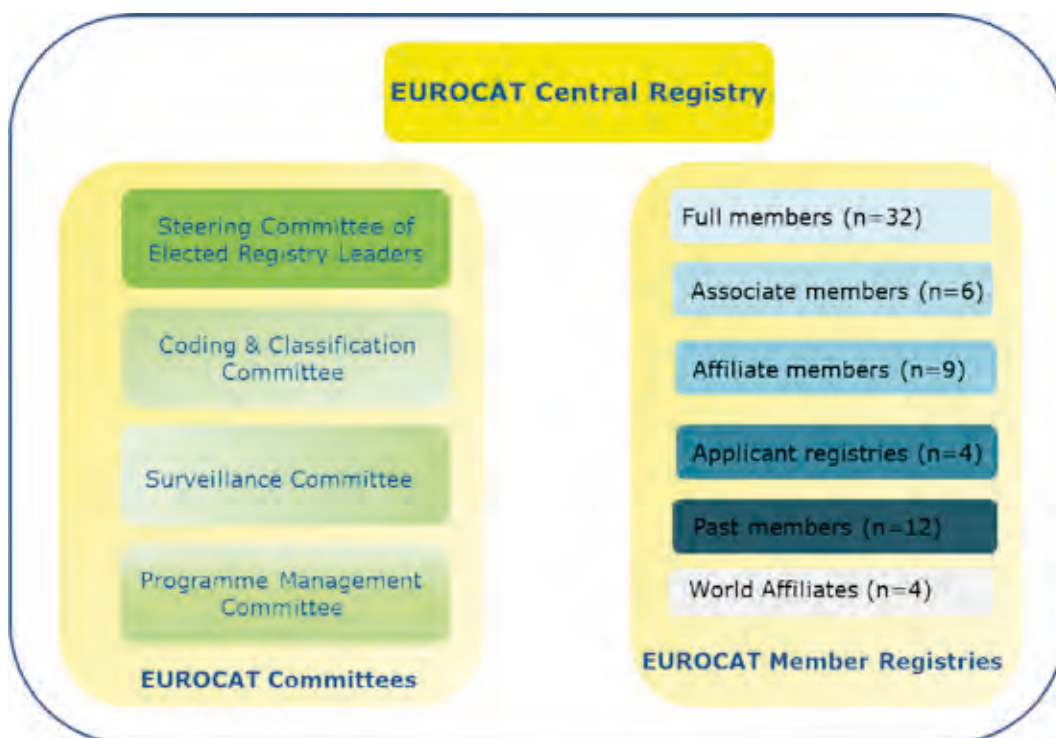


Figure 1. Composition of the EUROCAT network.

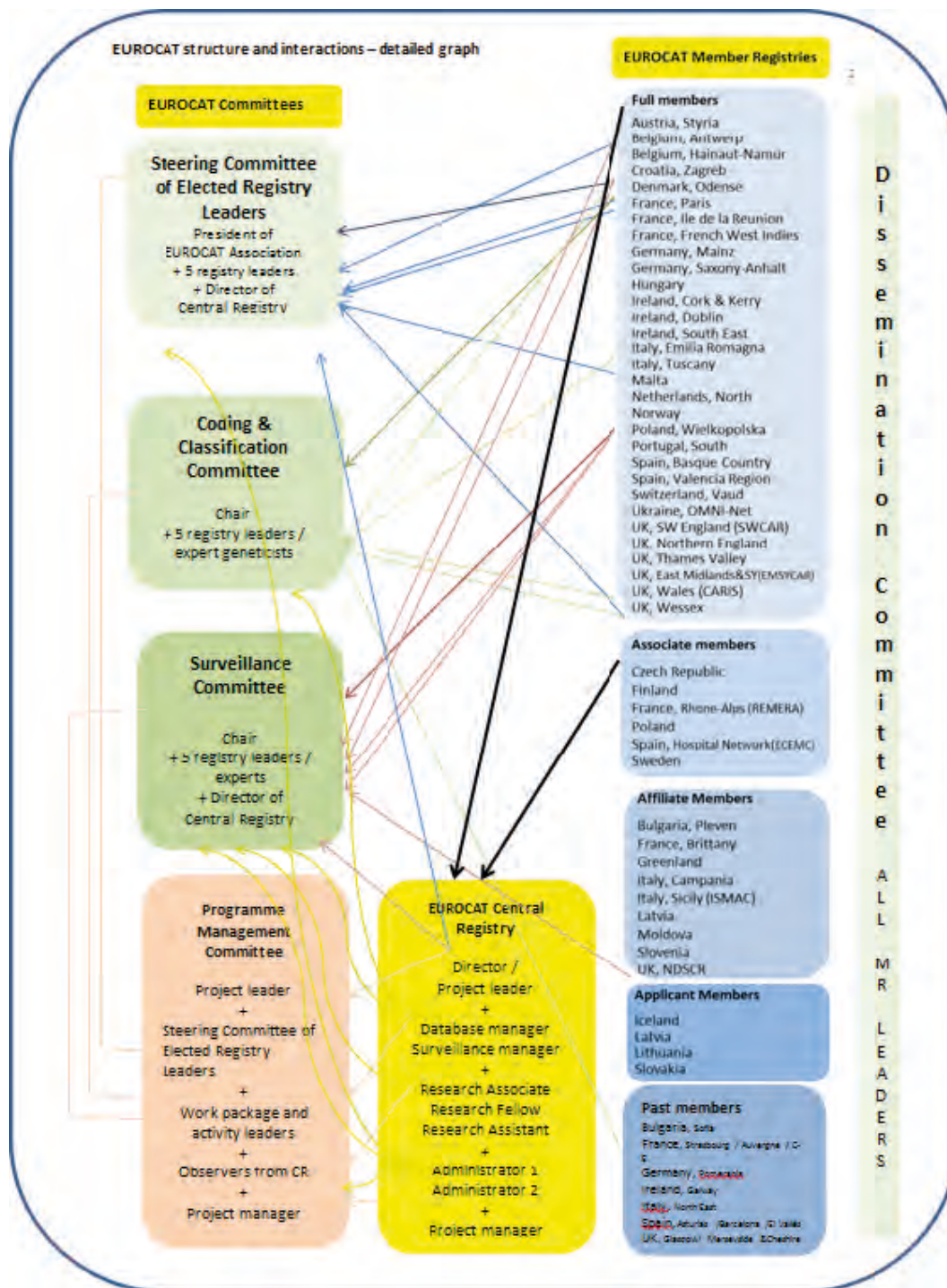


Figure 2. Detailed composition of the EUROCAT network and interactions between components.

2.2.4. EUROCAT IT subcontractor

The IT development, maintenance and update of the EUROCAT software has been done in the framework of EU grants by Biomedical Computing Ltd (www.bio-medical.co.uk/MeetTheTeam) led by James Densem, Managing Director, and Simon Mumford, Senior Software Developer.

2.3. Conclusion on the structures and activities to be transferred

The structures identified for the transfer to the JRC are:

- the Central Registry including the central database;
- the EUROCAT software (ECD, EDMP);
- the EUROCAT website.

With respect to the coordinating activities:

- the Steering Committee will merge with JRC representatives and will become the EUROCAT Management Committee;
- JRC will support the activities of the Management Committee, Coding and Classification Committee, other committees and working groups.

As a result, negotiations were conducted in relationship to the above mentioned structures and activities.

3 . Negotiation phase in view of the transfer

The negotiations between JRC and EUROCAT focused on two separate issues:

- the transfer of data and software including the website;
- the support of EUROCAT coordinating activities.

The negotiations took place on the occasion of meetings with the EUROCAT Steering Committee (November 2013, April, June and December 2014) and during the Annual Meeting with the registries' leaders (Belfast, June, 2014).

3.1. Meetings between JRC and the EUROCAT Steering Committee

3.1.1. EUROCAT Operating Grant

The negotiations between JRC and EUROCAT took place according to the EUROCAT Operating Grant No 20133307 under the EU Health Programme 2008-2013, UU_FY2014_FY2013(UU_FY2014).

3.1.2. Ispra, November 2013

The first meeting between JRC and the EUROCAT Steering Committee offered the opportunity for bilateral discussions and very welcome overviews on one hand on EUROCAT activities and way of working, on the other hand on the EU Platform on Rare Diseases Registration planned to be developed at the JRC. The next steps to be followed were explored. Three core areas of activities to be addressed were identified: database management and epidemiological data analysis; clinical coding and interpretation of surveillance results; software developments.

An internal EUROCAT Communication to Registry Members from 8 January 2014 presented the transfer to JRC as a 'promise of a sustainable future'.

3.1.3. London, April 2014

Following the kick-off meeting for the transfer held in November 2013 at the JRC in Ispra and an extensive exchange of documents on the structure and functioning of EUROCAT, its outputs and the work plan associated with the operating grant, at this meeting the different aspects of transferring and hosting the EUROCAT coordinating activities at the JRC were discussed in more detail.

It was agreed that in preparation of the transfer, EUROCAT will produce:

- a document on future sustainability–strategic planning in liaison with JRC/DG SANTE;
Deliverable: December 2014;
- a documented archive of the EUROCAT Database 1980-2012. Documentation includes:
 - EUROCAT Guides (for variables and coding schemes and exclusions) and years of data to which they refer;
 - contents of data (registries, years);
 - missing data tables, registry-specific data notes;*Deliverable:* December 2014;
- a unified EUROCAT Network Procedural Manual including or referring to all standard operating procedures (SOPs), Guidelines and Manuals–on membership application process, registration (variables, coding and classification, exclusions), data protection and data confidentiality, data transmission, data access (all data and medication data), authorship, EUROCAT Data Management Programme (EDMP) user instructions, calculation of EUROCAT prevalence rates, registry descriptions;
Deliverable: December 2014;
- EUROCAT will hand over the license for its IT product developed by Biomedical Computing Limited (subcontractor) for data collection and management to the JRC;
- the EUROCAT Website will be transferred to the JRC.

It was agreed that in preparation of the transfer, JRC will take action on:

- preparation of a roadmap document for the transfer to be presented at the 29th EUROCAT Registry Leaders' Meeting on 26th-27th June 2014 in Belfast;
- preparation of the transfer of the EUROCAT Central Database (ECD) to the JRC:
 - preparation of a contract template for the registries to be presented at the Registry Leaders' Meeting;
 - exploring the possibility that the ECD data assistant manager continues working for six months/one year in parallel with the JRC statistician responsible for the ECD;
- defining the activities that could be supported by the JRC:
 - meetings and teleconferences of the Steering Committee;
 - newsletters/year–e-mailed to 2140 recipients worldwide;
 - promotional leaflet;
 - biennial scientific symposia;
- finding a solution for maintaining
 - a EUROCAT Scientific Committee (composed of experts which are part of the actual Steering Committee) involved in the analysis and exploitation of data, clinical input, identification of clusters and trends, working on publications, etc.;
 - the Coding and Classification Committee;
 - three meetings x two days/year–essential activity that needs to be continued;
- activities to be offered to the member registries:
 - IT support for registries: computing developments made centrally to be available locally–to help member registries and increase attractiveness;
 - validation of codes for malformations (in collaboration with the Coding and Classification Committee) in order to avoid the need of extensive data cleaning for specific projects or interpretation of multiple malformations: Workshop on coding;
- activities for adding value to the EUROCAT data:
 - integration of the congenital anomalies data into larger health information systems; link to other databases–environmental data, etc.;
 - public health indicators (six defined already)–to be disseminated to policy makers for decisions on primary/secondary prevention;
- data quality indicators–eventually extended use to other registries.

3.1.4. Belfast, June 2014

The points mentioned under 3.1.3 were further discussed and detailed.

3.2. Meeting between JRC and the EUROCAT Registry Leaders

Following two meetings with the EUROCAT Steering Committee (November 2013 at the JRC-Ispra and April 2014 in London) and an extensive exchange of documents, JRC was invited to participate to the annual EUROCAT Registry Leaders' Meeting which is essentially involved in the scientific and operational organisation of the network. There were 62 participants at the meeting: 49 participants representing 32 registries and 13 participants from the Central Registry and non-members.

JRC presented the EU Platform on Rare Diseases Registration which is being developed at the JRC and detailed the Roadmap for the transfer of the EUROCAT database and coordinating activities to the JRC as follows:

1) **Transfer of the EUROCAT Central Database (ECD) to the JRC Staff**

Data management requires continuity of dedicated staff. In order to ensure transfer of knowledge and human resources support, a transition period of six months/one year was envisaged.

- Database management: recruitment procedure started at the JRC, personnel available Q4/2014.
- Database management at ECD Ulster: solution proposed by the JRC to maintain the ECD data assistant for six months/one year (starting January 2015).

During this period, the ECD data assistant and the JRC data assistant will work in parallel (exchanges, visits in Ulster and JRC, etc.).

2) **Governance/Coordination**

JRC ensures the solution for maintaining

- the *EUROCAT Coordination Committee* (name to be defined) composed of
 - members which are part of the actual Steering Committee
 - leaders of the current projects/registries' leaders

- experts involved in the analysis and exploitation of data, clinical input, identification of clusters and trends, working on publications, etc.
 - JRC representatives;
- JRC will organise
- three meetings of the EUROCAT Coordination Committee/year
 - three teleconferences/year.
- the *Coding and Classification Committee* (essential activity that needs to be continued)
 - three meetings x two days/year.

3) Dissemination

- the EUROCAT *Website* will be transferred to the JRC and will operate under 'eurocat.eu'.
The responsibility for the scientific content of the website will be under the EUROCAT Coordination Committee.
- JRC will produce in close collaboration with the EUROCAT Coordination Committee
 - two newsletters/year
 - promotional leaflets.

4) Activities offered by JRC to the member registries

- *IT support*: computing developments made centrally to be available locally.
- *Registry advisory service* – to be set up in collaboration with the EUROCAT Coordination Committee.
- *Training workshops*.
- *Workshop on coding* (2014/2015) in close collaboration with the Coding and Classification Committee
 - particularly needed for validation of codes for malformations to avoid the need of extensive data cleaning for specific projects or interpretation of multiple malformations.
- Biennial *scientific symposia* (2015).

5) Activities offered for adding value to EUROCAT data

- Integration of congenital anomalies data into larger health information systems; link to other databases – environmental data, genomics, etc.

- Public health indicators (six defined already) [12] – to be disseminated to policy makers for decisions on primary/secondary prevention.
- Data quality indicators [13] – extended use to other registries.

An extended Q&A session served to discuss in detail with the leaders/representatives of the member registries various transfer-related issues.

In a dedicated roundtable discussion, members of the EUROCAT Steering Committee, representatives of the JRC and DG SANCO addressed many specific points of the transfer with the following implications/actions:

- JRC will further explore the internal legal and administrative procedures for following the proposed roadmap for the transfer of the database, including the associated data protection and IP rights issues, as well as the procedures concerning the staff necessary for running the database.
- JRC will clarify the ways for the future collaboration with the EUROCAT experts and the possibilities for supporting the functioning of a ‘EUROCAT Scientific/Management Committee’.
- The direct contact with the IT company who developed and maintains the EUROCAT central database was established, different aspects of the transfer have been discussed in principle and the company’s director offered his availability to further support this process.
- EUROCAT will provide the documents related to the ethical approval under the network and the central database are functioning.
- EUROCAT will continue discussing with the registry leaders the different aspects and implications of the transfer, will conclude on their position and will inform the JRC as soon as possible about their decision.
- JRC and SANTE transmitted the message that the many new and additional requests of EUROCAT primarily concerning the preservation of the EUROCAT Central Registry staff cannot be accomplished.

In addition to the organisational/administrative aspects related to the transfer, the meeting covered a wide range of scientific topics provided by member registries, reflected in the contributions as listed below:

- Presentation 1 [Tribute to Prof Michel Lechat](#) (Helen Dolk)
- Presentation 2 [Update on the EU RD Policy](#) (Jaroslaw Waligora)
- Presentation 3 [EUROCAT's Place in the RD Platform 1](#) (Simona Martin)
- Presentation 4 [EUROCAT's Place in the RD Platform 2](#) (Simona Martin)
- Presentation 5 [Horizon 2020–InnoRARE Plans](#) (Victoria Hedley)
- Presentation 6 [EUROCAT/EUROPLAN](#) (Domenica Taruscio)
- Presentation 7 [Valencia RD Registry](#) (Oscar Zurriaga)
- Presentation 8 [Poland](#) (Anna Latos-Bielenska)
- Presentation 9 [Developmental Biology](#) (Adonis Ioannides)
- Presentation 10 [Collection of DNA Samples and Biobanking](#)
(Jorieke van Kammen-Bergman)
- Presentation 11 [Greenland](#) (Turid Skifte)
- Presentation 12 [Brittany](#) (Florence Rouget)
- Presentation 13 [Cyprus](#) (Adonis Ioannides)
- Presentation 14 [ICBDSR](#) (Pierpaolo Mastroiacovo)
- Presentation 15 [Global Burden of Diseases and Infant Mortality](#) (Helen Dolk)
- Presentation 16 [Pierre Robin Study in Relation to Methadone Exposure](#)
(Brian Cleary)
- Presentation 17 [Fetal Alcohol Syndrome](#) (Mary O'Mahony)
- Presentation 18 [NI Baby Hearts Study](#) (Nichola McCullough)
- Presentation 19 [Surveillance of Multiples](#) (Ester Garne)
- Presentation 20 [Evaluation of Clusters](#) (Maria Loane)
- Presentation 21 [Holoprosencephaly and Coarctation of Aorta](#) (Amanda Neville)
- Presentation 22 [Aortic Valve Atresia/Stenosis](#) (David Tucker)
- Presentation 23 [Amniotic Bands](#) (Jorieke van Kammen-Bergman)
- Presentation 24 [Pan-European Trends](#) (Ruth Greenlees)
- Presentation 25 [EUROmediCAT Asthma Study](#) (Ester Garne)
- Presentation 26 [Final Lamotrigine Study for GSK](#) (Maria Loane)
- Presentation 27 [Signal Detection Methodology](#) (Michiel Luteijn)

4

. Preparation phase for the transfer

4.1. Legal aspects

The legal and administrative frame for the transfer needed to be established. In order to proceed with this, the Rare Diseases Group (F.1. Health in Society Unit) started an intensive collaboration with the JRC Legal Advice Unit and the Intellectual Property Rights (IPR) Office. This resulted in the necessity to clarify the legal basis for the transfer as well as the ownership of the different structures to be transferred. It turned out that ownership and rights had to be defined for the following levels: the database infrastructure, the content and the particular data. In addition, ownership and rights/licensing rights had to be defined for the software and the website.

These clarifications required an extensive exchange between the JRC (Health in Society Unit and Legal Advice Unit) and the University of Ulster (Technology Transfer Unit), Belfast, UK.

