

**2012 REPORT ON THE STATE OF THE ART
OF RARE DISEASE ACTIVITIES IN EUROPE
OF THE
EUROPEAN UNION COMMITTEE OF EXPERTS
ON RARE DISEASES**



**STATE OF THE ART OF RARE DISEASE ACTIVITIES IN
GERMANY**

This work was financed by the EUCERD Joint Action: Working for Rare Diseases N° 2011 22 01

This document has been produced by the Scientific Secretariat of the European Union Committee of Experts on Rare Diseases (EUCERD, formerly the European Commission's Rare Diseases Task Force) through the EUCERD Joint Action: Working for Rare Diseases (N° 2011 22 01, Coordinator: Kate Bushby, University of Newcastle, United Kingdom), within the European Union's Second Programme of Community Action in the Field of Health.

More information on the European Union Committee of Experts on Rare Diseases can be found at www.eucerd.eu.

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To quote this document:

Aymé S., Rodwell C., eds., "2012 Report on the State of the Art of Rare Disease Activities in Europe of the European Union Committee of Experts on Rare Diseases", July 2012.

ISBN : 978-92-79-25355-3

DOI : 10.2772/50554

<http://www.eucerd.eu/wp-content/uploads/2012/09/2012ReportStateofArtRDAactivitiesDE.pdf>

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ACRONYMS

General

CAT - Committee for Advanced Therapies at EMA
CHMP - Committee for Medicinal Products for Human Use at EMA
COMP - Committee on Orphan Medicinal Products at EMA
DG - Directorate General
DG Enterprise - European Commission Directorate General Enterprise and Industry
DG Research - European Commission Directorate General Research
DG Sanco - European Commission Directorate General Health and Consumers
EC - European Commission
ECRD - European Conference on Rare Diseases
EEA - European Economic Area (Iceland, Switzerland, Norway)
EMA - European Medicines Agency
ERN - European reference network
EU - European Union
EUCERD - European Union Committee of Experts on Rare Diseases
EUROCAT - European surveillance of congenital anomalies
EUROPLAN - European Project for Rare Diseases National Plans Development
EURORDIS - European Organisation for Rare Diseases
FDA - US Food and Drug Administration
HLG - High Level Group for Health Services and Medical Care
HTA - Health Technology Assessment
IRDiRC – International Rare Diseases Research Consortium
JA - Joint Action
MA - Market Authorisation
MoH - Ministry of Health
MS - Member State
NBS - New born screening
NCA - National Competent Authorities
NHS - National Health System
PDCO - Paediatric Committee at EMA
RDTF - EC Rare Disease Task Force
WG - Working Group
WHO - World Health Organization

Pilot European Reference Networks

Dyscerne - European network of centres of expertise for dysmorphology
ECORN-CF - European centres of reference network for cystic fibrosis
Paediatric Hodgkin Lymphoma Network - Europe-wide organisation of quality controlled treatment
NEUROPED - European network of reference for rare paediatric neurological diseases
EUROHISTIONET - A reference network for Langerhans cell histiocytosis and associated syndrome in EU)
TAG - Together Against Genodermatoses – improving healthcare and social support for patients and families affected by severe genodermatoses
PAAIR - Patients' Association and Alpha-1 International Registry Network
EPNET - European Porphyrin Network - providing better healthcare for patients and their families
EN-RBD -European Network of Rare Bleeding Disorders
CARE-NMD -Dissemination and Implementation of the Standards of Care for Duchenne Muscular Dystrophy in Europe project
ENERCA - European network for rare and congenital anaemia – Stage 3

GENERAL INTRODUCTION TO THE REPORT ON THE STATE OF THE ART OF RARE DISEASE ACTIVITIES IN EUROPE OF THE EUROPEAN UNION COMMITTEE OF EXPERTS ON RARE DISEASES

The 2012 Report on the State of the Art of Rare Disease Activities in Europe was produced by the Scientific Secretariat of the European Union Committee of Experts on Rare Diseases (EUCERD), through the EUCERD Joint Action: Working for Rare Diseases (N° 2011 22 01), which covers a three year period (March 2012 – February 2015).

The report aims to provide an informative and descriptive overview of rare disease activities at European Union (EU) and Member State (MS) level in the field of rare diseases and orphan medicinal products up to the end of 2011. A range of stakeholders in each Member State/country have been consulted during the elaboration of the report, which has been validated as an accurate representation of activities at national level, to the best of their knowledge, by the Member State/country representatives of the European Union Committee of Experts on Rare Diseases. The reader, however, should bear in mind that the information provided is not exhaustive and is not an official position of either the European Commission, its Agencies or national health authorities.

The report is split into five parts:

Part I: Overview of rare disease activities in Europe

Part II: Key developments in the field of rare diseases in 2011

Part III: European Commission activities in the field of rare diseases

Part IV: European Medicines Agency activities and other European activities in the field of rare diseases

Part V: Activities in EU Member States and other European countries in the field of rare diseases

Each part contains a description of the methodology, sources and validation process of the entire report, and concludes with a selected bibliography and list of persons having contributed to the report.

The present document contains the information from Parts II and V of the report concerning Germany. A list of contributors to the report and selected sources are in annex of this document. For more information about the elaboration and validation procedure for the report, please refer to the general introduction of the main report¹.