4.2. Handover of EUROCAT documents to the JRC

The handover of EUROCAT Central Registry documents effectively started on October 13th 2014 with the visit of EUROCAT Project manager to the Public Health Policy Support Unit at JRC-Ispra. The aim of the visit was the handover of Part I of EUROCAT Procedural Manual.

The purpose of developing a EUROCAT Network Procedural Manual was to unify, include or refer to all SOPs, Guidelines and Manuals previously produced by the Network. Part I of the new Procedural Manual included the following chapters: EUROCAT Membership, Requesting EUROCAT Data, Website, Communication, Data Security, Confidentiality, Ethics and Consent.

The chapters were delivered in printed and electronic format (pdf and word files). In the following weeks the Manual was uploaded to EUROCAT website and it is now accessible to logged in members. The content of the Procedural Manual (Part I) is detailed below:

EUROCAT Membership

1. EUROCAT member registries Webpage
2. Membership Categories
3. EUROCAT Membership Criteria
4. New Applicant Registry Process Flowchart
5. EUROCAT Membership Application Form or Registry Description Questionnaire
6. EUROCAT Membership Map
7. Percentage Coverage of the European Birth Population
8. EUROCAT Registries: Population Definition, Geographic Area and Stillbirth Definition for Denominators
9. Number of Births (Live Births, Stillbirths and Total Births per EUROCAT Member Registry)
10. EUROCAT Registries: Upper Age Limit for Recording Congenital Anomalies
11. EUROCAT Member Registry Descriptions and Contact Details
12. Relevant Hyperlinks on the EUROCAT website
13. Expansion of the EUROCAT Network
14. The Role of the EUROCAT Steering Committee in Relation to Membership
15. Overview of EUROCAT Registry Advisory Service

Requesting EUROCAT Data

1. Requesting EUROCAT Data
2. Procedure for Obtaining EUROCAT Data
3. EUROCAT Terms and Conditions (include EUROCAT Authorship Guidelines)
4. EUROCAT Data Request Form
5. EUROCAT Registry Participation and Permission Form
6. EUROCAT Registries Participation and Permission Table Checklist
7. EUROCAT Data Request Contract

8. Guidance for EUROCAT Data Users
9. EUROCAT Member Author Affiliations and Email Addresses
10. EUROCAT/EUROmediCAT Medication Enquiry Form
11. EUROCAT Data Manual
12. Keeping the EUROCAT Network Informed of the Progress of the Use of Released Data

Website

1. Levels of Access
2. Version Controlled Publicly Available Documents or Lists of Documents that Change Over Time and Require Systematic Updating
3. EUROCAT Publications List
4. Registrations to Use the Website Tables
5. Website Dissemination Committee
6. Website Forum
7. Future Development of the EUROCAT Website

Communication

1. Internal Website Interface
2. Communication Emails
3. Maintenance of a Dynamic Up-to-date Stakeholder Email Database
4. Meetings
 - Annual Registry Leaders’ Meeting (includes Association and Registry Advisory Service Meetings)
 - Biennial EUROCAT Scientific Symposia
 - Steering Committee and/or Project Management Committee
 - Coding and Classification Committee
 - Registry Advisory Service
5. Ad Hoc Email, Phone and Fax Communications

Data Security, Confidentiality, Ethics and Consent

1. Regulation (Regulation of the European Parliament and of the Council) on the protection of individuals with regard to the processing of personal data and on the free movement of such data (General Data Protection Regulation)

2. Hosting the EUROCAT Central Database within the University of Ulster, United Kingdom
3. Ethics, Consent and Ethical Approval

Data Cleaning of Malformation Codes in the EUROCAT Central Database

Additional information such as registry descriptions and data security policy documents were provided together with historical files. The main archive system of EUROCAT is EUROCAT website where most working documents have been uploaded over time.

The first stage of the handover allowed JRC to understand how EUROCAT Central Registry can manage and operate key features of the network: membership application process, internal communication with members, use of the website for external communication and archive, requests for data, data security and data protection issues.

4.3. Practical training

The second stage of the handover of EUROCAT Central Registry took place with the visit of JRC staff to EUROCAT Central Registry in Belfast on 20-24 October 2014. The purpose of the visit was to learn directly from the Central Registry staff about

- Central Database management processes
- website content management
- core statistical monitoring procedures.

The practical sessions were coordinated by the EUROCAT Project Manager and hosted by the EUROCAT Project Leader and Central Registry Director. It was emphasised that the role of the Central Registry was not understood as a service; it was more about leadership and expertise and not only about procedures.

EUROCAT Central database processes were explained in detailed by EUROCAT Data Manager. The visit was organised shortly after the 2nd annual deadline for

data submission (15 October) and the practical work was performed on data files received for the current data campaign. The sessions covered the following topics:

- call for data instructions to registries;
- introduction to the EDMP (EUROCAT Data Management Programme) and ECD (EUROCAT Central Database software);
- check and import of individual and aggregated cases and denominators;
- feed-back to registries;
- generate prenatal diagnosis, perinatal mortality, missing frequency and prevalence tables for the test website;
- generate tables and reports for live website;
- confirmation and quality assurance; data quality indicators;
- statistical monitoring;
- maintenance of database;
- download of data for investigators.

A draft procedural manual chapter on data management was used and completed during the practical work sessions.

Epidemiologic surveillance is the core activity of EUROCAT Network. Central Registry scientific activities cover two areas: coding and statistical monitoring. Both activities are built on the automatic coding and analysis performed by the data manager running ECD software. These activities require specialised expertise to produce high quality and timely annual surveillance annual report. The tasks needed are the revision of multiple malformations coding, the pan-European trend analysis and the assessment of trends and clusters.

EUROCAT Website was presented by the web content administrator. The website is used for external communication with stakeholders and dissemination and also for internal communication with EUROCAT Members and archive. The session covered the

- custom content management system developed for EUROCAT website
- functionalities for different access levels.

4.4. Organisational issues

The final content of the transfer was agreed at the meeting between JRC and the EUROCAT Steering Committee in Ispra on 4 December 2014.

JRC informed on the organisation, resources and staff of the JRC-EUROCAT Central Registry based at the JRC in Ispra.

4.4.1. Governance

The new joint governance structure is the JRC-EUROCAT Management Committee. It is composed of:

- seven members from EUROCAT
 - five elected members including the President of the EUROCAT Association
 - two non-elected (permanent) members (Project Leader and Chair of the Coding Committee)
- two JRC representatives.

The EUROCAT Steering Committee will decide about the new Project Leader (which will be referred to as Scientific Leader).

The Management Committee can invite to its meetings other experts for reporting on or contribute to specific tasks (*e.g.* surveillance, new projects).

The rules of functioning of the current Steering Committee need to be adapted to the new situation. The necessary changes will be prepared in collaboration with the JRC Legal advice Unit.

The changes required to the EUROCAT Association Constitution will be discussed and voted at the next Registry Leaders Meeting.

4.4.2. Calendar of the meetings 2015

the calendar of the meetings 2015 was established:

- Management Committee meetings:
 - 24th March 2015
 - 21st May 2015
 - 11th November 2015;
- Annual Registry Leaders' Meeting:
 - 17-18 June 2015.

All meetings will take place at the JRC's site in Ispra, Italy.

4.4.3. Delivery of the EUROCAT Procedural Manual

The final version of the EUROCAT Procedural Manual Part I was delivered by the EUROCAT Steering Committee to the JRC, including chapters on Database processes and Data cleaning of malformation codes in Central Database.

Statistical monitoring part is still pending.

4.4.4. Approval of the transfer by the registries

Agreement was reached on the procedure for asking individually each member registry to approve the transfer of its data from the Central Registry in Belfast to the JRC.

In a concerted action with the EUROCAT Steering Committee and the EUROCAT Central Registry, JRC contacted every registry leader in order to explain the reasons for the transfer, the support that JRC will offer and the future JRC-EUROCAT activities by means of the letters below. In addition, a declaration form was prepared in collaboration with the EUROCAT Steering Committee, to be signed by the registries. Member registry leaders received guidance from Belfast Central Registry on how the transfer would be performed in practical terms, together with the template of the Declaration to be signed.

Ispra, 31.10.2014

Dear EUROCAT Registry Leader,

Since the establishment of EUROCAT in 1979 by the European Commission's Directorate General (DG) for Science, Research and Development, the EUROCAT central activities including the Central Registry with the central database and the Steering Committee have been funded by the European Commission in the frame of successive projects and health programmes: 1979-1990 by DG Science, Research and Development; 1991-1998 by DG Employment, Industrial Relations and Social Affairs, Health and Safety; 2000-2014 by DG Health and Consumers (DG SANCO).

This framework, combined with the dedication, competence and passion of the people who built and maintained every single register has led to EUROCAT becoming an EU-wide and internationally recognised reference network for the surveillance of congenital anomalies. The valuable scientific work done over those years has led to results of real relevance and importance for European public health.

In order to secure a sustainable solution for the continuation of the EUROCAT activities and faced with the actual situation in which

- the functioning of the EUROCAT Central Registry is ensured only until 31.12.2014 by an operating grant from DG SANCO/Chafea and
- DG SANCO, in close collaboration with the DG Joint Research Centre (JRC), started to develop the EU Platform on Rare Diseases Registration at the JRC site in Ispra, Italy,

EUROCAT will become part of the EU Platform. The Central Registry including the central database and the website will be moved to the JRC and will start to operate from the JRC as from the 01.01.2015. Therefore, the reception and treatment of the data will be coordinated by the JRC as and from that date. Registries will remain the owners of their data. JRC will not give the raw data to any third party without the explicit consent of each registry and will not publish any findings or results without the explicit consent of each registry. In fact, the JRC will ensure to give visibility to the registries.

The terms of the transfer and the future functioning of EUROCAT were agreed between JRC and the EUROCAT Steering Committee during several meetings: Ispra, 27-28.11.2013; London, 28-29.04.2014; Belfast, 26-27.06.2014. The handover of the EUROCAT documents to the JRC as well as the training of JRC staff on the operation of the central database are ongoing, according to the work plan of the operating grant.

The activities that will be provided by the JRC include:

- support to the coordinating activities of EUROCAT
- organising the meetings of the
 - Steering Committee
 - Coding and Classification Committee
 - other working groups
- organising the annual Registry Leaders' Meeting
- organising scientific symposia
- running the database
- support for dissemination activities:
 - website
 - newsletters, leaflets
- support offered to the individual registries:
 - coding workshop
 - trainings
 - IT support
- future actions aimed at adding value to the EUROCAT data by
 - integration into larger health information systems, links to other databases (*e.g.* environmental data)
 - dissemination of public health indicators to policy makers for decisions on primary/secondary prevention.

All the activities will be carried out in collaboration with and under the scientific responsibility of the Steering Committee (which may become the Management Committee) and in line with the unified EUROCAT Network Procedural Manual.

Thank you for the great work you've done up to now and we look forward to your continued and fruitful cooperation in the frame of the EUROCAT network.

Ciarán Nicholl
Head of Unit
European Commission, Joint Research Centre
Institute for Health and Consumer Protection
Public Health Policy Support

Ispra, 10.12.2014

Dear EUROCAT Registry Leader,

on 4 December 2014 at the JRC's site in Ispra, the EUROCAT Steering Committee met with JRC representatives.

The Steering Committee endorsed the following way forward to ensure the transfer of data on congenital anomalies to the JRC as soon as possible:

The Registries are asked to sign the attached declaration giving their consent for the data to be transferred to the JRC. The Registries are asked to return the signed and scanned copy of the declaration to the EUROCAT Central Registry at eurocat@ulster.ac.uk with JRC-EUROCAT@ec.europa.eu in copy by **16 December**. The registries which will not provide their consent by 22 December 2014 at the latest will be given back all the data by the Central Registry and will be asked to send the data to the JRC directly. In order to ensure the continuity of the activities and given the very limited timeframe it is crucial that the consent is given as soon as possible so that the Central Registry can effectuate the transfer before the end of the operating grant.

The JRC will handle the data in accordance with the EUROCAT rules and procedures specified in the EUROCAT Network Procedural Manual.

The JRC will ensure that any operation using the data is carried out in accordance with the relevant provisions of the applicable data protection law.

The JRC will ensure that all reasonable administrative, technical and physical safeguards are taken to protect the data from misuse, loss or any unauthorised access, modification or disclosure.

All the activities will be carried out in collaboration with and under the scientific responsibility of the Steering Committee (which may become the Management Committee). New staff (statistician, IT specialists) will be recruited at the JRC in order to ensure the functioning of the Central Database. JRC is presently negotiating with the University of Ulster to facilitate the transfer of the software and website. If negotiations don't succeed, JRC will develop the system from scratch.

The activities provided by the JRC will be offered to the registries who agree to transmit their data to the JRC and sign the declaration attached.

In order to remind you on the activities offered and the reasons for the transfer, I send you below an updated version of my previous letter to you:

Since the establishment of EUROCAT in 1979 by the European Commission's Directorate General (DG) for Science, Research and Development, the EUROCAT central activities including the Central Registry with the central database and the Steering Committee have been funded by the European Commission in the frame of successive projects and health programmes: 1979-1990 by DG Science, Research and Development; 1991-1998 by DG Employment, Industrial Relations and Social Affairs, Health and Safety; 2000-2014 by DG Health and Consumers (DG SANCO).

This framework, combined with the dedication, competence and passion of the people who built and maintained every single register has led to EUROCAT becoming an EU-wide and internationally recognised reference network for the surveillance of congenital anomalies. The valuable scientific work done over those years has led to results of real relevance and importance for European public health.

In order to secure a sustainable solution for the continuation of the EUROCAT activities and faced with the actual situation in which

- the functioning of the EUROCAT Central Registry is ensured only until 31.12.2014 by an operating grant from DG SANCO/Chafea and
- DG SANCO, in close collaboration with the DG Joint Research Centre (JRC), started to develop the concept for the EU Platform on Rare Diseases Registration at the JRC site in Ispra, Italy,

EUROCAT will become part of the EU Platform. Therefore, the receipt and treatment of the data will be coordinated by the JRC as and from the 01.01.2015. Registries will remain the owners of their data. JRC will not give the raw data to any third party without the explicit consent of each registry and will not publish any findings or results without the explicit consent of each registry. In fact, the JRC will ensure to give visibility to the registries.

The terms of the transfer and the future functioning of EUROCAT were agreed between JRC and the EUROCAT Steering Committee during several meetings: Ispra, 27-28.11.2013; London, 28-29.04.2014; Belfast, 26-27.06.2014, Ispra, 04.12.2014. EUROCAT documents were handed over to the JRC and a training session of a JRC staff member on the operation of the central database took place in October.

The activities that will be provided by the JRC include:

- support to the coordinating activities of EUROCAT
- organising the meetings of the
 - Steering Committee
 - Coding and Classification Committee
 - other working groups
- organising the annual Registry Leaders' Meeting
- organising scientific symposia (up 2016)
- running the database
- support for dissemination activities:
 - website
 - newsletters, leaflets
- support offered to the individual registries:
 - coding workshop
 - trainings
 - IT support
- future actions aimed at adding value to the EUROCAT data by
 - integration into larger health information systems, links to other databases (*e.g.* environmental data)
 - dissemination of public health indicators to policy makers for decisions on primary/secondary prevention.

Thank you for the great work you've done up to now and we look forward to your continued and fruitful cooperation in the frame of the EUROCAT network.

Ciarán Nicholl
Head of Unit
European Commission, Joint Research Centre
Institute for Health and Consumer Protection
Public Health Policy Support



Declaration

Considering the Letters to the Registry Leaders sent by the European Commission's Joint Research Centre–Institute for Health and Consumer Protection (JRC) on 31.10.2014 and 10.12.2014 regarding the transfer of the EUROCAT coordinating activities to the JRC as of 1 January 2015, the undersigned Registry agrees that its data on congenital anomalies stored at the EUROCAT Central Registry at the University of Ulster be transmitted to the JRC. The Registry reserves the right to modify its data prior to their transmission to the JRC in accordance with the applicable legislation. The undersigned Registry declares its willingness to continue transmitting data on congenital anomalies to the JRC in the future. The data will be released by the Registry under the same conditions as they have been released to the Central Registry at the University of Ulster.

Registry Name:

Registry Leader Name:

Date:

5. Transfer

Separate processes were conducted for the transfer of data, the transfer of software and the procurement of services. The transfer of data proceeded in close collaboration with the EUROCAT Central Registry.

5.1. EUROCAT data

Data on congenital anomalies are collated across Europe in population-based registries. The registries use multiple sources to ascertain cases but the ascertainment of cases is far from being a data linkage exercise. The registration of cases requires a multidisciplinary team that includes clinicians, epidemiologists, data managers and collectors, administrative staff as well as project coordination and leadership structure. EUROCAT is an internationally established network that provides essential epidemiologic information on congenital anomalies at the European level. The added value of the EUROCAT network comes from the pooling of standardised data to perform surveillance activities.

The Central Registry in Belfast hosted EUROCAT Central Database which contained data on approx. 500 000 cases of CA. Twice a year, Full and Associate member registries submit electronic data. Over time, EUROCAT network designed and developed efficient procedures to harmonise, validate and pool the data collected and submitted by registries. At an operational level, a dedicated and skilled team at Central Registry was in charge of processing the data and exchanging with member registries. In addition, working together with steering and specialised committees, it produced and disseminated summary tables and surveillance reports.

EUROCAT member registries keep the ownership of submitted data, even after the data is checked, modified and collated in the Central Database by Central Registry. This is why the effective transfer of data required the explicit approval of member registries.

The approval was formalised in the Declaration signed by the Registry Leader. The Declaration states the Member Registry agrees that its data stored at the EUROCAT Central Registry at the University of Ulster be transmitted to the JRC. The Member Registry also declares its willingness to continue transmitting data on congenital anomalies to the JRC in the future. The conditions for the release of data at JRC are the same that applied for University of Ulster.

Twenty-five registries signed the Declaration. EUROCAT Steering Committee decided to transfer as well the data of the 12 Past member registries, which data are used for in the prevalence tables.

The situation of the transfer as on December 23, 2014 was:

Transferred:

- **Active** registries: 25 registries (out of 38 active registries) (*Table 9*)
 - **Full** members (transmitting individual data): 22 registries (out of 32)
 - **Associate** members (transmitting aggregate data): three registries (out of six)
- **Past** registries: 12 registries (stored aggregate data; will not submit new data) (*Table 10*).

Table 9. EUROCAT member registries – Active data providers, transferred (n = 25).