The German Federal Ministry of Health can only verify the information and data which concern federal responsibilities. The information provided here is illustrative and not exhaustive, and that it is validated by the EUCERD Member State representative to the best of their knowledge.

¹ <http://www.eucerd.eu/upload/file/Reports/2012ReportStateofArRDActivities.pdf>

RARE DISEASE ACTIVITIES IN GERMANY

Definition of a rare disease

Stakeholders in Germany accept the European Regulation on Orphan Medicinal Products definition of a prevalence of no more than 5 in 10'000 individuals.

National plan for rare diseases and related actions

In the German health care system every patient is entitled to complete health care coverage consisting of preventive, diagnostic, therapeutic and rehabilitative measures. The medical care of patients is generally of high quality and the access to medical doctors and specialists is on a high international standard. . There is no national plan for rare diseases in Germany at the moment, and there are no specific funds allocated to rare diseases in the health care system, although ad hoc funding for rare disease projects does exist.

However, the first steps are being made to establish a national plan for rare diseases. An in-depth evaluation of the situation of patients affected by rare diseases in Germany was published by the Federal Ministry of Health in August 2009 .The study is entitled "Maßnahmen zur Verbesserung der gesundheitlichen Situation von Menschen mit Seltenen Erkrankungen in Deutschland" ("Strategies for improving the health care situation of patients with rare disease in Germany"). The study analyses the current situation of care for persons with rare diseases in Germany from the perspective of various actors in the health care system by evaluating the perspective of public organisations, service providers and patient organisations on the basis of quantitative and qualitative surveys in the form of questionnaires, individual interviews and group discussions. In the process, the priority spheres for action in the areas of the general care situation, specialised forms of care, diagnosis, therapy, exchange of information and experience as well as research, are identified. This provides the basis for discussions regarding the first implications of implementing a national action forum as well as a national action plan for rare diseases in Germany. Subsequently, possible solutions for individual areas will finally be developed in co-ordination with existing and planned activities at EU level.

The Federal Ministry of Health in Germany initiated a national action league for people with rare diseases - *Nationales Aktionsbündnis für Menschen mit Seltenen Erkrankungen* (NAMSE)² – in Berlin on 8 March 2010. NAMSE is a co-ordination and communication platform comprising all key bodies and organisations. The following stakeholders are part of this platform and the steering committee: the Federal Ministry of Health, the Federal Ministry of Education and Research, the Federal Ministry of Labour and Social Affairs, the Federal Ministry for Family Affairs, Senior Citizens, Women and Youth, the 16 Federal *Laender* (*federal states*), health insurance funds (sickness funds), associations of panel doctors, hospital associations, the Federal Joint Committee, medical societies, scientific societies, patient representatives, including the National Alliance for Rare Diseases "ACHSE". NAMSE is coordinated in a joint effort by the Ministry of Health, the Ministry of Education and Research and ACHSE.

This platform provides the basis for further concerted action, including the implementation of a National Action Plan on Rare Diseases. All partners, the major institutions and stakeholders of the German health care system, adopted a common declaration to improve the health situation for people with rare diseases in Germany. By this declaration all partners of the action league declare their willingness to contribute towards the implementation of the established goals through their active participation in the action league. One established goal is to contribute to implementing the Recommendation of the Council of the European Union. This includes the drafting of a National Action Plan for Rare Diseases and its implementation and monitoring as recommended in the EU Council Recommendation on an action in the field of rare diseases, the coordination of measures for improving the health situation of persons with rare diseases, supporting the establishment of centres of expertise, initiating pilot projects and further action in the field of rare diseases, and assembling initiatives and making all actors involved cooperate in a coordinated and goal-orientated manner to put patients' care first. The process is organised in a steering committee and four working groups. Amongst others they try to identify ways how to improve the information on rare diseases, how to speed up the diagnosis of a rare disease, how centres of rare diseases could be structured, how to reach the experts and how research can more easily benefit the patients. At the end of this process the national action league for

² <http://namse.de/>

people with rare diseases will recommend different actions for the German National Action Plan for Rare diseases.

Centres of expertise

The implementation of national centres of expertise in Germany is challenged by the decentralised, federal structure of the German health care system, since the provision of sufficient structural resources for health care is a matter solely concerning the *Laender* (federal states).

Hospitals next to outpatient physicians are entitled to provide outpatient care for rare diseases patients if they have received prior authorisation by the competent Land authority (Social Code V, Section 116b): however this applies only to certain rare diseases according to a list which has been stipulated by law (Social Code V, Section 116b). The Federal Joint Committee (*Gemeinsamer Bundesausschuss, G-BA*) can extend this list. The Federal Joint Committee (*G-BA*) is the supreme decision-making body of the so-called self-governing system of service providers and health insurance funds in Germany. Physicians, dentists, hospitals and health insurance funds are represented in the *G-BA*. Since 2004 national groups representing patients were given the right to file applications and to participate in the consultations of the *G-BA*. The *G-BA* issues the directives that are necessary for safeguarding medical service provisions. The latter aims to ensure that medical services for persons ensured under the statutory health insurance in Germany are adequate, appropriate and efficient. The *G-BA* issues directives and thus determines the benefit package of the statutory health insurance (*gesetzliche Krankenversicherung, GKV*) covering about 70 million people. The *G-BA* is responsible for reimbursement decisions in the statutory health insurance (*GKV*). In the field of outpatient care for rare diseases provided by hospitals according to Social Code Book V, Section 116b, the *G-BA* has to regulate both the structural and personnel resources needed for outpatient care provided by hospitals as well as the cross-institutional measures for quality assurance. In this context, for the purpose of ensuring the quality of treatment, the *G-BA* may also lay down certain minimum numbers of patients treated per year in a certain 'Section 116b centre'.