		Registry			Declaration
		No.	Name	Leader	
TRANSFERRED as December 23, 2014	Full Members	R02	Hainaut-BE	Verellen-Dumoulin, Christine	Yes
		R08	Tuscany-IT	Bianchi, Fabrizio	Yes
		R13	N Netherlands-NL	deWalle, Hermien	Yes
		R18	Emilia Romagna-IT	Neville, Amanda	Yes

Table 9. (cont.)

	Registry			Declaration	
	No.	Name	Leader		
TRANSFERRED as December 23, 2014	Full Members	R20	Vaud-CH	Addor, Marie-Claude	Yes
		R21	Zagreb-HR	Barisic, Ingeborg	Yes
		R23	Malta-MT	Gatt, Miriam	Yes
		R28	S Portugal-PT	Dias, Carlos Matias	Yes
		R29	Antwerp-BE	Nelen,Vera	Yes
		R30	Basque Country-ES	Arriola, Larraitz	Yes
		R33	Saxony Anhalt-DE	Rissmann, Anke	Yes
		R34	Mainz-DE	Queisser-Luft, Annette	Yes
		R39	Styria-AT	Haeusler, Martin	Yes
		R49	Cork&Kerry-EI	O'Mahony, Mary	Yes
		R59	Norway-NO	Ebbing, Marta	Yes
		R60	Auvergne-FR	Perthus, Isabelle	Yes
		R66	Reunion-FR	Randrianaivo, Hanitra	Yes
		R67	Wielkopolska-PL	Latos-Bielenska, Anna	Yes
		R68	Thames Valley-UK	Kurinczuk, Jenny	Yes
		R70	Wessex-UK	Wellesley, Diana	Yes
		R81	French West Indies-FR	Schaub, Bruno	Yes
	R86	Valencia Region-ES	Zurriaga, Oscar	Yes	
	Associate Members	R55	Spain Hospital Network-ES	Martínez-Frías, María-Luisa	Yes
		R76	Poland-PL	Latos-Bielenska, Anna	Yes
R83		Czech Republic-CZ	Sipek, Antonin	Yes	

Table 10. *EUROCAT member registries – Past data providers (n= 12).*

TRANSFERRED	Past Full Members	R11	Galway-El	(1981-2000)
		R14	Glasgow-UK	(1980-2000)
		R19	Strasbourg-FR	(1982-2007)
		R25	North East Italy-IT	(1981-2003)
		R32	Asturias-ES	(1990-2004)
		R35	Barcelona-ES	(1992-2007)
		R41	Sofia-BG	(1996-1999)
		R43	North West Thames-UK	(1991-2005)
		R50	Sicily-IT	(1991-2005)
		R51	Campania-IT	(1996-2007)
	R52	Merseyside & Cheshire-UK	(1995-2000)	
	Past Assoc. Members	R54	Central East France-FR	(1980-2004)

Not yet transferred (*Table 11*):

- **Active registries:**
 - **Full** members (10 out of 32)
 - **Associate** members (three out of six)
- **Past registries:** none.

Table 11. *EUROCAT member registries – Active data providers, not yet transferred (n=13).*

		Registry			Declaration
		No.	Name	Leader	
NOT YET transferred	Full Members	R03	Odense-DK	Garne, Ester	No
		R05	Paris-FR	Khoshnood, Babak	No
		R10	Dublin-EI	McDonnell, Bob	No
		R57	Wales-UK	Tucker, David	No
		R62	Ukraine-UA	Zymak-Zakutnya, Natalya	No
		R72	E Midlands & S Yorkshire-UK	Draper, Elizabeth	No
		R73	Northern England-UK	Rankin, Judith	No
		R75	Hungary-HU	Csaky-Szunyogh, Melinda	No
		R79	SE Ireland-EI	Lynch, Catherine	No
	R84	South West England-UK	Stoianova, Sylvia	No	
	Associate Members	R38	Finland-FI	Ritvanen, Annukka	No
		R71	Sweden-SE	Kallen, Karin	No
		R80	Rhone-Alpes-FR	Amar, Emmanuelle	No

The main reasons for not signing the Declaration in the short allocated period were:

- the need for an extensive documentation about data security and data protection issues at the new Central Registry setting;
- the need to have the Declaration signed by a representative of the organisation of the Registry.

Table 12. EUROCAT member registries – Active Non-data providers (n = 17).

NON-Data Providers	Affiliate Members	Greenland	Flemming Kleist Stenz
		Pleven-BG	Katya Kovacheva
		Brittany-FR	Florence Rouget
		Campania-IT	Gioacchino Scarano
		Sicily-IT	Sebastiano Bianca
		Latvia CDPC-LV	Ieva Grinfelde
		Moldova-MV	Vladimir Egorov
		Slovenia-SL	Gorazd Rudolf
		R87	Nat. Down Syndrom CR-UK
	Applicant	Iceland	Helga Sol Olafsdottir
		Latvia	Iveta Volkovska-Cielava
		Lithuania	Algirdas Utkus
		Slovakia	Elena Szabová
	World Affiliates	Argentina	Rosa Liascovich
		Iran	Saeed Dastgiri
		New-Zealand	Barry Borman
		Saudi Arabia	Ahmed M Kurdi

On 23 December 2014, Central Registry at Belfast issued its last internal Communication and informed on the success of the full transfer to JRC of data from 25 Registries who signed the Declaration.

The data files from two thirds of EUROCAT member registries (37/50) in 16 countries were secured at JRC-Ispra.

5.2. EUROCAT software

EUROCAT software includes two software products:

- the data management programme
- the website.

EUROCAT software was developed in the framework of EU grants awarded to University of Ulster, which was the affiliation of the Project Leader and the Central Registry. The IP rights are on University of Ulster.

The two pieces of software are instrumental to complete EUROCAT data cycle. First, the data management programme with two versions, for use in member registries and in Central Registry. Second, the website with different access levels and two salient features: an interactive system for producing customised prevalence tables and an archive of EUROCAT documentation.

5.2.1. EUROCAT Data Management Programme

EUROCAT Data Management Programme was designed by Central Registry to streamline the EUROCAT Database processes and obtain high quality data for surveillance in a timely manner. The system ensures that all data is coded according to agreed guidelines and verifies each case.

The two versions of the programme are: one for member registries (EUROCAT Data management Programme, EDMP) and one for Central Registry (EUROCAT Central Database, ECD).

EDMP

EDMP is designed for the management of data at individual registry level. EDMP is provided to all EUROCAT registries (full, associate and affiliate members). It is used by local registries for checking data before submission and for statistical monitoring of local clusters and trends. It is now used by nearly 40 EUROCAT registries. The Data check part can be purchased by non-EUROCAT registries; the surveillance part is exclusive of EUROCAT registries.

ECD

The ECD is only used by EUROCAT Central Registry. It is aimed at facilitating the operations of:

- 1) central database management;
- 2) public health statistical monitoring;
- 3) research activities (e.g. [EUROmediCAT](#)).

EDMP functionalities are included in ECD. In addition ECD can manage, analyse and report on data from different centres. Both programmes were created and are maintained and updated by [Biomedical Computing](#).

Tasks operated by ECD (*Table 13*):

1) Central Database management:

- *Import* of individual cases data (csv files).
- *Check data* and provide an ‘Error Report’ if importing failure is due to fatal conversion errors or an ‘Imported Data Summary’ with details of validation errors.
Information on ‘Data checks’ should be detailed in the ‘Procedural Manual on EUROCAT Software’ to be provided with the software. It took several years of a closed collaboration between Central Registry and the IT company to develop the software to its present form. Continuous maintenance and frequent updates are required.
- Provide an ‘History of Imported Data’ with notes from previous data submission.
- Import denominator data: two modalities, with an import facility or by entering data manually.
- *Input* aggregate *data*, manually typed in a table.
- *Edition* of existing cases, manually by entering Centre Name and Local ID Number; and feeding ‘Edit History’.
- *Select data* for upload to test website through a ‘Manage Web Data’ page that allows to select a Centre Name, year, subgroups of cases.

Table 13. Tasks operated with ECD software at Central Registry.

Tasks	Resources				Without ECD
	EDMP	ECD	Partners	IT company	
1) DATA MANAGEMENT and DESCRIPTIVE ANALYSIS					
Data submission	Y		Y		Data management routine needed
Data Import		Y			Data management routine needed
Data Check and derived variables	Y	Y	Y		Data Constraints and Integrity rules are not documented. Software development needed
Error report		Y			Software development needed
Import data report		Y			Software development needed
History of imported data		Y			–
Data Input		Y			Data management routine needed
Data Edition		Y			Data management routine needed
Data Selection		Y			Data management routine needed
Frequency distributions		Y			Statistical programming needed
Epidemiologic measures		Y			Statistical programming needed
Quality indicators		Y			Statistical programming needed
Data Upload to Test website				Y	Software development needed
Data Upload to Live website				Y	Software development needed
Data Export		Y			Data management routine needed
2) PUBLIC HEALTH					
Statistical monitoring					
Clusters and trends	Y	Y			Statistical programming and software development
Pan Europe trend analysis					Performed by Central registry staff. Statistical programming needed

Table 13. (cont.)

Tasks	Resources				Without ECD
	EDMP	ECD	Partners	IT company	
3) RESEARCH					
Download data for a Project		Y			Data management routine needed

- Use the ‘Reports’ functionality > ‘Missing Data Frequencies’ > ‘Missing values by Centre for selected years’ to obtain an Excel file with *computed* missing values *frequencies* by variable/year/centre.
- *Generate epidemiologic measures*: prevalence data files, perinatal mortality and prenatal diagnosis files for test and live website. These estimations are computed from ‘cases’ and ‘denominators’ data. The files obtained are sent to the administrator of EUROCAT website at Biomedical Computing who will upload them. The data for test website are uploaded on a Biomedical Computing server and will only be accessed by EUROCAT partners. The data for live website are uploaded on the public EUROCAT website.
- *Export* data to from UK, EI and FR registries to ‘UK+EI’ and to French network.
- *Quality indicators* report: compute and display QI.

2) EUROCAT public health statistical monitoring:

ECD includes a module for *statistical analysis of clusters and trends*. The statistical module included in EDMP is limited to the analysis of one registry. A complex routine called *Pan-Europe trend analysis* is run on Stata by the central registry staff.

3) EUROCAT Research:

Customised data download is routinely performed for approved research projects. Some projects require the use of all ECD functions, e.g. EUROmediCAT.

ECD/EDMP Technical description

ECD/EDMP are written in MS Access and VBA, C Sharp, Java Script, SQL Server and Perl. System requirements are Windows Server 2003 and later.

New versions are downloaded from EUROCAT website. ECD/EDMP are installed locally.

The EUROCAT Central Database is comprised of four MS Access databases. One is the user interface and the remaining three are the data containers (Case data, extra data and history). The case data database currently holds around 490 000 records. The user interface provides the facilities to manage, export, analyse and report the data.

5.2.2. EUROCAT website (www.eurocat-network.eu)

The EUROCAT website allows Central Registry members to update and modify content via the custom developed Content Management System by Biomedical Computing Ltd.

The websites are closely linked with the Database and many of online data sources used are updated via uploads specifically generated from the central database. The online summary data allows users to apply selection criteria and generate prevalence and detection rate tables in a number of formats. Test data for registries is uploaded for their approval prior to use.

Routine data management includes importing data from registries, uploading data for interactive website tables and producing routine data quality indicators (DQI) and statistical monitoring outputs. In addition there is the manual update of annualised associate registry aggregate data.

The [Site Map](#) is detailed below:

- Coding Committee
- ABOUT US
 - What Is EUROCAT?
 - What is EUROCAT?
 - EUROCAT Association
 - EU Rare Diseases Policy
 - WHO Collaborating Centre
 - Member registries
 - Data Collection
 - Guidelines for Registration
 - Guide 1.4
 - Guide 1.3 Instruction Manual
 - Malformation Coding Guides
 - Previous Coding Guides/ Instruction Manuals
 - EDMP
 - Introduction/Purchase for Non-European Members
 - EDMP User Guide
 - Ethics & Consent
 - Data Security & Confidentiality
 - Data Management
 - Data Transmission to Central Registry
 - Data Quality
 - Data Quality Indicators
 - Cases Diagnosed After 1 Year
 - Missing Frequency Rates per Variable
 - Requesting EUROCAT Data
 - Publications
 - Media Interest
 - EUROCAT Press Releases
 - EUROCAT Symposia & Workshops
 - Zagreb Symposium 2013
 - Antwerp Symposium 2011
 - Bilbao Symposium 2009
 - Naples Symposium 2007
 - Poznan Symposium 2005

- Heidelberg Symposium 2003
 - Sicily Symposium 2001
 - Environmental Pollution Workshop 2007
- CODING & CLASSIFICATION
 - Coding Committee
 - Members
 - ICD11
- ACCESS PREVALENCE DATA
 - Prevalence Tables
 - Key Public Health Indicators
 - Interpretation Guide
 - Calculation of Prevalence Rates
 - Interpretation of Prevalence Rates
- PREVENTION & RISK FACTORS
 - Primary Prevention
 - Folic Acid
 - Medication During Pregnancy
 - Medication Introduction
 - Medication Publications
 - Medication Posters
 - EUROmediCAT
 - ATC Coding
 - Relevant Websites
 - Environmental Pollution
- PRENATAL SCREENING & DIAGNOSIS
 - General Information
 - Introduction
 - Policies in European Countries
 - Prenatal Diagnosis Publications
 - Prenatal Detection (PD) Rates
- CLUSTERS & TRENDS
 - Statistical Monitoring
- USEFUL LINKS
- CONTACT US
- GALLERY

- A simple statistical test
- Affiliate Members
- All Members
- Applicant Members
- Application for Membership
- Application Form
- Associate Members
- Completed Cluster Investigations
- Coverage of European Population
- Environmental Risk Factors
- EUROCAT Membership Criteria
- Full Members
- Home Page
- How Unusual is an Observed Cluster?
- Introduction
- Members & Registry Descriptions
- New Prevalence Tables
- Past Members
- Privacy Policy
- Terms of Use
- World Affiliate Members

It took several years of a closed collaboration between Central Registry and the IT company to develop the software to its present form. Continuous maintenance and frequent updates are required.

The transfer of the EUROCAT software (Data Management Programme and website) was finalised via a purchase contract between JRC and the University of Ulster.

6. JRC-EUROCAT Collaboration Agreement

The JRC and the EUROCAT Network member registries have established a legal framework for the transfer and the continuation of EUROCAT European-level coordinating activities at the JRC in the context of the EU Platform for Rare Diseases Registration.

In December 2014 the EUROCAT member registries able to transfer data to the JRC before the end of the year signed a Declaration (see 4.4.4). In early 2015, the JRC Legal Advice Unit proposed to have a Collaboration Agreement signed between the JRC and the individual Registries covering the objectives of the collaboration, roles and responsibilities of the parties, governance and coordination, protection of the results of the collaboration.

Following the approval of the text by the JRC-EUROCAT Management Committee in May 2015, the final draft of the Collaboration Agreement was presented at the EUROCAT Registry Leaders Meeting in June 2015, and its details were extensively been discussed with the participants. After this comprehensive discussion and in line with its conclusions, the Collaboration Agreement was sent for signature in September-November 2015, once the legal representatives of the registries were notified to the JRC.

The Collaboration Agreement entered into effect in December 2015 when signed by at least seven member registries.

As of 7 March 2016, 26 out of 34 organisations (27/39 registries) have signed the collaboration agreement. See *Figure 3* and *Table 14*.

6.1. Objectives of the Collaboration Agreement

The collaboration takes place in the frame of the EU Platform on Rare Diseases Registration being developed at the JRC in agreement and close collaboration with DG SANTE.

EUROCAT network member registries

(as of March 7th, 2016)

Member registries (n=39):

Full members, n=33

Associate members, n=6

Collaboration Agreement signed (n=27)

additionally, in the process of signature (n=9)

under legal considerations (n=3)

Data submitted in 2015 (n=27)

in 2016 (n=11)

Complete data available

at Central registry (n=32)

Figure 3.

Specific objectives of the agreement are:

- To secure a sustainable solution for the continuation of EUROCAT activities and to secure the results of the previous work.
- To ensure further functioning of the Central Registry and Central database of congenital anomalies, as well as of the European-level coordination activities of EUROCAT.

Table 14. EUROCAT member registries that signed the JRC-EUROCAT Collaboration Agreement, as of 7 March 2016.

Central Registry assigned No.	Central Registry assigned Name	EU Member State /European Country		Signed JRC-EUROCAT Collaboration Agreement
39	Styria	Austria	AT	YES
2	Hainaut	Belgium	BE	NO
29	Antwerp	Belgium	BE	YES
21	Zagreb	Croatia	HR	YES
83	Czech Republic	Czech Republic	CZ	NO
3	Odense	Denmark	DK	NO
38	Finland	Finland	FI	YES
5	Paris	France	FR	NO
60	Auvergne	France	FR	YES
66	Isle de la Reunion	France	FR	YES
80	Rhone-Alps	France	FR	NO
81	French West Indies	France	FR	YES
88	Brittany	France	FR	YES
33	Saxony-Anhalt	Germany	DE	YES
34	Mainz	Germany	DE	YES
75	Hungary	Hungary	HU	NO
10	Dublin	Ireland	IE	YES
49	Cork and Kerry	Ireland	IE	YES
79	SE Ireland	SE Ireland	IE	YES
8	Tuscany	Italy	IT	YES

Table 14. (cont.)

Central Registry assigned No.	Central Registry assigned Name	EU Member State /European Country		Signed JRC-EUROCAT Collaboration Agreement
18	Emilia Romagna	Italy	IT	YES
23	Malta	Malta	MT	YES
13	N Netherlands	Netherlands	NL	YES
59	Norway	Norway	NO	YES
67	Wielkopolska	Poland	PL	YES
76	Poland	Poland	PL	YES
28	S Portugal	Portugal	PT	YES
30	Basque Country	Spain	ES	YES
55	Spain Hospital Network	Spain	ES	YES
86	Valencia Region	Spain	ES	YES
71	Sweden	Sweden	SE	NO
20	Vaud	Switzerland	CH	YES
62	Ukraine	Ukraine	UA	YES
57	Wales	United Kingdom	UK	YES
68	Thames Valley	United Kingdom	UK	NO
70	Wessex	United Kingdom	UK	NO
72	East Midlands & S York	United Kingdom	UK	NO
73	Northern England	United Kingdom	UK	NO
84	South West England	United Kingdom	UK	NO

6.2. Responsibilities of the Parties

6.2.1. Responsibilities and roles of the JRC

a) Operates the JRC-EUROCAT Central Registry.

The role of the Central Registry is:

1. To maintain and further develop a centralised database of congenital anomalies according to established coding methodologies. The JRC shall be the owner of the central database.
2. To coordinate and operate data collected from the Registries.
3. To ensure data security/safety including the process of data transmission.
4. To manage data including data checking, standardisation, quality assessment, validation, statistical analysis for monitoring of clusters and trends, to provide the output of analysis for further dissemination.
5. To manage the website–administration, maintenance, updates, development.
6. To communicate with the Registries and give feedback on data-related issues and results of the monitoring.
7. To offer support to individual registries for the implementation of EUROCAT procedures.
8. To produce and disseminate to the Registries the monthly ‘Communication’.
9. To maintain and establish relations with other organisations.
10. To process and evaluate new applications for membership and requests for data use.

b) Participates to and supports the coordinating activities of EUROCAT.

c) Organises meetings of the JRC-EUROCAT Management Committee, Coding and Classification Committee, other committees and working groups.

d) Organises the annual Registry Leaders’ Meeting.

e) Organises scientific symposia, workshops.

f) Offers support for dissemination activities: newsletters, leaflets.

g) Offers support to the individual registries – e.g. IT support, etc.

h) Supports the organisation of trainings.

i) Ensures to give visibility to the Registries.

j) Disseminates the output of data analysis whilst ensuring anonymity of the Registries.

- k) Supports actions aimed at adding value to the EUROCAT data by: integration into larger health information systems, links to other databases (*e.g.* environmental data), dissemination of public health indicators to policy makers for decisions on primary/secondary prevention.
- l) Promotes the registration of congenital anomalies across Europe.

6.2.2. Responsibilities and roles of the Registries

- a) Transmit data to the Central Registry (full members: individual data; associate members: aggregate data), according to the annual calendar for data transmission (deadlines: February and October). The Registries remain the owners of their data and the JRC is granted rights of use on the data for the purposes of the activities set out in this Collaboration Agreement.
- b) Provide feed-back on the data processed at the Central Registry and on the output of data analysis; collaborate with the Central Registry for data validation.
- c) Contribute to the analysis and interpretation of the monitoring results and reports related to the data they provided.
- d) Approve the prevalence data and give permission to the JRC to publish the results of the monitoring on the EUROCAT website.
- e) Decide on giving permission to the JRC for any use of individual data.
- f) Inform local/regional/national health authorities on the issues of concern from the results of the monitoring.
- g) Obtain ethical approvals if required by the applicable law at their site.

6.3. Coordination

The JRC-EUROCAT Management Committee consisting of 7 representatives of the EUROCAT Network and two representatives from the JRC co-ordinates EUROCAT activities as follows:

- a) Prepares and takes decisions on the JRC-EUROCAT activities under the Collaboration Agreement.
- b) Decides on membership issues including applications for membership.
- c) Supervises the security and confidentiality of data held at the Central Registry including data transmission.

- d) Facilitates the discussions between the Registries and the Central Registry concerning the execution of the activities under the Collaboration Agreement.
- e) Supervises and supports the organisation of the annual Registry Leaders' Meeting.
- f) Decides on applications for additional meetings, workshops and working groups.
- g) Decides on applications for studies regarding protocol, data and authorship.
- h) Establishes policies and adopts documents related to the Management Committee and the Central Registry.
- i) Supports the activities and collaborates with the Central Registry.

Decisions of the JRC-EUROCAT Management Committee are taken by consensus.

7 JRC-EUROCAT Central Database –Part of the European Platform on Rare Diseases Registration

The JRC-EUROCAT Central Database (CDB), component of the JRC-EUROCAT Central Registry operates from the JRC since the 1st of January 2015. The operation of the CDB includes all processes aimed at strengthening the value and quality of the CDB. This comprises, among other functions, maintaining the CDB, updating the CDB annually with data submissions from registries, and extending the network of data providers.

7.1. Maintaining the CDB

The added value of the EUROCAT network of registries comes from the pooling of standardised data into the CDB to perform monitoring and research activities.

The effective hosting and maintenance of the EUROCAT Central Database at the JRC is the outcome of two different processes, the transfer of EUROCAT data and the transfer of the EUROCAT software.

Set-up of the CDB

The previous Central Registry (Ulster) transferred to the JRC the individual data sets fragmented by registry. Registry data were transferred in separate Access files. IHCP IT Support team rebuilt the CDB. All Access files had the same structure. Starting with an empty Access database, individual data tables were linked to the CDB and imported by appending all records of each linked table to the corresponding table in the CDB. The process was performed for datasets with individual and aggregate data. In addition, the CR team developed a set of relational spreadsheets to manage and update the content of the CDB as new files were received.

Table 15 shows the sequence of the data transfer from the previous Central Registry in Belfast to JRC-EUROCAT Central Registry. In December 2014, CDB at Belfast CR included data from 50 registries: 33 registries provided individual data and

17 aggregate data. The transfer was performed in two phases. First, CR at JRC received individual data from 22 full registry members and aggregate data from 15 associate and past registries. Later in March, more aggregate data were received from 10 full registry members and three associate members.

Table 15. *Transfer of data to JRC-EUROCAT Central Registry (50 registries, as 24/03/2015).*

EUROCAT Central Database							
		31/12/2014		Jan-Mar 2015		24/03/2015	
Member	n	Data	n	Data	n	Data	n
Full	32	Individual	32	Individual	22	Individual	22
				Not transferred (n = 10)		Aggregate	10
Associate	6	Aggregate	5	Individual	1	Individual	1
				Not transferred (n = 3)		Aggregate	5
				Aggregate	2		
Past	12	Aggregate	12	Aggregate	12	Aggregate	12
		50	50	37		50	

JRC Central Registry hosts EUROCAT Central Database which contains data on more than 700 000 cases of CA. The data in the CDB correspond to individual cases or to aggregate cases, depending on the registry membership (full, associate, affiliate, past member) and on the decision of registries to transfer data before or after the signature of the Collaboration Agreement with JRC.

Table 16 and *Figure 4* show a summary of data hosted at JRC CR as of September 2015.

At this stage (2015) the CDB includes data transferred to the CR and data transmitted for the first data submission deadline in 2015 (in red in the table). Number of cases is presented by registry, birth year and type of data. The CDB contains individual data from 30 registries, and aggregate data from 24 registries: 12 past registries, five associate and seven full member registries.

The Central Registry team is in charge of processing the data and exchanging with member registries, to work with the MC and other committees (Coding and Classification Committee), to produce summary tables and statistical monitoring analysis, to disseminate results and to coordinate together with the MC data requests and applications for membership.

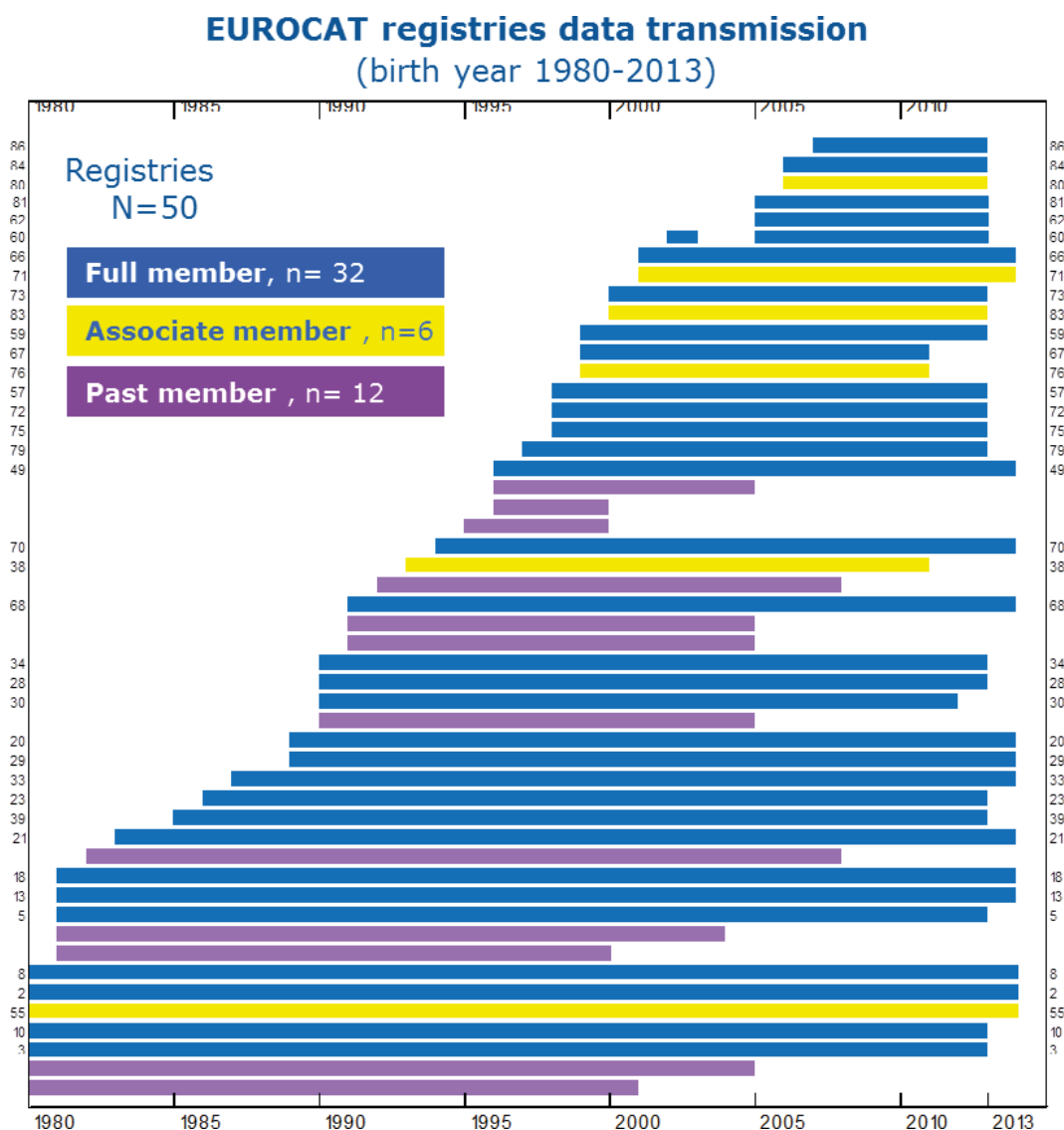


Figure 4. EUROCAT Central Database data, by type of registry and birth year (1980-2013; 50 registries, as 24/03/2015).

EUROCAT software

During the process of transferring the EUROCAT software to the JRC, the CR team developed data management tools to perform tasks such as rebuilding the CDB, reporting on data submission, providing feed-back to registries, analysing new variables. Before the accomplishment of the transfer, it was not possible to process submitted data according to EUROCAT procedural manual or to produce standard EUROCAT summary tables and statistical monitoring.

7.2. Update of the CDB

To achieve the main purpose of monitoring changes in time and place in the occurrence of births with congenital anomalies, the CDB needs to be regularly updated by registry members across Europe. The EUROCAT network established a calendar for performing all tasks necessary to achieve its main objective. The calendar foresees two data submission deadlines annually which are directly related with an output in terms of monitoring. The first data submission is February 15, the second October 15. The annual monitoring process is mainly reliant on the first annual submission deadline. One of EUROCAT data quality indicators (DQI) is related with timeliness for February data submission. These last years, two thirds of registries submitted data for the first deadline. Registries that did not submit for the first deadline are expected to submit for the second one. Registries that did submit for the first deadline can update their submission in terms of new cases for a certain year or new/modified data for a case already submitted.

The first step in the annual update of the CDB is the confirmation by the Management Committee of the deadline for submission. At the meeting of the JRC-EUROCAT Management Committee in December 2014, the data submission calendar for year 2015 was discussed. By default, the first 2015 deadline would be February 15. The main benefit of keeping the deadline was to send a positive signal to the network that the MC and CR at JRC intended to achieve their objectives in terms of monitoring. The main risk was that in order to ensure continuity with previous EUROCAT practices in terms of data checking and processing and statistical monitoring, CR should use ECD software. At that time, December 4, 2014 the purchase of ECD software by JRC was not done but an early completion was

foreseeable. The MC decided to keep the EUROCAT calendar and not to change the first data submission deadline.

The February deadline was confirmed by CR in January 2015 to EUROCAT member registries through the monthly emailed bulletin (EUROCAT Communication 2015/01).

Table 17 shows timeliness with February deadline submission for full registry members that agreed to transfer individual data to JRC Central Registry (n=22). Timeliness with February deadline submission is one of EUROCAT data quality indicators for full registry members. Out of the 22 full members that transferred individual data to JRC at the end of 2014, 80% of registries complied with 2015 February deadline, *i.e.* 11 out of 13 or 14 that usually submit in February did so in 2015.

Registries should strictly follow EUROCAT Guide 1.4 for the transmission of data [14]. Before transmission to CR, registries should check their data with EDMP software.

Table 17. *Timeliness with February data submission deadline for full registry members.*

Registry		Birth year submitted (1 = yes)				
Code	Name	2013	2012	2011	2010	2009
2	Hainaut-BE		1	1	1	1
8	Tuscany-IT	1	1	1	1	1
13	N Netherlands-NL	1	1	1	1	1
18	Emilia Romagna-IT	1	1	1	1	1
20	Vaud-CH	1	1	1	1	
21	Zagreb-HR	1	1		1	1
23	Malta-MT					1
28	S Portugal-PT					1

Table 17. (cont.)

Registry		Birth year submitted (1 = yes)				
Code	Name	2013	2012	2011	2010	2009
29	Antwerp-BE	1	1	1	1	1
30	Basque Country-ES				1	
33	Saxony Anhalt-DE	1	1	1	1	1
34	Mainz-DE			1	1	
39	Styria-AT					1
49	Cork & Kerry-IE	1	1			
59	Norway-NO		1	1		
60	Auvergne-FR					
66	Reunion-FR	1	1	1		1
67	Wielkopolska-PL					
68	Thames Valley-UK	1	1	1	1	1
70	Wessex-UK	1	1	1	1	1
81	French W Indies-FR		1	1	1	
86	Valencia Region-ES					
Full member, individual data transferred, n = 22		11	14	13	13	13

For data transmission, local registries had the choice between two procedures. Registries could send a data file in a password protected email. Most registries were used to this mechanism. Some required a more secure way of transmitting data through a data transmission portal.

The IT Support Team established a web-based system for safe upload of data files from EUROCAT registries to JRC servers via SSL encryption (HTTPS). The directory for the upload of files was only accessible with a combination of username and password in a URL address administered by the JRC (e.g. <https://gmoextranet>).

jrc.ec.europa.eu/Rare-Diseases/UKPHE). The URL address and the username are emailed in different messages. The password is provided through a secure e-mail address or by phone. From next data submission campaign, this data transmission system will be the only way for registries to transmit data to Central Registry.

Figure 5 shows the management panel of the data transmission portal.

Following the reception of the case data file, CR performs a set of pre-specified data checks. These checks are one of the functions of ECD software. ECD was not yet available at CR when data were transmitted. CR performed logical checks consistent with the description of variables in EUROCAT Guide 1.4. The analyses were discussed with the MC and a feed-back report was sent to registries.

CR performed an analysis of the new variables as they were received in 2015 data submission. This analysis was discussed at the MC in May and at the annual network meeting in June. It was considered very useful by registries for developing recommendations and improving the collection of new and related variables.

7.3. Legal considerations

Following the entry into force of the Collaboration Agreement between the JRC and the registries, the JRC has rights on the network's central database and website.

As a European Commission's DG, JRC needs to comply with specific legal requirements in terms of data protection and information security.

7.3.1. Data protection

The [EU Charter of Fundamental Rights](#) [15] (Art.8 on human rights to privacy and protection of personal data), the [Treaty on the Functioning of the EU](#) [16] (Art. 16) and the [Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 'on the protection of individuals with regard to the processing of personal data and on the free movement of such data'](#) [17] provide a legal framework for the processing of personal data in the EU.

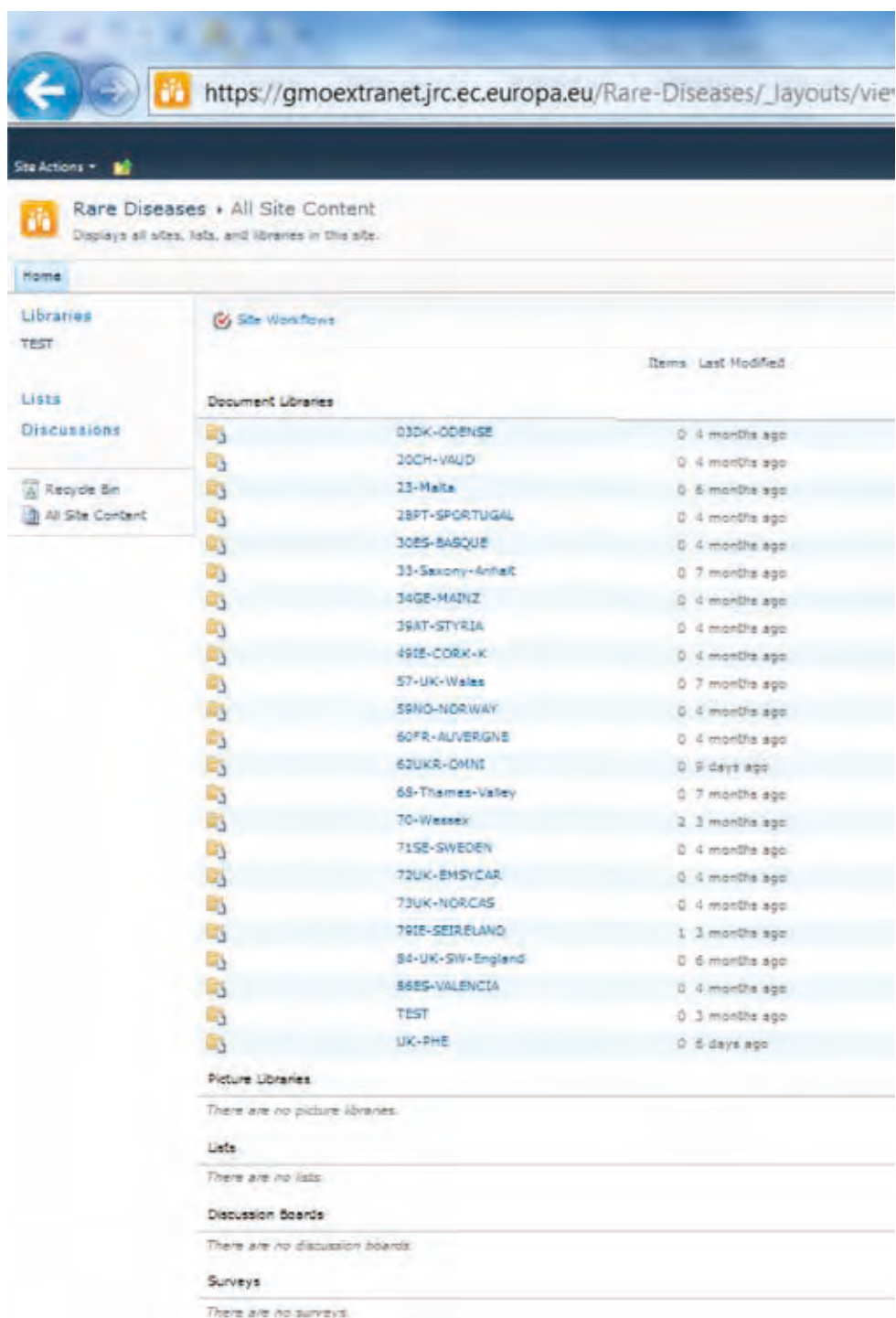


Figure 5. JRC-EUROCAT Data transmission portal, management panel.