In addition to the so-called 'Section 116b centres', other centres like social-paediatric centres (Social Code V, Section 119) or university clinics for outpatient care (Social Code V, Section 117) may also be involved in the treatment of rare disease patients. This applies also to specialised ambulatory care offered by authorized physicians in hospitals.

Legislation provides the basis for the contracting of *Ambulante Spezialfachärztliche Versorgung* (highly specialised care) for a limited number of diseases (see above), some of which are rare.

There are already several self-appointed centres for rare diseases in Germany. However, these do not share a nation-wide concept and are not reviewed in respect of any specific quality criteria for rare diseases. Therefore, it falls to the NAMSE process to define and develop national framework conditions for centres and networks dedicated to rare diseases. This also includes topics such as the setting up of registries and biobanks as it does the drafting of criteria and eligibility procedures for the certification of future centres.

Pilot European Reference Networks

German teams participate, or have participated, in the following European Reference Networks for rare diseases: Dyscerne, ECORN-CF (main partner), ENERCA, EPI, EPNET, EUROHISTIONET, NEUROPED, Paediatric Hodgkin Lymphoma Network (main partner), PAAIR, EN-RBD and Treat-NMD (Main partner).

Registries

There are some registries for rare diseases in Germany. There is no public central clinical trial registry dedicated solely to rare diseases. However the German Clinical Trials Register (Deutsches Register Klinischer Studien, DRKS) which is funded by the Federal Ministry of Education and Research (BMBF) aims at registering all trials performed in Germany, including those for rare disorders. All federal states are obliged to register cancers, including rare cancers, in existing population based cancer registries. An analysis based on the Orphanet database identifies about 80 registries, most of them belonging to academic institutions. Some of these registries are implicated in international networks or covers the whole European region. Germany contributes to European registries such as EUROCAT, TREAT-NMD, EBAR, EHDN, EIMD, EurIPFnet, E-IMD, EURIPEDES, European Alport registry, EuroDSD, EUROSCA-R, EUTOS, and RegiSCAR.

Genetic testing and Newborn Screening Policy

On 1 February 2010, a law passed by the German Bundestag regulating genetic testing in humans officially came into effect. The Genetic Diagnostics Act (Gen DG) regulates the practice of testing on humans as well as the handling of samples and data but does not extend to testing and data/samples undertaken for research

purposes. Notably, the legislation prohibits prenatal testing for diseases that typically have onset after the age of adulthood (age 18). All persons undergoing genetic testing for medical purposes must be offered counselling before and after testing. The scope of the regulation includes predictive, prenatal and postnatal genetic testing. The Act seeks to reduce discrimination and to enhance the quality of testing in Germany.

Since 2005 there has been a mandatory legalised screening program covering fourteen conditions: phenylketonuria, biotinidase deficiency, galactosaemia, MCAD deficiency, VLCAD deficiency, LCHAD deficiency, CPT1, CPT2, CAT deficiencies, maple syrup urine disease, glutaric aciduria type 1, isovaleric acidaemia, congenital adrenal hyperplasia and congenital hypothyroidism.

Newborn screening is a genetic test as defined in the GenDG. As such, it is subject to the exclusive right of medical professionals to practise medicine as well as the requirements for informed and written consent. The Joint Federal Committee - as the joint self-administration body representing health insurance funds, the medical profession and hospitals - specifies in a binding guideline the conduct of newborn screening and the diseases and conditions the screening for which is eligible for reimbursement by the statutory health insurance system.

Diagnostic tests are registered as available in Germany for 1449 genes and an estimated 1479 diseases in the Orphanet database³.

National alliances of patient organisations and patient representation

In Germany, the German National Alliance for Chronic Rare Diseases (ACHSE) is a network of more than 100 patient organisations of people living with a specific rare disease. Through ACHSE, rare disease patient organisations support each other, exchanging know-how so as to strengthen their influence in the political arena and improve the quality and duration of life of people living with a rare disease. ACHSE is an active member of EURORDIS and a member of its Council of National Alliances.

In Germany, health-related self-help groups and organisations are eligible for financial support from the statutory health insurance funds. A legislative reform (1 January 2009) has made access to funding easier and the distribution of the funding earmarked by the statutory health insurance funds is guaranteed: this means about €40 million in 2011.

The Ministry of Health currently supports different projects concerning the participation of patients with rare diseases at the Charité Berlin. One of these projects deals with the "Contribution of self-help groups/patient organisations to the organisation of interfaces within the health care system", aimed at improving patient participation and orientation. The Ministry of Health also supports other activities in the field of rare diseases such as conferences, brochures, workshops.

An important role is played in the regulation of the medical services of the German health care system by self-governing bodies such as patient associations: since 2004, national groups representing patients participate in the consultations of the Federal Joint Committee.

Sources of information on rare diseases and national help lines

Orphanet activities in Germany

The Orphanet portal on rare diseases is available in German⁴ and is widely used as a major information source on rare diseases in Germany. Since 2001 there is a dedicated Orphanet team in Germany, currently hosted by the Human Genetics department of the Hannover Medical School (MHH). This team is in charge of collecting data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials and patient organisations) in their country for entry into the Orphanet database. This team was officially designated as the Orphanet national team for Germany by the Federal Ministry of Health in 2010. In 2010, the Orphanet-Germany national website was launched⁵. This German language page is maintained by the Orphanet-Germany team and features information, news and events specific to field of rare diseases in Germany. Users can access the main Orphanet site in any of the five available languages, as usual, from this page.

Official information centre for rare diseases

There is no official information centre on rare diseases in Germany.

³ Information extracted from the Orphanet database (September 2011), no verification by the German Federal Ministry of Health.

⁴ www.orphanet.de

⁵ <http://www.orpha.net/national/DE-DE/index/startseite/>

Help line

There is currently no official help line for rare diseases in Germany. However, ACHSE offers a privately funded help line for people living with a rare disease since 2006 and answers about 600 to 800 requests per year. The help line is also open for professionals, but not often addressed by them. The help line is financed solely with donations and through charity events.

Other sources of information on rare diseases

All medicinal products, including orphan medicinal products, are included in a database called PharmNet, run by the German Institute of Medical Documentation and Information (DIMDI)⁶ ensuring public access to package leaflet, summary of product characteristics (Fachinformation in Germany) and the assessment report (publicly accessible version).

On 1 January 2011 Section 42b AMG (Arzneimittelgesetz, Medicinal Products Law) came into force stipulating pharmaceutical companies and sponsors of clinical trials to report results of clinical trials to the federal higher authorities for purposes of publication in a public database run by DIMDI.

The ACHSE website⁷ provides a platform for information on rare diseases. This platform is a validated and patient-orientated source of information. It encourages patient organisations to improve their information continuously. ACHSE has also established a help line to inform patients and their families in particular those without a diagnosis or an established patient organisation.

The KINDERNETZWERK⁸ offers a service line for patients with rare diseases together with patient oriented online diseases descriptions. The KINDERNETZWERK additionally holds a database for registering parents with children suffering of rare diseases. Information on patient groups can also be found at the NAKOS website⁹ (The National Clearing House for the Encouragement and Support of Self-Help Groups). Other non-rare disease specific help lines are available to help patients understand the health care system.

Beside the above mentioned internet information sources for rare diseases there exist several informational websites for rare diseases run by e.g. patient organisations, learned societies and university institutions. Some (genetic) diagnostic labs also offer information about tested diseases in detail. Several other internet databases are offering information on common diseases which imply also information on rare diseases: DermIS (www.dermis.net) an internet based information system for dermatology (recently public funded by the Federal Ministry of Education and Research, now private funding by Bayer Health Care), ONKODIN (www.onkodin.de) with focus on hematological diseases, public funding, www.patienten-information.de (www.patienten-informationen.de) of the ÄZQ (Agency for Quality in Medicine) – an initiative of the Bundesärztekammer (German Medical Association) and the Kassenärztliche Bundesvereinigung (National Association of Statutory Health Insurance Physicians) and others. The University Rostock, Albrecht-Kossel-Institut for Neurodegeneration is hosting the data-base www.selteneerkrankungen.de, mainly focusing on rare neurogenerative diseases and the laboratories that are apparently qualified for diagnosis (Funding is unclear.). There is also the Rare Metabolic Diseases Database which receives public funding from the German Federal Ministry of Education and Research, and is hosted by the Bielefeld University, Bioinformatics Department. It also represents a patient registry for rare metabolic diseases.

Good practice guidelines

For some rare diseases there exist practice clinical guidelines (i.e. cystic fibrosis, diagnostic of myopathy, congenital adrenal hyperplasia) from the AWMF (Association of the Scientific Medical Societies, *Arbeitsgemeinschaft Wissenschaftlicher Medizinischer Fachgesellschaften*). In 2011 the Institute for Quality and Efficiency in Health Care (IQWiG) published a rapid report (V 10-01) concerning the question “What type of evidence is currently being considered in the development of clinical practice guidelines for rare diseases?”¹⁰.

Training and education initiatives

Germany is elaborating a national catalogue of learning objectives for medicine for medical students. In this process criteria are being developed to integrate rare diseases in this catalogue to better incorporate them in basic medical training.

⁶ <http://www.dimdi.de/static/de/amg/pharmnet/index.htm>

⁷ www.achse.info

⁸ www.Kindernetzwerk.de

⁹ www.nakos.de

¹⁰ https://www.iqwig.de/download/V10-01_Executive_Summary_Evidence_for_guidelines_on_rare_diseases.pdf

National rare disease events in 2011

The German Society of Human Genetics (GfH) holds an annual conference (Regensburg, 16-18 March 2011) in association with the Swiss and Austrian Societies of Human Genetics, where topics concerning rare diseases are given a spotlight. Several paediatric subspecialties have a tradition of focussing on rare diseases, especially the Arbeitsgemeinschaft Pädiatrische Stoffwechselerkrankungen (Paediatric Metabolic Medicine), Paediatric nephrology, Deutsche Gesellschaft für Kinderendokrinologie und –diabetologie (DGKED) e.V. (Paediatric endocrinology) and Paediatric rheumatology, all holding yearly meetings often including patient organisations. ACHSE organises meetings for patient organisations twice a year.