The processing of personal data by EU institutions and bodies has a specific legal framework. For operating the JRC–EUROCAT Central Database, the JRC needs to comply with [Regulation \(EC\) 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’](#) [18].

The definition of personal data contained in the data protection Directive reads as follows:

Personal data shall mean any information relating to an identified or identifiable natural person (‘data subject’); an identifiable person is one who can be identified, directly or indirectly, in particular by reference to an identification number or to one or more factors specific to his physical, physiological, mental, economic, cultural or social identity.

This definition reflects a wide notion of ‘personal data’ and includes all information concerning an identifiable individual. It includes objective and subjective information, sensitive and more general information on any format. [*Any information*]

It includes information about a person or information with the purpose of evaluating a person or information which use may have an impact on the person. [*Related to*]

The person may be identified by identifiers (*e.g.* name) or by all the means likely reasonably to be used by the controller or by any other person. [*Identified or identifiable person*] The information refers to living individuals with special considerations with deceased persons.

In different circumstances *information may be considered not to be personal data*. This is the case where the data cannot be considered to relate to an individual, or because the individual cannot be considered to be identified or identifiable. When the information that is processed does not fall within the concept of ‘personal data’, the consequence is that the Directive does not apply. This does not mean, though, that individuals may be deprived of any kind of protection in the par-

ticular situation. If the Directive does not apply, national data protection law may apply. It may therefore very well happen that certain situations not involving processing of personal data as defined in the Directive are nevertheless subject to protective measures under national law.

Processing of personal data refers to any operation or set of operations which is performed upon personal data, whether or not by automatic means, such as collection, recording, organisation, storage, adaptation or alteration, retrieval, consultation, use, disclosure by transmission, dissemination or otherwise making available, alignment or combination, blocking, erasure or destruction.

The Regulation (EC) 45/2001 describes a procedure and identifies players and responsibilities in the processing of personal data in EU institutions:

- Data subjects are persons or individuals that have the rights to be protected and informed. For JRC-EUROCAT Central Database, the data subjects are the individual cases registered in the database.
- The Data Controller takes the responsibility of the processing. For JRC-EUROCAT Central Database, the Head of the Public Health Policy Support Unit is the Data Controller.
- The Data Protection Coordinator (DPC) advises the Controller and relates with the Commissions' Data Protection Officer (DPO).
- The DPO approves the notification of the processing, sends the notification to the European DP Supervisor (EDPS), accepts and registers the notification.

Figure 6 represents the simplified procedure for the registration by the DPO of a notification for processing personal data.

All personal data processing operations or sets of operations in the Commission, intended to serve a single purpose or several related purposes must be notified by the controller to the Data Protection Officer of the Commission. The information provided shall include a description of the data processing operations, security safeguards, retention period, etc.

Processing operations likely to present specific risks to the rights and freedoms of data subjects must also be declared to the EDPS. The EDPS will examine whether the processing respects the Regulation and, if the notification qualifies for prior checking, *i.e.* if the opinion is given prior to the start of the processing operation, will deliver an opinion within a period of two months. In his opinion, the EDPS may make recommendations to the institution or body concerned so as to ensure compliance.

7.3.1.1. Notification

A notification is a prior notice by the Data Controller to the Data Protection Officer of any processing operation in which personal data is involved. It contains a description of the processing operations, security, safeguards, data transfer, retention period, legal basis.

The actors involved are (*Figure 6*):

- the Data Controller: determines the purposes and means of the processing and is the contact person;
- Commission's Data Protection Officer (DPO): advises and makes recommendations on rights and obligations [19];
- European Data Protection Supervisor (EDPS): independent authority, responsible that privacy rights are respected, particularly when risky processing of personal data are notified by DPO [20].

In early 2015, the Health in Society Unit prepared a notification to the DPO for processing of personal data related to JRC EUROCAT Central database. The notification was prepared in collaboration with JRC-Ispra Data Protection Coordinator (DPC) and submitted to the DPO through the DPO-2 system.

The DPO sent comments to the Controller. The notification was modified to address DPO comments and resubmitted by the DPC. Following further exchange between PHPS, DPC and DPO, the notification was resubmitted [Notification 3768.1]. *Figure 7* represents the workflow on the DPO-2 System for the acceptance of a notification to the DPO.

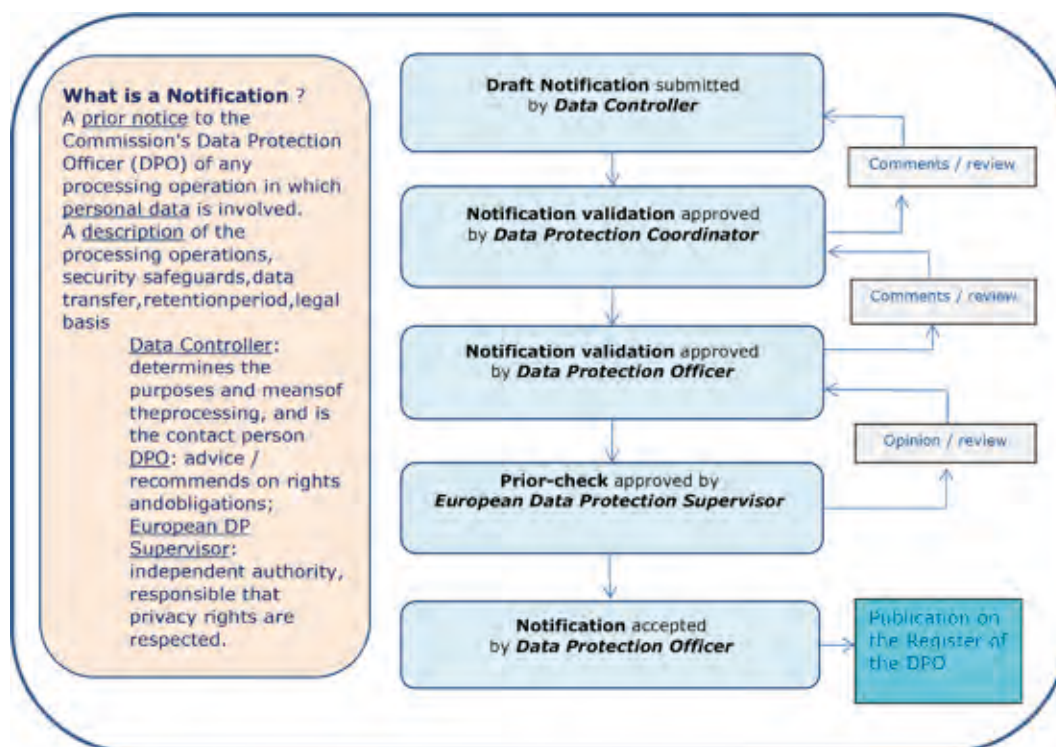


Figure 6. Simplified procedure for the registration of a notification by DPO.

7.3.1.2. DPO approval, EDPS opinion

The DPO approved the notification in October 2015 and sent it to EDPS. Notifications are sent to EDPS by DPO when the processing is considered of ‘high risk level 1’. Following exchanges between DPC, DPO and EDPS, the notification was considered for prior-check [Case number 2015-0982]. On 17 February 2016, EDPS sent a request for information to the Controller. PHPS prepared a reply in collaboration with DPC and LISO and sent it to DPO on 26 February.

The main points of the reply to EDPS related to clarifying the purpose of the notification, providing the legal provisions for the processing, the legal agreements with the registries, detailing the functioning of registration and information to participants at the local registry level, and the risk assessment at the Central Registry level.

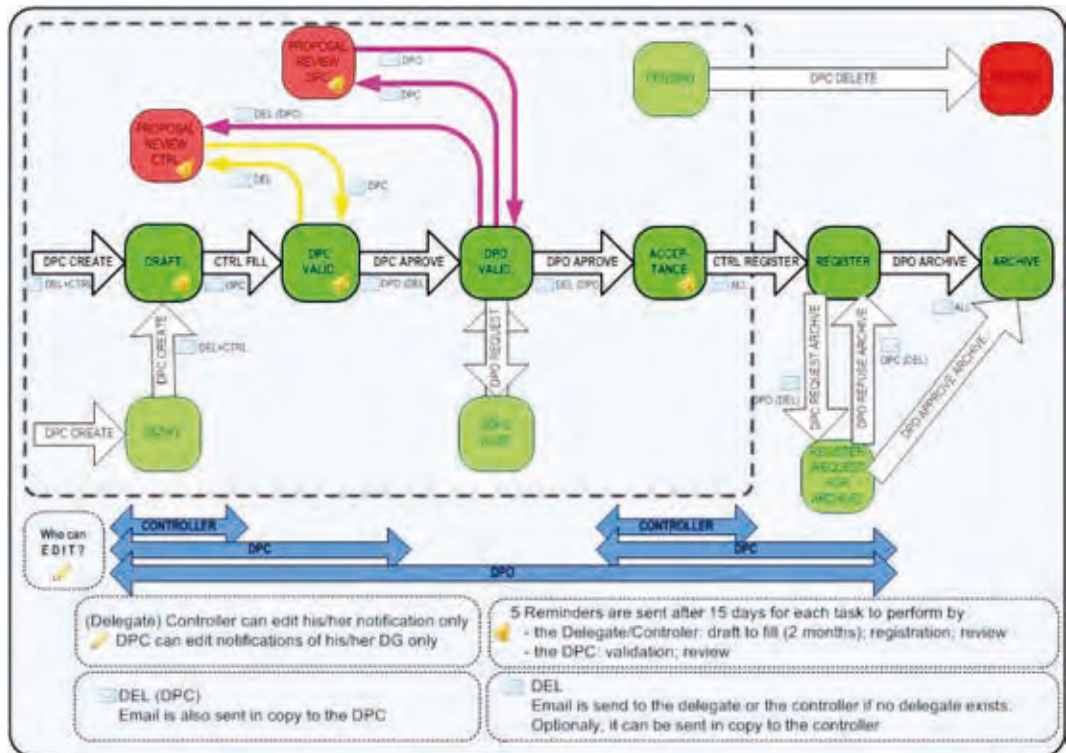


Figure 7. Workflow on the DPO-2 System for the acceptance of a notification to the DPO.

- The *purpose of the Notification* is to cover the possibility of identifying data subjects. This possibility is only theoretical. The databases do not include data subject names or other identifiers that could be connected by the JRC to a concrete patient (that can be done only by the national registry which submitted the data to the JRC). The databases include data such as date of birth of the subject and of the mother or residence codes that in themselves do not allow for identification of an individual without an extensive effort and access to other databases, to which JRC has no access and would not allow its staff to access or combine the data in them.

- The *legal basis* for processing can be found in
 - Treaty on the Functioning of the EU (Art. 168)
 - Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions on Rare Diseases: Europe’s Challenges [Com(2008) 679 final] (5.11) [1]
 - Council Recommendation of 8 June 2009 on an action in the field of rare diseases (2009/C 151/02) (II.5) [2]
 - Directive 2011/24/EU of the European Parliament and of the Council of 9 March 2011 on the application of patients’ rights in cross-border healthcare (12.2.(e),13) [21].

- The *legal obligation* (necessity of the processing):
 - Report from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions. Implementation report [COM(2014) 548 final] on the Commission Communication on Rare Diseases: Europe’s challenges [COM(2008) 679 final] and Council Recommendation of 8 June 2009 on an action in the field of rare diseases (2009/C 151/02) [3]
 - European Union Committee of Experts on Rare Diseases Core Recommendations on Rare Disease Patient Registration and Data Collection to the European Commission, Member States and all stakeholders (EUCERD, 5 June 2013) [22]
 - *Administrative Arrangement* between DG SANCO and JRC on the ‘Development and maintenance of the European Platform for Rare Diseases Registration’ [17.030600/13/669748].

- Functioning of the *registration and information to patients*: the registries are the only ones who collect data from the patients/cases (the JRC has no contact with the patients). The registries, at their local, regional or national level are responsible for obtaining the necessary approvals and for complying with the institutional and national requirements on data protection. The fact that they transmit the data annually to the Central Registry is implicitly the confirmation of their compliance with their national legislation.

Table 18 shows the DPO-2 History log of Notification 3768.1, as of 29 February 2016.

Table 18. History of Notification 3768.1 on the DPO-2 system, as of 29 February 2016.

Profile	Status	Date	Action	Due date
DPO	EDPS Validation	–	Under EDPS validation	–
DPO	EDPS Validation	29/01/2016	Validation by the DPO	–
DPC	DPO Validation	28/10/2015	Validation approved by DPC	11/11/2015
Controller	DPC Validation	13/10/2015	Review by the controller	08/04/2015
DPO	Comments/Review	09/03/2015	Validation rejected by DPO for major modifications	08/04/2015
DPC	DPO Validation	05/03/2015	Validation approved by DPC	01/04/2015
Controller	DPC Validation	04/03/2015	Completed	01/04/2015
DPC	Draft	04/03/2015	Draft created	01/04/2015

7.3.1.3. Next steps on Data Protection

EDPS' opinion can either confirm or deny that the processing of JRC-EUROCAT Central Database involves personal data.

- If EDPS' opinion confirms the processing of personal data, it can make recommendations on the security counter-measures to be implemented at JRC-EUROCAT Information System.

Before completing the acceptance process, the DPO will re-open the notification for further input from the controller and DPC.

Following the update of the notification, the DPO registers the notification in the *Register of the Data Protection Officer*. After the registration, any significant change to the processing should be notified to the DPO.

- In case EDPS opinion does not justify the application of Regulation 45/2001 and considers that the processing of JRC-EUROCAT Central Database does not involve personal data, DPO will provide an official reply on DPO-2 sys-

tem and invite to withdraw the notification. If the Directive does not apply, it should be explained to the registries that this opinion is not in contradiction with national laws which consider that the data processed by registries is personal data. The non-application of the Regulation 45/2001 at the JRC level should not be considered a motive for not providing data that are considered personal data at the national level.

In both cases, following EDPS opinion and DPO decision, PHPS would be compliant with Commission's requirements in terms of Data Protection.

EU Data Protection Reform: a political agreement on the new General Data Protection Regulation was reached on 15 December 2015. The final text will be formally adopted by the European Parliament and Council at the beginning 2016. The new rules will become applicable two years thereafter.

The Regulation updates and modernises the principles enshrined in the 1995 Data Protection Directive to guarantee privacy rights. It focuses on: reinforcing individuals' rights, strengthening the EU internal market, ensuring stronger enforcement of the rules, streamlining international transfers of personal data and setting global data protection standards.

The networks' registries and the Central Registry will have to update their registration procedures in the light of the new Regulation but no major changes are expected. In practical terms, the new text still considers important alternatives to seeking individual consent for processing data with historical, statistical or scientific research purposes.

7.4. Use of Data

The Platform on RD Registration promotes the use of data hosted at CR. The use of EUROCAT data is described as a function of three types of activities:

- 1) monitoring of CA occurrence
- 2) data request for research or policy purposes
- 3) developing dissemination elements.

7.4.1. Monitoring of congenital anomalies in Europe

EUROCAT public health monitoring strategy is aimed at producing two types of output: summary CA prevalence tables and an analysis of clusters and trends. Most statistical analyses required for both outputs are performed with ECD software. For this reason, CR has not developed yet CA monitoring activities.

Summary CA prevalence tables: ECD generates epidemiologic measures in prevalence data files, perinatal mortality and prenatal diagnosis files. These estimations are computed from ‘cases’ and ‘denominators’ data. The files obtained are first uploaded on a test website where registries can check the results obtained from their data. Once checked, the data are uploaded to EUROCAT public website. A simple interface allows registered users to produce and download prevalence tables and graphs by CA, registry, country and year.

Statistical monitoring: ECD includes a module for statistical analysis of clusters and trends. In addition a complex routine called Pan-Europe trend analysis is run on Stata. The output of both set of analyses is used to build EUROCAT annual surveillance report.

Next steps: CR will perform these analyses following the reception of ECD software. In addition, the collaboration with EUROCAT experts will be continued for producing the necessary work on coding and classification, and the surveillance report.

7.4.2. Request of data for research

The JRC and EUROCAT registries encourage the use of EUROCAT data for research or policy purposes. Ensuring the protection of complete confidentiality of the data and ensuring that existing knowledge is fully brought to bear on the interpretation of its data are the main requirements established by EUROCAT network.

EUROCAT network developed a detailed procedure for data request which includes a data request form and a data request contract to be completed by the lead investigator, and a written permission to be signed by registries included in

the data request form (see 9.4). Behind most EUROCAT publications there is a formal data request that started with the submission of a study outline or study proposal, initially processed by the CR and further assessed and approved by the MC. A specific function of ECD software facilitates the extraction of the study dataset from the CDB.

7.4.3. Dissemination

EUROCAT Website

EUROCAT website is part of the software developed by Biomedical Computing. The two main features of the website are an interactive system for producing customised prevalence tables and an archive of EUROCAT documentation. A Content Management System allows CR to upload and update documents. Most of the reference documents of EUROCAT are available on the website (from procedural manuals, guides, surveillance reports, minutes and publications).

The more accessed website section is the one allowing registered users to customise prevalence tables by congenital anomaly, registry, country and birth year. Twice a year, six weeks approximately after each submission deadline, the Central Registry uploads an updated a database, derived from the central database, with aggregate data from which the prevalence tables are obtained. Each registry has previously checked its data on a test website. Other data published on the website as summary tables are annually updated (prenatal detection rates, perinatal mortality, data quality indicators).

Functional mailbox

The CR has established a functional mailbox (FMB) at JRC-EUROCAT@ec.europa.eu to manage the email exchanges within and outside the network. Queries from registry members on the network activities are answered on a daily basis. The FMB is also the CR external contact address. The most frequent topic of external queries is on access to EUROCAT data and publications on the website.