A number of actions and events were organised to mark Rare Disease Day 2011 in Germany. Events were organised by ACHSE members with support and coordination of ACHSE in 11 German cities: Bad Oeynhausen, Berlin, Dessau, Essen, Hamburg, Hannover, Cologne, Magdeburg, Stuttgart, Würzburg. People from different rare disease patient organisations teamed up to organise different events. In Dessau, Magdeburg and Cologne there were events in the hospitals organised by the hospitals' staff. This day provided the opportunity to raise awareness, and to inform public about the problems and needs of people living with rare diseases. As in the previous year, at all the events hundreds of red ACHSE-balloons were released to rise into to sky. Apart from these awareness events the Eva Luise and Horst Köhler foundation for people with rare diseases in cooperation with ACHSE awarded another Eva-Luise-Köhler- Award for a research project that has not been realised yet, thus strengthening research for rare diseases.

A short film was produced for the ACHSE-project "Wissenskarawane für die Seltenen" (caravan of knowledge for people with rare diseases) by SympathieFilm which was financed by the statutory health insurance funds Barmer GEK, TK, DAK, KKH, HEK.

On 26 February the 2nd Rare Disease Day Symposium was organised by Orphanet at the Medical School of Hanover. This event was well attended by 36 different support groups taking part by presenting information booths to the public. The motto of Rare Disease Day "rare but equal" was reflected by 8 interesting talks from experts presenting different aspects of the actual health care situation for patients with rare diseases in Germany. Different structures were highlighted, including a report of experiences of the first official centre for rare diseases in Germany during its first year of existence. The audience also learned about the structure of different networks and their impact on patient care, the latest developments in the field of orphan medicinal products and how to improve quality of specialised centres by certifying them. About 250 people visited this event. The press also attended the meeting, with the local print media publishing a report on this day, along with reports on television of the Symposium.

A symposium on rare diseases was held at the Heidelberg University Hospital on 15 April 2011. The event was well attended and several support groups took part in the meeting by presenting information booths to the public. Talks covered different topics in the field of rare diseases were given by representatives of associations and of the German Parliament, clinicians and researchers as well as a round table discussion with people living with a rare disease and clinicians was presented. The topics included: health policy, the latest scientific developments on rare diseases and the role of networks to improve the care of rare disease patients. The event was reported on in the local print media and on television.

Rare diseases were also one of the topics of the Year of Science 2011 – Research for Our Health – which was organised by the Federal Ministry of Education and Research (BMBF) in collaboration with Wissenschaft im Dialog (WiD) - an initiative by the German Science - and numerous partners from different fields such as science, industry, politics and culture. One of the events was a photo exhibition titled "Orphans of Medicine – Living with a rare disease" which was hosted in Munich June 29 to July 22 2011. The exhibition was organised by ACHSE and funded by the BMBF. In addition, rare diseases were one of the topics presented in the exhibition titled "Discoveries" on the island of Mainau from 20 May to 4 September 2011.

A meeting of the networks for rare diseases funded by the German Federal Ministry for Education and Research (BMBF) was held on 20 September 2011 in Munich. The participants included representatives of the funded networks, PT-DLR (Project Management Organization at the DLR, acting on behalf of the BMBF) and ACHSE.

Hosted rare disease events in 2011

Amongst the rare diseases events hosted by Germany and announced in OrphaNews Europe were: 3rd International Adrenal Cancer Symposium: From Molecular Pathogenesis to Clinical Outcome (17-19 February 2011, Würzburg), Fourth Berlin Conference on IP in Life Sciences: Rare Diseases – Blockbusters in the Niche (18 February 2011, Berlin), 3rd Symposium on Disorders of Sex Development (20-22 May 2011, Lubeck), The World Orphan Drug Summit (31 May – 1 June 2011, Frankfurt), International Conference on Inherited Disorders of Muco-Ciliary Clearance (Focus on PCD) (20-22 May 2011, Muenster), 2011 International Expert Meeting: Large

Congenital Melanocytic Nevi/Neurocutaneous Melanocytosis (6-7 May 2011, Tuebingen, Germany), 15th International Workshop on Fragile X and Early-Onset Cognitive Disorders (4-7 September 2011, Berlin), 1st CURE-Net International Conference for Congenital Uro-Rectal Malformations (21-22 October, Heidelberg).

In addition to these events, the 4th International Postgraduate Course on Lysosomal Storage Disorders: Diagnostic Background and Clinical Therapy took place at the University of Rostock in Berlin from 14-15 November 2011.

Research activities and E-Rare partnership

National research activities

In 2003, the Federal Ministry for Education and Research (*Bundesministerium für Bildung und Forschung, BMBF*) funded ten networks of national academic groups, clinical centres, specialised laboratories and patients organisations for basic and clinical research for an initial three years. After a successful interim evaluation, nine of the networks for rare diseases were funded for another two years. The budget of this rare disease research programme was €31 million.

In 2007, the BMBF opened a new funding programme on rare diseases research with a substantial increase in budget to €24 million for the first 3 year period and a possible extension of the maximum funding duration of 3 times renewable 3 year periods for new networks. Starting in October 2008, 16 networks are currently being funded. Six of these are extensions of previously funded networks, while the other 10 networks are new. In 2010, the networks have been granted €6 million additional funds for investments in shared research equipment, most notably next generation sequencing. In September 2010, a new call for proposals for the possible extension of the 10 networks which started in 2008 and the creation of new networks was published. After the evaluation of 39 proposals by a review board of international rare disease experts, the BMBF has selected 12 networks for funding starting in 2012 with more than €21million for three years.

Additional funding of rare disease research is ongoing in other funding initiatives of the BMBF such as the National Genome Research Network (NGFN), Innovative Therapies, Regenerative Medicine, Molecular Diagnostics, Clinical Trials and others with about €20 million in 2011. All these activities are funded within the framework programme "Health research". In co-operation with the Federal Ministry of Health, the BMBF assumes responsibility for the programme which is financed with funds from the BMBF.

The *Eva Luise und Horst Köhler Stiftung für Menschen mit Seltenen Erkrankungen*, a foundation of the former First Lady and the former president of the Federal Republic of Germany, is dedicated to patients with rare diseases and supports research projects into rare diseases annually since 2006.

Regional sources of funding are also available.

Participation in European research projects

German teams participate, or have participated, in European research projects for rare diseases including: AUTOROME, ANTEPRION, BIOMALPAR, BNE, CAV-4-MPS, CRANIRARE, CURE-FXS, CHD PLATFORM, CILMALVAC, CUREHLH, EDEN, EMVDA, ENRAH, ENCE-PLAN, EURADRENAL, EUCILIA, EUNEFRON, EURIPFNET, EUROBONET, EUROBFNS, EUROSD, EURO-CDG, EURO-LAMINOPATHIES, EUROPEAN LEUKEMIA NET, EUROSCA, EURO-SCAR, EUROTRAPS, EURORETT, EUROSPA, ERMION, EuPAPNet, EUBNFS, EURO-CGD, ELA2-CN, EMINA, EPINOSTICS, EUREGENE, EUROPEAN LEUKEMIA NET, EMSA-SG, ESDN, FASTEST-TB, GETHERTHAL, GENOMIT, HMA-IRON, HAE III, HDLOMICS, HUE-MAN, HMANASP, IPF-AE, INTHER, KINDLERNET, LEISHDRUG, MANASP, MITOTARGET, MTMpathies2, MYORES, MIMOVAX, MOLDIAG-PACA, NEUROSIS, NSEuroNet, NEUTRONET, NEMMYOP, NEWTBDRUGS, PULMOTENSION, OVCAD, OSTROPETR, PODONET, PEMPHIGUS, RD PLATFORM, RevertantEB, RHORCOD, RATSTREAM, RARE-G, RISCA, SKIN-DEV, TRANSPOSMART, WHIM-Thernet, WHIPPLE'S DISEASE and TB-VIR.

E-Rare

Germany is a partner of the E-Rare project, represented by the BMBF and the Project Management Agency of the German Aerospace Centre (*PT-DLR*). Germany participated in the E-Rare joint transnational calls in 2007, 2009 and 2011 and funds the participating German research groups of 35 transnational research projects with a total of about €10 million.

IRDiRC

The Federal Ministry of Education and Research (BMBF) is a committed member of IRDiRC.

Orphan medicinal products

Orphan medicinal product committee

No specific information reported.

Orphan medicinal product incentives

Orphan medicinal products are also exempted from the mandatory rebate to the statutory and private health insurance funds on sales of products outside the German maximum reimbursement prices (*Festbeträge*) system, though evidence for the need of this exemption must be provided by the company¹¹. See further under chapter "Orphan medicinal product reimbursement policy".

Orphan medicinal product market availability situation

No specific information reported.

Orphan medicinal product pricing policy

All orphan medicinal products are reimbursed directly after market authorisation. As the German maximum reimbursement prices scheme (*Festbeträge*) normally does not cover orphan medicinal products, they were excluded from any on reimbursed prices. Only generic products and those considered to belong to the same pharmacological or therapeutic group can be subject to maximum reimbursement prices that eventually set the retail-price of the manufacturer. Effective 1 January 2011, for every new drug with patented or non-generic substances a binding ex-factory price based on the value of the drug have to be negotiated on Federal Level. This is carried out by the Federal Association of Sickness Funds and the manufacturer. If no agreement can be achieved, the price is set by arbitrage committee, in which both contract parties are represented. For the first 12 months following marketing authorisation each new drug is still reimbursed at the full price set by the manufacturer. Mandatory Price Negotiations have been introduced by the Act for the New Order for the Drug Market in Social Health Insurance (AMNOG). According to this law, previous to price negotiations the value of the drug is evaluated. The manufacturer issues a Dossier when they enter the market. It is assessed by the German Institute for Quality and Efficiency in Health Care (IQWiG). The Federal Joint Committee (G-BA) appraises and decides on the added value of the drug compared to standard therapy.

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Once authorised at European level, all orphan medicinal products are fully reimbursed by the statutory health insurance (*GKV*). Until 31 December 2010, all newly authorised drugs could be put on the marketplace without any restrictions on reimbursed prices. Only generic products and those considered to belong to the same pharmacological or therapeutic group could be subject to maximum reimbursement prices that eventually set the retail-price of the manufacturer. Effective 1 January 2011, the act on new regulations for the drug-market (AMNOG) is mandating that all drugs with patented substances are subject to a cost/benefit analysis followed by a price negotiation. However, while this procedure that is limited to 12 months following marketing authorisation, is running, the product is still reimbursed at the price set by the manufacturer. Orphan medicinal products authorised by EMA under EU-regulation 141/2000 with an annual turnover below 50 million Euros are exempted from the benefit assessment, because the benefit is taken as granted. Still, price negotiations are mandatory also for these drugs.