JRC-EUROCAT Information System

The JRC-EUROCAT Information System includes the JRC-EUROCAT web data exchange system, the JRC-EUROCAT Central Database and the JRC-EUROCAT website (*Figure 8*).

8.1. Information security

The JRC-EUROCAT Central Registry undertakes to put in place appropriate technical and organisational security measures having regard to the risks inherent in the processing, to the nature of the personal data concerned and in line with the rules and regulations applicable to it in order to:

- a) prevent any unauthorised person from gaining access to computer systems processing personal data, and especially:
 - i) unauthorised reading, copying, alteration or removal of storage media;
 - ii) unauthorised data input, as well as any unauthorised disclosure, alteration or erasure of stored personal data;
 - iii) unauthorised use of data-processing systems by means of data transmission facilities;
- b) ensure that authorised users of a data-processing system can access only the personal data to which their access right refers;
- c) record which personal data have been communicated, when and to whom;
- d) ensure that, during communication of personal data and transport of storage media, the data cannot be read, copied or erased without authorisation.

The Central Registry applies the following rules and standards on Security of Information Systems:

- a) *Commission Decision* of 29 November 2001 amending its internal Rules of Procedure [23]
- b) *Commission Decision* of 16 August 2006 C(2006)3602 concerning the security of information systems used by the European Commission [24]

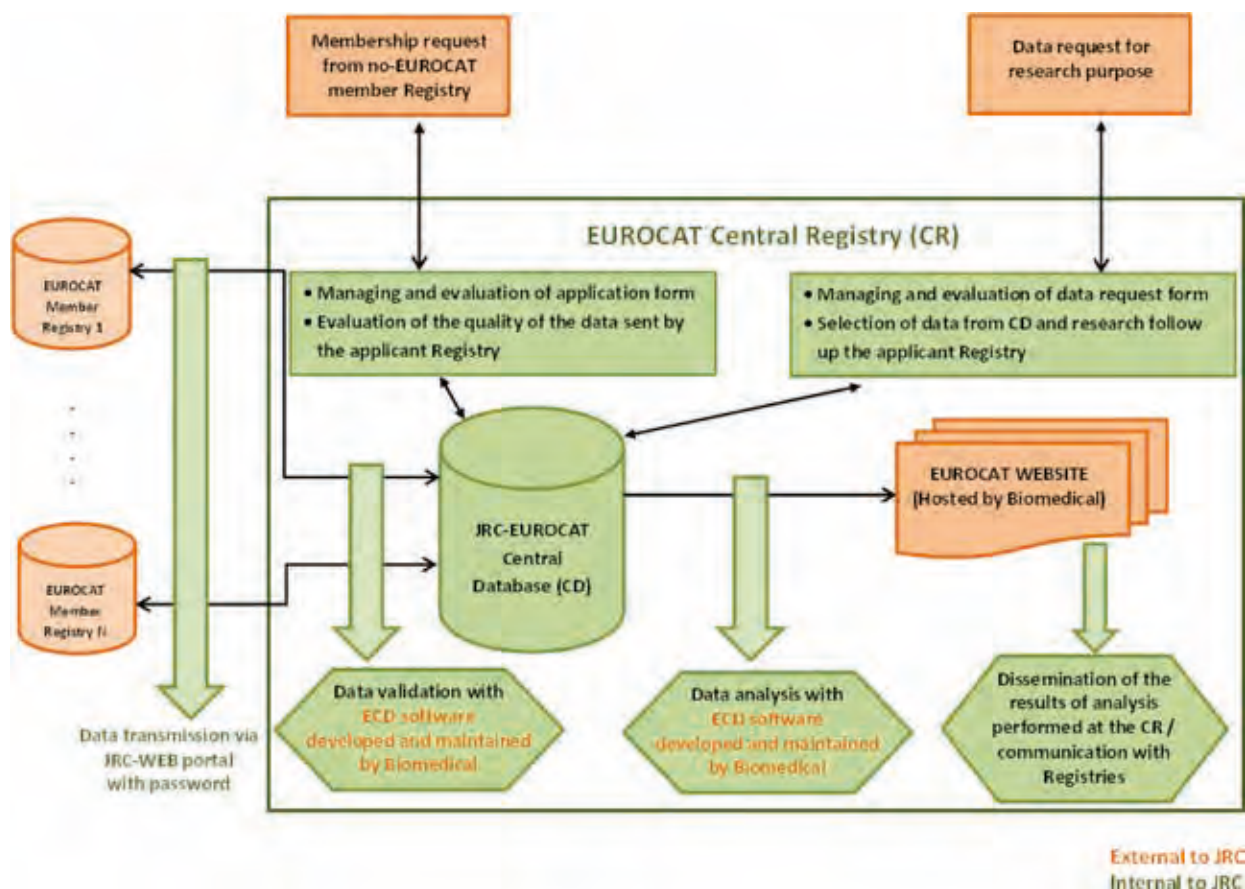


Figure 8. Data security procedure for the JRC-EUROCAT Information System.

c) *Implementing Rules* for Commission Decision C(2006)3602 of 16.8.2006 concerning the security of information systems used by the European Commission and the Security Standards adopted in accordance with Article 10(3) of the mentioned Decision:

- Standard on asset management
- Standard on business continuity management
- Standard on logging and monitoring
- Standard on backups
- Standard on physical and environmental security
- Standard on access control and authentication
- Standard on secure systems development

- Standard on controls against malicious code
- Standard on accreditation process for communication and information systems handling EU classified
- Standard on information cryptography and public key infrastructure
- Standard on removable media
- Standard on information security risk management
- Standard on mobile code
- Standard on operational management
- Standard on sanitisation of media
- Standard on information systems security incident management
- Standard on technical vulnerability management
- Standard on compliance.

The Commission Decisions, Implementing Rules and related Standards and Guidelines provide for security measures for the protection of the involved information systems and the information processed therein against threats to their availability, integrity and confidentiality. The legal provisions apply to all Directorates-General and departments in all places of work, including the Joint Research Centre and the delegations in third countries, offices linked administratively to the Commission and all Executive Agencies or other bodies using the Commission's information systems.

To comply with the legal requirements, the responsible of the Information System must start by performing a proper Business Impact Assessment (BIA) and Risk Analysis (RA) to ensure sufficient and appropriate security measures are in place. Based on the BIA and RA, the responsible of the Information System may end-up by elaborating an IT Security Plan (ITSP).

The JRC Local Informatics Security Officer (LISO) coordinates information and communications technology (ICT) security and adapts the Commission standards and guidelines on ICT security to the JRC.

Figure 9 presents the activities involved in the preparation of the Security Plan for JRC-EUROCAT information System.

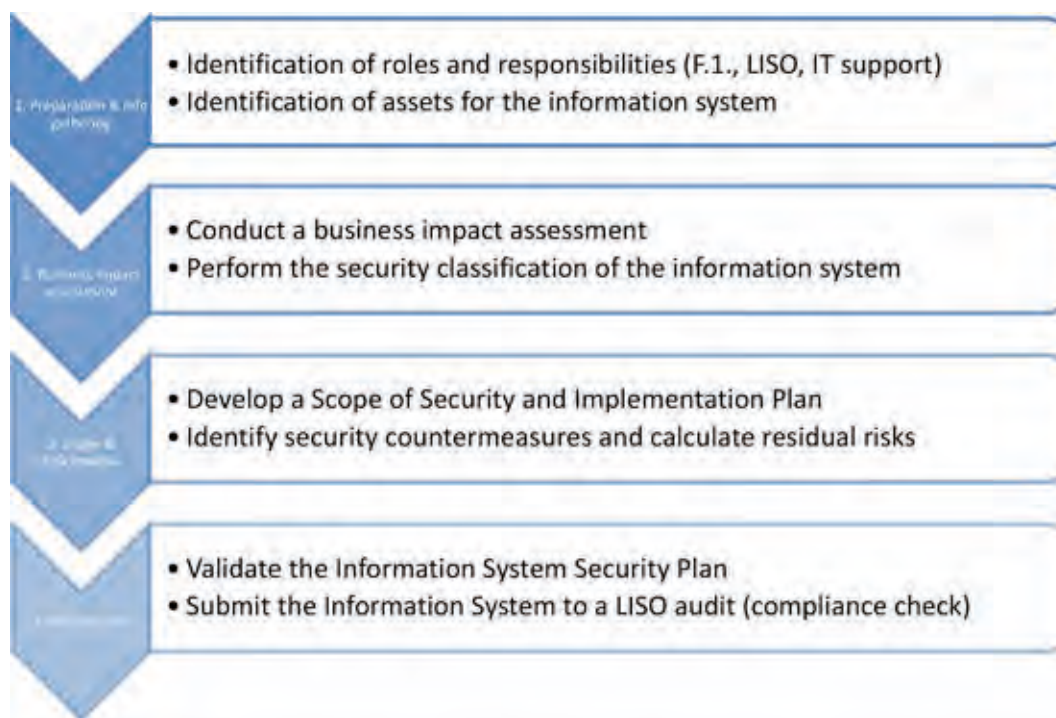


Figure 9.

8.1.1. Security plan

The Central Registry addressed all information security issues related to the JRC-EUROCAT information system in close collaboration with JRC LISO and IT support teams.

All Communication and Information Systems (CIS) of the European Commission processing shall have a documented Security Plan. In the EC regulations on information security, a CIS is any system enabling the handling of information in electronic form. A CIS shall comprise the entire assets required for it to operate, including the infrastructure, organisation, personnel and information resources.

A ‘Security Plan’ can be summarised as the collection of material which defines the end to end implementation of security of an information system. This may be achieved through a single top level document which contains security informa-

tion and provides reference to other material providing such information. Hence the 'Security Plan' is not a single document but the combination of all security material necessary to describe security implementation in total.

LISO has a key role in 1) supporting in the establishment of a security plan for information systems in the EC, and in 2) monitoring the correct informatics security of the Commission's internal security rules.

As a first step, the Central Registry prepared the JRC-EUROCAT information system Business Impact Assessment (BIA) document. The BIA is a task establishing the security needs of the system in terms of confidentiality, integrity and availability.

The BIA summarises in classification levels the business impacts for the Commission of a loss of confidentiality, integrity and availability of its information. The classification process is used to classify all physical and logical assets based on the classification of the information they are storing or processing. CIS can be allocated to one of two system categories, 'Standard' and 'Specific'.

A system is classified as 'SPECIFIC':

- with a confidentiality level of LIMITED HIGH or above, and integrity and availability levels of STRATEGIC or CRITICAL; or
- handling EU classified information; or
- handling personal data falling under Articles 10 or 27 of Regulation (EC) No. 45/2001.

Following the initial system assessment by LISO, the Central Registry started assembling the material needed to build the security plan, including the System Security Scope, a Threat and Vulnerability Analysis (to determine what security threats exist at different locations that the system is operated or used at, and how vulnerable the location is to those threats), a Risk Assessment and Determination of Candidate Security Countermeasures, Risk Treatment Plan, Definition of Selected Security Requirements applicable to the system and Risk Report.

It should be noted that a system which handles personal data is SPECIFIC and hence subject to a risk assessment. The sensitivity and impact due to a security breach of that personal data is reflected in the systems BIA. The associated required risk assessment shall only be as onerous as required by the ratings determined during that BIA.

Based on the BIA findings, the JRC-EUROCAT Information System was classified in terms of confidentiality, integrity and availability (CIA) and as a whole:

- Confidentiality: Limited High
- Integrity: Critical
- Availability: Moderate
- Classification: SPECIFIC.

The level of rigour to be applied during the risk assessment depends upon the CIA classification associated with the system.

Being classified as ‘SPECIFIC’ the JRC-EUROCAT information system required a detailed and documented Threat and Vulnerability assessment.

The standard project management methodology PM² replaced the previous Business Impact Assessment, Scope of Security of the System, Implementation Plan, Security Plan. The Central Registry developed following documents:

- PM² Project Initiation Request
- PM² Business Case
- PM² Project Charter.

8.1.2. Next steps on Information Security

The Central Registry and LISO are waiting for EDPS opinion to, respectively, validate and approve the Security Plan. The opinion will have an impact on the countermeasures that will put in place.

Once the final documents are ready to be validated and approved, LISO will perform an audit to check the compliance with European Commission's requirements.

8.2. Website management

The EUROCAT network developed a website that was purchased in the frame of the EU Platform on Rare Disease Registration by the JRC from University of Ulster. The website contents include (1) public information about EUROCAT activities; (2) an interactive application for obtaining summary data on congenital anomalies that requires completing a registration form for first time users; (3) a member access to EUROCAT documents.

The JRC-EUROCAT Central Registry manages the content of the website.

The website has been hosted by Biomedical Computing, UK, the company that developed it. The JRC has established a service contract with the above IT firm to host and adapt the existing website.

JRC-EUROCAT Website and Dissemination Working Group is developing a project for updating the organisation of website content.

Before launching, the EUROCAT website is being registered in the JRC web registry.

The following sections cover what has been done to date at the JRC and what is planned to be done in relation to the EUROCAT website.

8.2.1. Adapting the website

The collaboration established with the IT firm is aimed at hosting the website and at

- 1) adapting the website to the Commission Requirements in terms of visual identity and IT security
- 2) converting the existing website into a responsive website
- 3) implementing a first reorganisation of contents.

8.2.2. Updating the website

The JRC-EUROCAT Website and Dissemination Working Group started to develop (1) a series of modifications in the navigation and tree structure to be implemented by the IT company; (2) a work plan for updating contents until the Registry Leaders' Meeting (June, 2016) where progress will be presented, discussed and approved.

8.2.3. Website registration

All JRC & JRC-hosted websites have to be recorded in the JRC web registry, as well as FTP sites and web services and third-party websites hosted or maintained by the JRC (*Figure 10*).

The JRC Website Registry is an information system set up to meet the following aims:

- Maintain an accurate and detailed inventory of all JRC websites and services, as well as third-party websites hosted or maintained by the JRC.
- Improve consistency and quality control of these websites, including compliance with data protection and IT security rules.
- Monitor each website project from the definition of website requirements to the launch and maintenance of the website, up to its archival and decommissioning.
- Help rationalising the JRC web-presence by avoiding unnecessary multiplication of JRC websites.

The registration process of the EUROCAT website is planned under the URL <http://eurocat-network.jrc.ec.europa.eu>. *Figure 18* summarises the website registration process.

The steps for recording the website are:

- Definition and Development
- Approval and Validation
- Allowance and Compliance
- Activation and Production
- Revalidation and Deactivation

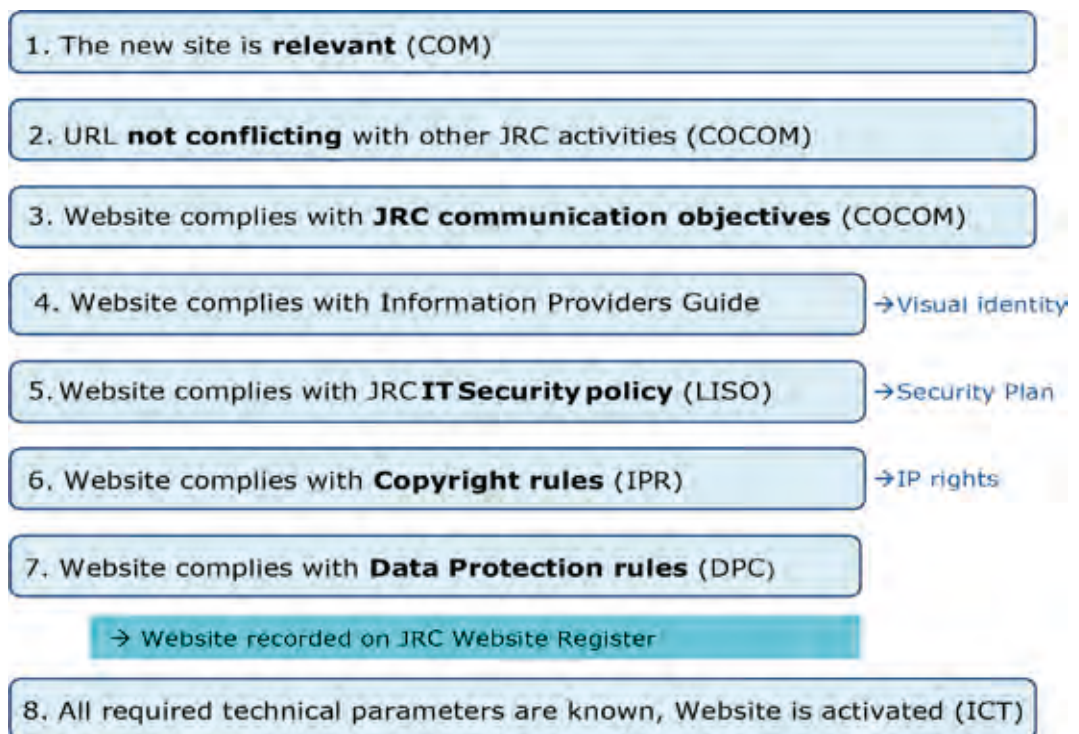


Figure 10. JRC web registration.

Different roles are identified for the recording:

- Site Owner or project leader
- Web Master or web administrator
- Head of Unit
- The Global Controllers:
 - Communication Unit/DG (COM)
 - Communication Correspondent (COCOM)
 - Local Informatics Security Officer (LISO)
 - Intellectual Property Rights Unit (IPR).

The outcome of the registration process is a clear understanding of website-related ownership, data protection, information security and intellectual property rights and a full compliance with Commission’s requirements, also in terms of communication objectives and visual identity.

9. Data management

This section covers activities performed at JRC-Central Registry regarding all steps of data management, from acquisition of data by individual registries to addressing data requests and data use. The data management steps are described in detail in two key EUROCAT documents: EUROCAT Guide and EUROCAT procedures. Next steps in data management are also identified.

EUROCAT procedures include two data transmission deadlines annually: 15 February and 15 October. A series of actions are related with each of these two deadlines both for individual registries and for central registry: submission of data, data checks and analysis, publication of prevalence tables together with some public health indicators, statistical monitoring, data quality indicators, availability for data requests.

Since 1 January 2015 EUROCAT Central Database is operated at the JRC-EUROCAT Central Registry. Up to now, JRC Central Registry has managed three data transmission deadlines (February and October 2015 and February 2016) from 28 different registries (out of 39). The most recent birth year in 2015 data transmission was 2013; in 2016, it was 2014. In addition, registries often submitted some previous birth years (complete, with updated information) or all previous years (in addition or in lieu of the data transfer). See *Table 19*.

9.1. Data acquisition

The process of data acquisition in the EUROCAT network is described at the individual register level (*Figure 11*) and at the Central Registry level (*Figure 12*) with emphasis on updates from January 2015.

9.1.1. Registry data processing

Over the years the EUROCAT network has developed a set of guidance documents and tools for registries.

Table 19. *EUROCAT (Full and Associate) member registries that transferred standard data (individual data for full members and aggregate data for associates) in December 2014 and transmitted new data in 2015-16 (up to 2012 birth year, 2013 or 2014).*

EUROCAT registry		EU Member State /European Country		Transferred Up to 2012	Transmitted		
No.	Name				Up to 2012	2013	2014
2	Hainaut	Belgium	BE	YES		YES	
3	Odense	Denmark	DK				
5	Paris	France	FR				
8	Tuscany	Italy	IT	YES	YES	YES	YES
10	Dublin	Ireland	IE		YES		
13	N Netherlands	Netherlands	NL	YES	YES	YES	YES
18	Emilia Romagna	Italy	IT	YES	YES	YES	YES
20	Vaud	Switzerland	CH	YES	YES	YES	
21	Zagreb	Croatia	HR	YES		YES	
23	Malta	Malta	MT	YES	YES	YES	
28	S Portugal	Portugal	PT	YES		YES	YES
29	Antwerp	Belgium	BE	YES	YES	YES	
30	Basque Country	Spain	ES	YES	YES	YES	
33	Saxony-Anhalt	Germany	DE	YES		YES	YES
34	Mainz	Germany	DE	YES			
38	Finland	Finland	FI	YES			
39	Styria	Austria	AT	YES			
49	Cork and Kerry	Ireland	IE	YES	YES	YES	
55	Spain Hospital Network	Spain	ES	YES	YES	YES	
57	Wales	United Kingdom	UK		YES	YES	

Table 19. (cont.)

EUROCAT registry		EU Member State /European Country		Transferred Up to 2012	Transmitted		
No.	Name				Up to 2012	2013	2014
59	Norway	Norway	NO	YES			
60	Auvergne	France	FR	YES	YES	YES	
62	Ukraine	Ukraine	UA		YES	YES	
66	Isle de la Reunion	France	FR	YES	YES	YES	YES
67	Wielkopolska	Poland	PL	YES	YES	YES	
68	Thames Valley	United Kingdom	UK	YES	YES	YES	
70	Wessex	United Kingdom	UK	YES	YES	YES	
71	Sweden	Sweden	SE		YES	YES	
72	East Midlands & S York	United Kingdom	UK				
73	Northern England	United Kingdom	UK				
75	Hungary	Hungary	HU				
76	Poland	Poland	PL	YES			
79	SE Ireland	Ireland	IE		YES	YES	YES
80	Rhone-Alps	France	FR			YES	YES
81	French West Indies	France	FR	YES	YES	YES	YES
83	Czech Republic	Czech Republic	CZ	YES	YES	YES	
84	South West England	United Kingdom	UK				
86	Valencia Region	Spain	ES	YES	YES	YES	
88	Brittany	France	FR		YES	YES	

The EUROCAT Guide is the main reference document for enabling registries to organise data collection and data transmission according to the network methodologies.

As part of JRC purchase of the EUROCAT software, the Central Registry provides EUROCAT members with EDMP software. JRC-EUROCAT Central Registry issued a new EDMP version (6.10) on 11/01/2016 including new checks on the variables that were more recently added to recommended data collection.

The new checks were developed at JRC Central Registry and implemented externally by Biomedical Computing Ltd through a service contract.

<http://www.eurocat-network.eu/aboutus/datacollection/edmp/downloadedmp>

Member registries are encouraged to use EDMP for checking their data and formatting prior to transmitting to Central Registry. Preliminary data checks at Central Registry suggest that registries do not always take full advantage of EDMP features for checking data.

9.1.2. The JRC-EUROCAT Data Portal

The IT support team set a data portal for secure exchange of files between member registries and Central Registry.

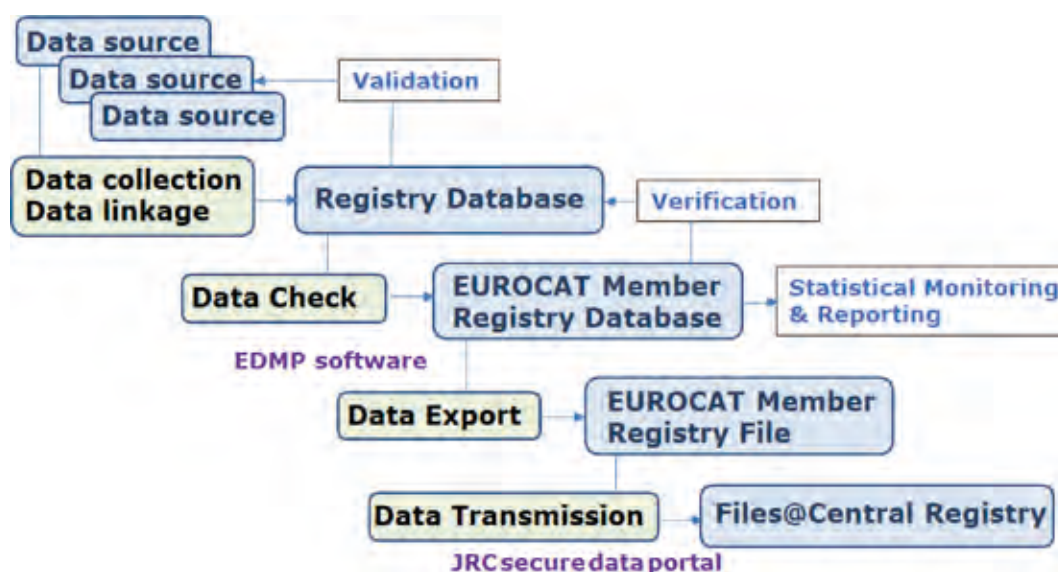


Figure 11. Data acquisition at EUROCAT member registry level.

This is a web-based system set-up at JRC-EUROCAT Central Registry for secure upload of data files from EUROCAT registries to JRC servers via SSL encryption (HTTPS). The address for the upload directory is specific for each registry, e.g. <https://gmoextranet.jrc.ec.europa.eu/Rare-Diseases/1oIEDublin>.

Access to data portal requires username and password. The Central Registry manages the registry access details: (1) for each new registry willing to transmit data, Central Registry asks the IT support to provide username and password; (2) Central Registry manages a file with all contact details; (3) One username per registry is sent to registry leaders (data managers in cc:) from JRC-EUROCAT FMB; the password is sent only to the registry leader from a Central Registry staff email.

The Central Registry downloads registry data files (cases, denominators) and cancels them from the portal.

EUROCAT full or associate member registries transmitting data to the JRC should only use the data transmission portal. Up to now, affiliate members do not have access to the data portal. The data protection and information security setting for affiliate members will be developed.

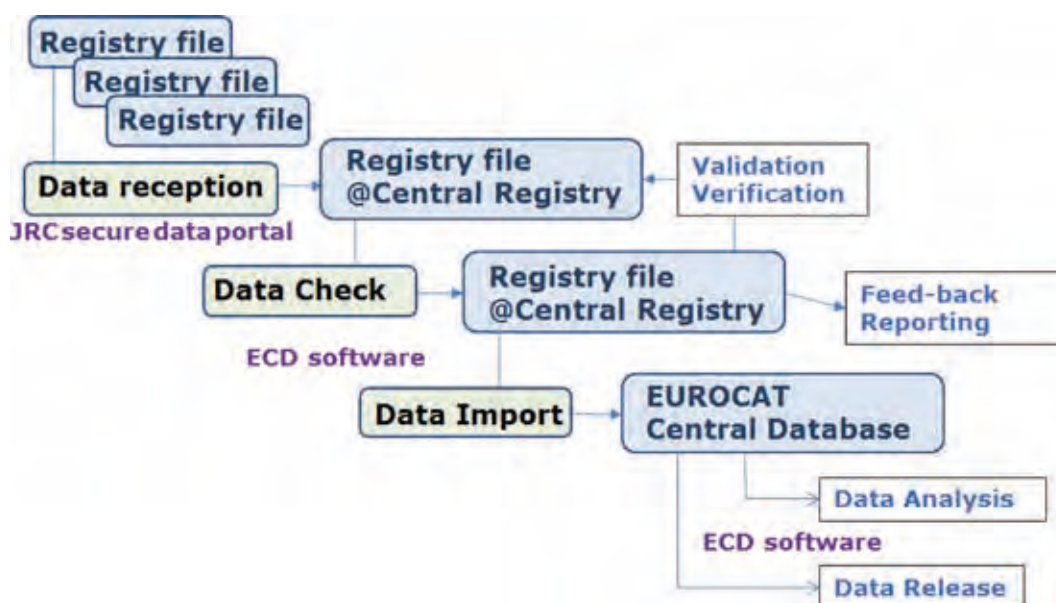


Figure 12. Data acquisition at JRC-EUROCAT central registry level.

Next steps: JRC-EUROCAT Central Registry is considering to develop a data portal for EUROCAT similar to the ones developed for the European Network of Cancer Registries (ENCR) and the network for the Surveillance of Cerebral Palsy in Europe (SCPE) data submissions. The new portal would replace the existing one and include data quality features.

9.2. Data Quality

Data quality assessment of EUROCAT central database data is a continuous process over the annual work programme: it starts with the data checks performed at Central Registry with EUROCAT ECD software and continues with coding and classification checks performed by the ad hoc committee (contract service). It is summarised annually with the publication of the Data Quality Indicators. In addition, each time a new study is approved, specific variables are thoroughly checked and updated.

9.2.1. Central data checks and data analysis

ECD includes both data checks and data analysis features.

Central Registry recently developed new checks that Biomedical Computing Ltd implemented in a new ECD version.

ECD is an Access application. Central Registry has identified limitations in its functioning due to code programming language used and size of the database. Main limitations are the instability of the system (not unusual breakdowns) and the running time (excessively time consuming for most functions).

The data validated with ECD data checks are automatically imported in the central database.

When data files from all member registries that transmitted data have been validated and imported, the analysis procedure can be initiated. The main analysis outcomes are the prevalence tables, the indicators (public health and data quality), the statistical monitoring. Some are embedded in ECD; others are implemented with a STATA routine.

9.2.2. Registry prevalence tables and analysis check

The analyses at Central Registry are open to checks and comments by member registries and committees.

The prevalence tables are uploaded on a website only accessible to members for a limited period of time (three weeks approx.). Registries can check, feed-back to central registry and validate the results obtained from the analysis of their data before publishing the tables.

The results of the statistical monitoring are discussed by the Management Committee before being sent to member registries with enough time to react and prepare the discussion at the RLM.

9.2.3. Next steps on data quality

Central registry is considering developing a data portal for data transmission that would include the data checks presently in ECD.

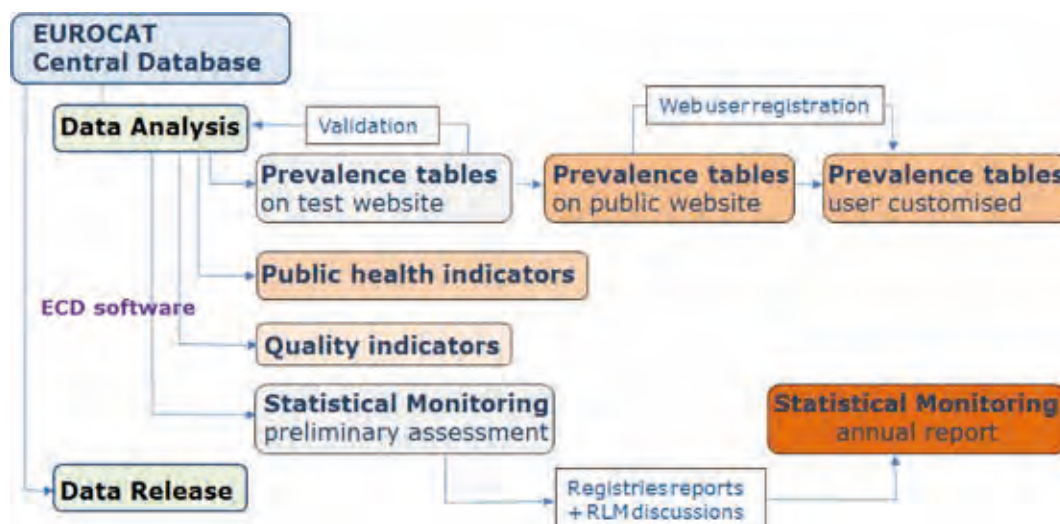


Figure 13. Data presentation at JRC-EUROCAT central registry level/1.

The analysis, reporting and other functions will be separated from the data check and import functions.

9.3. Data Presentation

EUROCAT produces on a regular basis different types of summary results (*Figure 13*). In the following the different types of output are presented as this was performed at the EUROCAT Central Registry in Ulster, a manner that will be continued and further developed at the JRC-EUROCAT Central Registry.

9.3.1. Prevalence tables

The prevalence tables are updated twice annually, approximately four to five weeks after deadline for data transmission. The tables provide aggregated data by registry, country, group of congenital anomalies, and year or period (*Figure 14*).

The results are presented in tabular or graphical format. The user can customise the tables with a menu or access already produced outputs.

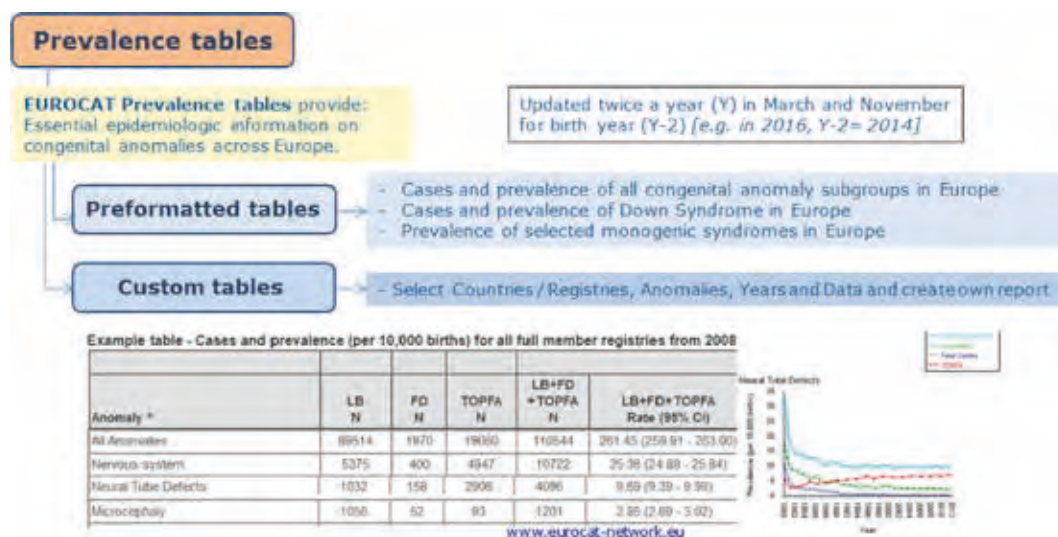


Figure 14. Data presentation at JRC-EUROCAT central registry level/2.

9.3.2. Public health indicators

The results needed for developing the Public Health Indicators (PHI) can be obtained with the prevalence tables, see *Figure 15*. EUROCAT has produced specific analysis on PHI in 2011 (publication) and in 2015 (RLM presentation).

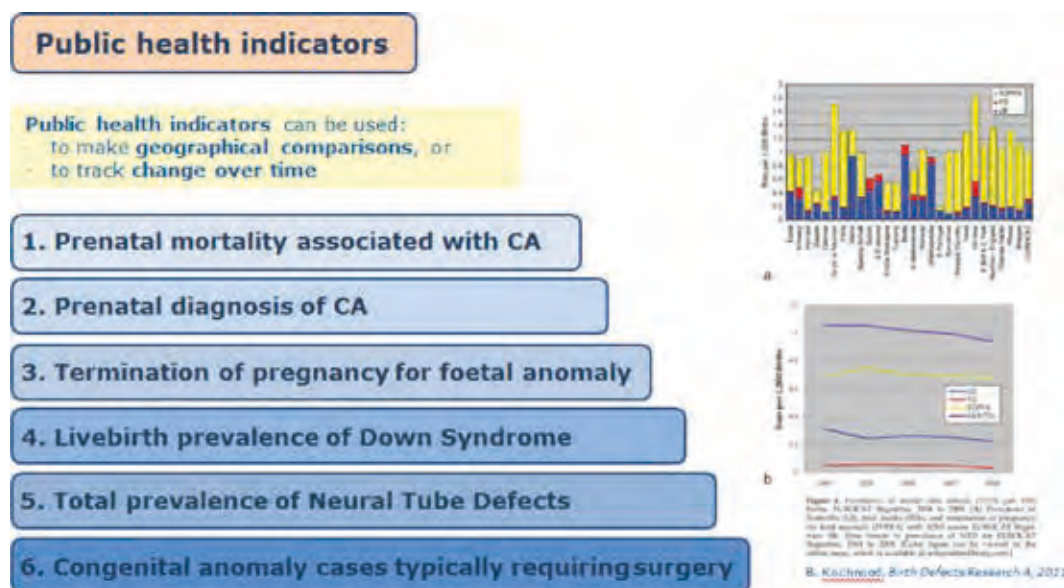


Figure 15. Data presentation at JRC-EUROCAT central registry level/3.

9.3.3. Data Quality Indicators

The Data Quality Indicators (DQI) are produced annually and discussed at network meetings (*Figure 16*). ECD includes a special function to produce the DQI.

9.3.4. Statistical Monitoring

A service contract is under preparation for ensuring the contribution of expert input to the analysis performed at Central Registry/statistical monitoring (*Figure 17*).

Data quality indicators

Data quality indicators:

- serve to highlight the strengths and weaknesses of the data.
- help to focus the attention of registries on areas needing improvement.
- are useful to data users for the interpretation of data.

Updated annually
www.eurocat-network.eu

1. **Ascertainment** (8 indicators; e.g. "Prevalence of severe cardiac defects")

2. **Accuracy of diagnosis** (8 indicators; e.g. "Prevalence of selected unspecified Q codes")

3. **Completeness of information** (8 indicators; e.g. "Number of core variables 90% completed")

4. **Timeliness** (1 indicator; "Timeliness for February deadline")

5. **Denominator information** (2 indicators; e.g. "Years with 80% maternal age denominators")

Figure 16. Data presentation at JRC-EUROCAT central registry level/4.

Statistical Monitoring

EUROCAT Central Statistical Monitoring is a screening method to scrutinise data regularly and systematically, to detect any previously unrecognised increases in frequency.

Performed annually; preliminary investigations at local registries are a key component; discussed at RLM in June; final report by end of the year.