Other initiatives to improve access to orphan medicinal products

Irrespective of the prevalence of the disease, the off-label use of drugs is reimbursed by the statutory health insurance (*GKV*) on the following conditions: the drug will be used to treat a life-threatening or fatal disease; there is an absence of pharmaceutical therapy with a marketing authorisation in Germany; and there is scientific evidence of positive therapeutic effects¹².

In Germany, as in many other European countries, it has been basically possible to administer promising medicinal products for severely ill patients before authorisation in case no alternatives exist. In 2005, on the basis of the Regulation (EC) No 726/2004 the German government implemented general rules providing such medicinal products in form of so-called Compassionate Use Programmes in Section 21 sub-section 2 no. 6 of the German Medicinal Products Act. In 2009 it was added that the provision of a medicinal product in such cases has to be free of charge. An ordinance, coming into force 2010, contains special regulations for the proper procedure of Compassionate Use Programmes. An overview on Compassionate Use Programmes

¹¹ *Orphan Drugs in Europe : Pricing, Reimbursement, Funding and Market Access Issues*, Donald Macarthur (2011)

¹² *Orphan Drugs in Europe : Pricing, Reimbursement, Funding and Market Access Issues*, Donald Macarthur (2011)

confirmed by the Federal Institute for Drugs and Medical Devices (BfArM) is available on the website¹³. Once authorised, all orphan medicinal products are fully reimbursed by statutory health insurance.

Orphan devices

No specific information reported.

Specialised social services

No specific activity reported.

DEVELOPMENT OF RARE DISEASE ACTIVITIES IN 2011 IN GERMANY

National plan for rare diseases and related actions

The national action league for people with rare diseases - *Nationales Aktionsbündnis für Menschen mit Seltenen Erkrankungen* (NAMSE)¹⁴, a co-ordination and communication platform comprising all key bodies and organisations, continues work on the implementation of a National Action Plan on Rare Diseases. The process is organised in a steering committee and four working groups. At the end of this process the national action league for people with rare diseases will recommend different actions for the German National Action Plan for Rare Diseases.

Sources of information on rare diseases and national help lines

Other sources of information on rare diseases

On 1 January 2011 Section 42b AMG (Arzneimittelgesetz, Medicinal Products Law) came into force stipulating pharmaceutical companies and sponsors of clinical trials to report results of clinical trials to the federal higher authorities for purposes of publication in a public database run by the German Institute of Medical Documentation and Information (DIMDI)¹⁵.

Good practice guidelines

In 2011 the Institute for Quality and Efficiency in Health Care (IQWiG) published a rapid report (V 10-01) concerning the question "What type of evidence is currently being considered in the development of clinical practice guidelines for rare diseases?"¹⁶.

Training and education initiatives

Germany is elaborating a national catalogue of learning objectives for medicine for medical students. In this process criteria are being developed to integrate rare diseases in this catalogue to better incorporate them in basic medical training.

National rare disease events in 2011

The German Society of Human Genetics (GfH) holds an annual conference (Regensburg, 16-18 March 2011) in association with the Swiss and Austrian Societies of Human Genetics, where topics concerning rare diseases are given a spotlight. Several paediatric subspecialties have a tradition of focussing on rare diseases, especially the Arbeitsgemeinschaft Pädiatrische Stoffwechselerkrankungen (Paediatric Metabolic Medicine), Paediatric nephrology, Deutsche Gesellschaft für Kinderendokrinologie und –diabetologie (DGKED) e.V. (Paediatric

¹³ www.bfarm.de

¹⁴ <http://namse.de/>

¹⁵ <http://www.dimdi.de/static/de/amg/pharmnet/index.htm>

¹⁶ https://www.iqwig.de/download/V10-01_Executive_Summary_Evidence_for_guidelines_on_rare_diseases.pdf

endocrinology) and Paediatric rheumatology, all holding yearly meetings often including patient organisations. ACHSE organises meetings for patient organisations twice a year.

A number of actions and events were organised to mark Rare Disease Day 2011 in Germany. Events were organised by ACHSE members with support and coordination of ACHSE in 11 German cities: Bad Oeynhausen, Berlin, Dessau, Essen, Hamburg, Hannover, Cologne, Magdeburg, Stuttgart, Würzburg. People from different rare disease patient organisations teamed up to organise different events. In Dessau, Magdeburg and Cologne there were events in the hospitals organised by the hospitals' staff. This day provided the opportunity to raise awareness, and to inform public about the problems and needs of people living with rare diseases. As in the previous year, at all the events hundreds of red ACHSE-balloons were released to rise into to sky. Apart from these awareness events the Eva Luise and Horst Köhler foundation for people with rare diseases in cooperation with ACHSE awarded another Eva-Luise-Köhler- Award for a research project that has not been realised yet, thus strengthening research for rare diseases.

A short film was produced for the ACHSE-project "Wissenskarawane für die Seltenen" (caravan of knowledge for people with rare diseases) by SympathieFilm which was financed by the statutory health insurance funds Barmer GEK, TK, DAK, KKH, HEK.