Trend analysis

- To detect changes in time within individual registries, and also to detect trends across all registries (Pan-Europe trends) on 81 anomaly subgroups.
- It provides information on a 10-year period, e.g. in 2016, on 2005-2014.

Cluster analysis

- To detect aggregation of cases in time or space, which appears to be unusual
- The most recent 5 years data are used to test each registry/country/ subgroup

Figure 1. To test a population of severe CHD for 10 years from 2005-2014 among individual registries and the pan-European trend.

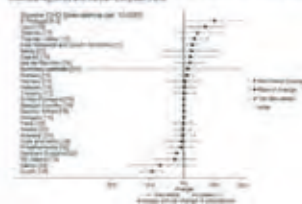


Figure 2. Severe CHD showing an anomaly trend and that trend when the registries with a statistically significant rise in prevalence are excluded.

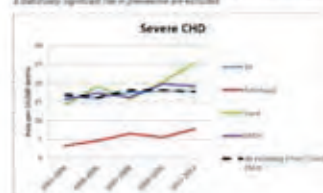


Figure 17. Data presentation at JRC-EUROCAT central registry level/5.

9.4. Data request and use of data

The Central Registry at JRC has developed a new procedure for data request in the frame of the Collaboration Agreement. The procedure refers only to data from registries that signed the Collaboration Agreement. The Management Committee approves first the Data request and then the Data release.

The Data Request Declaration is a document that recaps on participating registries and specifics established by the Management Committee. When the requester is not part of a registry that signed the Collaboration Agreement, it is proposed that the Data Request Declaration should be co-signed by the leader of a registry which is part of JRC-EUROCAT agreement.

Figure 18 describes the data request procedure.

Central registry has managed one data request in 2015 on Epidemiology of Congenital Heart Disease (CHD) in Europe. *Table 20* lists registries agreeing to participate to the CHD study. Data release is conditional on final approval of data release request.

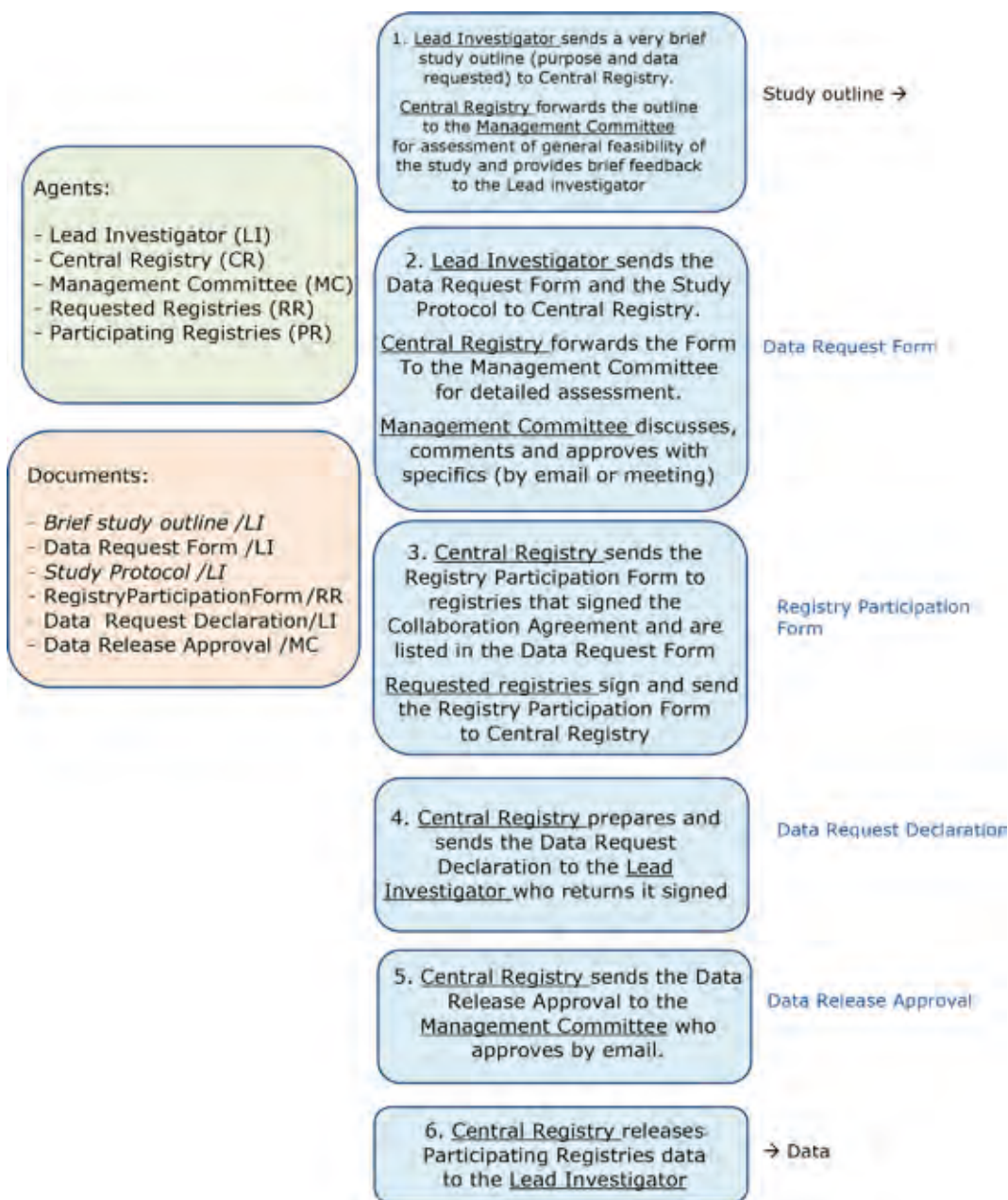


Figure 18. Procedure for obtaining EUROCAT Data from JRC-EUROCAT Central Registry.

Table 20. EUROCAT member registries that gave permission to transmit data for the ‘Congenital Heart Diseases (CHD) Study, 1990-2012: a registry-based study’, as of 7 of March 2016.

Central Registry assigned No.	Central Registry assigned Name	EU Member State /European Country		Signed Registry Participation Form
39	Styria	Austria	AT	YES
2	Hainaut	Belgium	BE	N/A
29	Antwerp	Belgium	BE	YES
21	Zagreb	Croatia	HR	YES
83	Czech Republic	Czech Republic	CZ	N/A
3	Odense	Denmark	DK	N/A
38	Finland	Finland	FI	N/A
5	Paris	France	FR	N/A
60	Auvergne	France	FR	YES
66	Isle de la Reunion	France	FR	YES
80	Rhone-Alps	France	FR	N/A
81	French West Indies	France	FR	YES
88	Brittany	France	FR	YES
33	Saxony-Anhalt	Germany	DE	YES
34	Mainz	Germany	DE	NO
75	Hungary	Hungary	HU	N/A
10	Dublin	Ireland	IE	YES
49	Cork and Kerry	Ireland	IE	NO
79	SE Ireland	Ireland	IE	YES
8	Tuscany	Italy	IT	YES

Table 20. (cont.)

Central Registry assigned No.	Central Registry assigned Name	EU Member State /European Country		Signed Registry Participation Form
18	Emilia Romagna	Italy	IT	YES
23	Malta	Malta	MT	YES
13	N Netherlands	Netherlands	NL	YES
59	Norway	Norway	NO	YES
67	Wielkopolska	Poland	PL	NO
76	Poland	Poland	PL	N/A
28	S Portugal	Portugal	PT	YES
30	Basque Country	Spain	ES	YES
55	Spain Hospital Network	Spain	ES	N/A
86	Valencia Region	Spain	ES	YES
71	Sweden	Sweden	SE	N/A
20	Vaud	Switzerland	CH	YES
62	Ukraine	Ukraine	UA	YES
57	Wales	United Kingdom	UK	YES
68	Thames Valley	United Kingdom	UK	N/A
70	Wessex	United Kingdom	UK	N/A
72	East Midlands & S York	United Kingdom	UK	N/A
73	Northern England	United Kingdom	UK	N/A
84	South West England	United Kingdom	UK	N/A

10. JRC-EUROCAT coordinating activities

10.1. JRC-EUROCAT Management Committee

The governing structure of JRC-EUROCAT collaboration is the JRC-EUROCAT Management Committee (MC) with seven representatives of the EUROCAT Network and two representatives of the JRC.

The JRC-EUROCAT Collaboration Agreement details the role of the Management Committee:

- Prepares and takes decisions on the JRC-EUROCAT activities.
- Decides on membership issues including applications for membership.
- Supervises the security and confidentiality of data held at the Central Registry including data transmission.
- Facilitates the discussions between the Registries and the Central Registry concerning the execution of activities under the Collaboration Agreement.
- Supervises and supports the organisation of the annual Registry Leaders' Meeting.
- Decides on applications for additional meetings, workshops and working groups.
- Decides on applications for studies regarding protocol, data and authorship.
- Establishes policies and adopts documents related to the Management Committee and the Central Registry.
- Supports and collaborates with the Central Registry for the activities carried out under the Collaboration Agreement.

The Management Committee meets in person at least three times a year. Additional meetings may be arranged via tele/videoconference.

In 2015, the Management Committee met in March, May and November in addition to meeting at the end of the annual meeting. A conference call was organised in September.

Main topics of the MC in 2015-16 were:

- The development, signature and follow-up process of the Collaboration Agreement;
- The acquisition of EUROCAT software;
- The transfer of the central database;
- The preparation and operation of the data transmission campaigns;
- The update, adaptation, and development of EUROCAT procedures at JRC;
- The organisation of annual and scientific meetings.

10.2. Other committees

The JRC supports the activities and meetings of other EUROCAT committees and working groups.

10.2.1. Coding Committee

The Coding Committee met once in 2015, in relation with the annual meeting. Next meeting is planned in relation with 2016 annual meeting.

Following the work performed at Central Registry on the newly adopted variables—prenatal diagnosis and genetic testing, the committee included modifications in EUROCAT Guide.

A service contract was established with the Chair of the Coding Committee to support Central registry in issues related with coding and classification.

Another service contract was established with a member of the coding Committee to explore harmonisation in the genetic testing field.

10.2.2. Website and Dissemination Working Group

The Web-dissemination Committee met for the first time on March 8, 2016 and collaborate with Central Registry (1) to identify modifications to be implemented by the subcontractor IT firm by end of March in the new website; (2) to plan the

development and reorganisation of the website—to be presented at annual meeting in June 2016.

10.3. Registry Leaders Meeting and Scientific Symposium

The annual EUROCAT Registry Leaders Meeting (RLM) is the central event in EUROCAT network calendar and it is a key tool to personally meet the leaders of the registries, to strengthen the collaboration between EUROCAT representatives and JRC-EUROCAT Central Registry team and to build motivation for further collaboration.

10.3.1. Registry Leaders Meeting 2015

EUROCAT RLM 2015 was organised by the JRC on 17-18 June 2015 in Baveno, Italy. Registry Leaders from all member registries were invited to the RLM. Leaders and representatives of 36 registries from 21 European countries attended the meeting. In addition, invited speakers from EUROCAT collaborating organisations and European Commission staff from DG SANTE, JRC-IES and JRC-IHCP also attended. There were 41 presentations and 64 participants.

The meeting met the expectations with regard to the continuation of the EUROCAT activities in the new setting and consolidated the trust basis for the future collaboration between JRC and EUROCAT registries.

10.4. Communication

The Central Registry operates a functional mailbox [JRC-EUROCAT@ec.europa.eu].

10.4.1. JRC-EUROCAT Communication

JR-EUROCAT Central registry has sent 11 issues of JRC-EUROCAT Communication to member registries in 2015. The recipients profile was extended to Affiliate and Applicants members, and to collaborators in individual registries—and not only to Registry Leaders.

Following discussions at the Management Committee meeting in November, the Communication format was modified and made more reader friendly: it includes a short list of contents with hyperlinks. The same email text is sent as an attached file (ARES).

10.4.2. Individual communication with registries and external queries

The Central Registry receives, assesses and answers members and external queries. When appropriate, queries are forwarded to management committee members depending on the topic: general scientific content queries are forwarded to the Scientific Leader, Coding queries to the chair of the Coding Committee, and Organisation and Registry related queries to the President of the Association.

The Central Registry presents a summary and analysis of queries at MC meetings.

11 Extension of the network to new registries

There are 39 registries approved for providing data to the Central Database. Full registry members (n=33) submit individual case data. Associate member registries usually transmit aggregate data. The Collaboration Agreement refers only to Full and Associate member registries.

Affiliate and applicant members work to set-up a registry. These registries should send data to the Central Registry together with an updated registry description to be assessed jointly with the Management Committee (*Table 21*).

Since the JRC-EUROCAT Central Registry started to operate at JRC in January 2015, there were changes regarding all categories.

In 2015, one registry, Brittany, France, which was previously Affiliate member was approved as Full member, adding up the number of Full members to 33.

There are still six Associate members. One of them, Czech Republic, sent individual case data for evaluation and, if applicable, be considered Full member.

One of the Applicants was approved as Affiliate: Navarre, Spain, following the assessment of the registry questionnaire. It has submitted individual data for evaluation and, if applicable, be considered Full member.

Several Affiliate members sent data for evaluation: Latvia, Pleven, Greenland.

The Western Australia Developmental Anomalies Registry (WARDA) was approved as World Affiliate member. WARDA has a long track of achievements in the field of monitoring congenital anomalies and research. The initial contact was taken by a WARDA partner interested in participating in EUROCAT activities. Some collaborative research initiatives between Australian and EUROCAT registries are already ongoing.

Table 21. *EUROCAT (Affiliate and Applicant) member registries that transmitted individual data in 2015-16 (up to 2012 birth year, 2013 or 2014).*

EUROCAT registry		EU Member State /European Country		Transferred Up to 2012	Transmitted		
No.	Name				Up to 2012	2013	2014
Affiliates							
50	Sicily	Italy	IT				
51	Campania	Italy	IT				
69	Slovenia	Slovenia	SL				
78	Latvia	Latvia	LV		YES		
82	Moldova	Moldova	MD				
87	NDSCR	United Kingdom	UK				
89	Greenland	Denmark	DK			YES	YES
90	Pleven	Bulgaria	BG			YES	
93	Navarre	Spain	ES				YES
Applicants							
85	Slovakia	Slovakia	SK				
91	Iceland	Iceland	IS				
94	Lithuania	Lithuania	LT				

Next steps regarding membership:

- Central Registry will process data transmitted for evaluation and Management Committee will decide on change of membership status and report back to all registries that sent data for evaluation.
- A new registry applied for Associate membership (North Italy). The registry description will be evaluated by the management committee members and discussed at next meeting in April 2016.

- The processing of data from Affiliate registries is not covered by the collaboration agreement. In case EDPS issues a positive opinion regarding processing of personal data at Central Registry, and before approval of the notification by the DPO, a short mention to processing of data from affiliate members should be included (see section on DP).
- Registry descriptions and contact details are available on EUROCAT website at <http://www.eurocat-network.eu/pagecontent.aspx?tree=allmembers>. The adapted website to be launched later in spring 2015 will give higher visibility to registries information, starting with a map.

It is planned to address registries and update the information already available. In addition a questionnaire extending the coverage of registration methods and practices could be added. This survey could document some of the items identified in the review of guidelines for new registries drafted by the Central Registry in 2015. Data could be collected with an online questionnaire.

- The Management Committee will assess (1) what membership status should have Full or Associate member registries that are members of EUROCAT Association but have not signed the agreement with the JRC; (2) if to be approved as Full or Associate members, registries need to sign JRC-EUROCAT Collaboration Agreement.

12 . Conclusions

The development of the European Platform on Rare Diseases Registration, as agreed between DG JRC and DG SANTE, started with a comprehensive activity in order to secure a sustainable solution for the internationally recognised, long-lasting network of 55 population-based registries for the surveillance of congenital anomalies in Europe, EUROCAT.

The transfer of the European-level coordinating activities of EUROCAT to the JRC was an intensive and complex process carried out over about two years. In addition to achieving the objective of having in place and operational at the JRC the new JRC-EUROCAT Central Registry, the intense exchanges with EUROCAT representatives—members of the former Steering Committee, registry leaders, members of scientific committees and working groups was an enriching experience, giving us valuable insights into their scientific work done with highest expertise and dedication over several decades.

The work on this transfer turned out to be an opportunity for a concerted action between different services of the Commission/JRC. The result could be achieved due to the continuous and fruitful involvement of the legal advice Unit, IT support group, local information security office, intellectual property rights office, data protection coordinator, procurement service. The interaction with all these services was a very helpful and instructive experience which paves the way for the next task: the transfer of the European-level coordinating activities of SCPE, the network for the surveillance of cerebral palsy in Europe, to the JRC. This objective will be addressed as well in close collaboration with DG SANTE.

Overall, this process was not a simply ‘transfer’, but the establishment of a whole new system, with new structures, which often required to go in minute detail of the topics addressed. It was a challenging experience which, most importantly, builds the fundament for continuing the work on the surveillance of congenital anomalies in Europe. Bringing together the information of the registries involved, the output of the JRC-EUROCAT Central Registry provides a source of knowl-

edge for healthcare providers, patients, researchers, policy makers, as well as for the general public.

The next steps in giving added-value to EUROCAT data will be to put this data in the wider context of health and health-related data in the context of European health information systems. A challenging purpose is linking these data with environmental and 'omics' datasets.

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Abbreviations

AA	Administrative Arrangement
CA	Congenital Anomalies
CDB	Central Database
CHD	Congenital Heart Disease
CIS	Communication and Information System
CR	JRC-EUROCAT Central Registry
DG JRC	European Commission's Directorate-General Joint Research Centre
DG SANTE	European Commission's Directorate-General Health and Food Safety
DP	Data Protection
DPO	European Commission's Data Protection Officer
DQI	Data Quality Indicators
EC	European Commission
ECD	EUROCAT Central Database software
EDMP	EUROCAT Data Management Programme
EDPS	European Data Protection Supervisor
ENCR	European Network of Cancer Registries
EU	European Union
EUROCAT	Network of population-based registries for the Surveillance of Congenital Anomalies in Europe <i>(Acronym derived from the name of the first initiative 'European Concerted Action on Congenital Anomalies and Twins')</i>
FMB	Functional Mailbox
IHCP	Joint Research Centre's Institute for Health and Consumer Protection
IPR	Intellectual Property Rights
IS	Information Security
MC	Management Committee
PHI	Public Health Indicators
PHPS	Public Health Policy Support Unit
RAS	Registry Advisory Service

RLM	Registry Leaders' Meeting
RD	Rare Diseases
SCPE	Network of registries for the Surveillance of Cerebral Palsy in Europe
SOPs	Standard Operating Procedures

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