On 26 February the 2nd Rare Disease Day Symposium was organised by Orphanet at the Medical School of Hanover. This event was well attended by 36 different support groups taking part by presenting information booths to the public. The motto of Rare Disease Day "rare but equal" was reflected by 8 interesting talks from experts presenting different aspects of the actual health care situation for patients with rare diseases in Germany. Different structures were highlighted, including a report of experiences of the first official centre for rare diseases in Germany during its first year of existence. The audience also learned about the structure of different networks and their impact on patient care, the latest developments in the field of orphan medicinal products and how to improve quality of specialised centres by certifying them. About 250 people visited this event. The press also attended the meeting, with the local print media publishing a report on this day, along with reports on television of the Symposium.

A symposium on rare diseases was held at the Heidelberg University Hospital on 15 April 2011. The event was well attended and several support groups took part in the meeting by presenting information booths to the public. Talks covered different topics in the field of rare diseases were given by representatives of associations and of the German Parliament, clinicians and researchers as well as a round table discussion with people living with a rare disease and clinicians was presented. The topics included: health policy, the latest scientific developments on rare diseases and the role of networks to improve the care of rare disease patients. The event was reported on in the local print media and on television.

Rare diseases were also one of the topics of the Year of Science 2011 – Research for Our Health – which was organised by the Federal Ministry of Education and Research (BMBF) in collaboration with Wissenschaft im Dialog (WiD) - an initiative by the German Science - and numerous partners from different fields such as science, industry, politics and culture. One of the events was a photo exhibition titled "Orphans of Medicine – Living with a rare disease" which was hosted in Munich 29 June to 22 July 2011. The exhibition was organised by ACHSE and funded by the BMBF. In addition, rare diseases were one of the topics presented in the exhibition titled "Discoveries" on the island of Mainau from 20 May to 4 September 2011.

A meeting of the networks for rare diseases funded by the German Federal Ministry for Education and Research (BMBF) was held on 20 September 2011 in Munich. The participants included representatives of the funded networks, PT-DLR (Project Management Organization at the DLR, acting on behalf of the BMBF) and ACHSE.

Research activities and E-Rare partnership

National research activities

In September 2010, the BMBF launched a new call for proposals for the possible extension of the 10 rare disease research networks which started in 2008 and the creation of new networks was published. After the evaluation of 39 proposals by a review board of international rare disease experts, the BMBF has selected 12 networks for funding starting in 2012 with more than €21 million for three years.

Additional funding of rare disease research is ongoing in other funding initiatives of the BMBF such as the National Genome Research Network (NGFN), Innovative Therapies, Regenerative Medicine, Molecular Diagnostics, Clinical Trials and others with about €20 million in 2011. All these activities are funded within the framework programme "Health research". In co-operation with the Federal Ministry of Health, the BMBF assumes responsibility for the programme which is financed with funds from the BMBF.

The *Eva Luise und Horst Köhler Stiftung für Menschen mit Seltenen Erkrankungen*, a foundation of the First Lady and the president of the Federal Republic of Germany, is dedicated to patients with rare diseases and supports research projects into rare diseases annually since 2006, including in 2011.

E-Rare

Germany participated in the E-Rare joint transnational calls in 2007, 2009 and 2011 and funds the participating German research groups of 35 transnational research projects with a total of about €10 million.

IRDiRC

The Federal Ministry of Education and Research (BMBF) is a committed member of IRDiRC.

Orphan medicinal products

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LIST OF CONTRIBUTIONS¹⁷

Contributions in 2010

Manfred Stuhmann-Spangenberg and Kathrin Rommel (*Orphanet Germany, Medizinische Hochschule Hannover*)

Ralph Schuster (*PT-DLR*)

Georg F. Hoffmann (*Department of Pediatrics, University of Heidelberg*)

Gabriele Dreier

Daniela Eidt-Koch (*First author of the study "Strategies for improving the health care situation of patients with rare disease in Germany"*)

Birgit Schnieders (*Federal Ministry of Health*)

Andreas Reimann (*ACHSE*)

Contributions in 2011

Manfred Stuhmann-Spangenberg (*Orphanet Germany, Medizinische Hochschule Hannover*)

Ralph Schuster (*PT-DLR*)

Georg F. Hoffmann (*Department of Pediatrics, University of Heidelberg*)

Olaf Hiort (*Universitätsklinikum Schleswig-Holstein*)

Birgit Schnieders and Véronique Héon-Klin (*Federal Ministry of Health*)

Contributions in 2012

Birgit Schnieders and Véronique Héon-Klin (*Federal Ministry of Health*)

Georg F. Hoffmann (*Department of Pediatrics, University of Heidelberg*)

Olaf Hiort (*Universitätsklinikum Schleswig-Holstein*)

Ute Rehwald (*Federal Ministry Of Research And Education*)

Manfred Stuhmann-Spangenberg (*Orphanet Germany, Medizinische Hochschule Hannover*)

Miriam Mann (*ACHSE*)

Thomas Wagner (*Klinikum der Johann Wolfgang Goethe-Universität*)

Validated by: Birgit Schnieders and Véronique Héon-Klin (*EUCERD Representative and EUCERD Alternate Representative Germany, Federal Ministry of Health*)

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¹⁷ The contributors and validators of the report have contributed information which is accurate to the best of their knowledge. However, readers should take note that the contents of this report are illustrative and not exhaustive.

¹⁸ All websites and documents were last accessed in May 2012. A more detailed list of sources is available in the full report: <http://www.eucerd.eu/upload/file/Reports/2012ReportStateofArtRDActivities.pdf>

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