EUROPLAN National Conference organized by ACHSE in Germany 13th and 14th of October 2010 in Berlin

CONFERENCE FINAL REPORT

I. General information

Country	Federal Republic of Germany
Date & place of the National Conference	13th and 14th of October 2010 in Berlin
Website	www.achse-online.de
Organisers	ACHSE – the German Alliance for Rare Diseases
Members of the Steering Committee	--
Names and list of Workshops	Workshop 1: Improving Information Workshop 2: Standards of Care, Centres of Expertise/Reference Centres and Orphan Drugs Workshop 3: Research Workshop 4: Monitoring and Indicators
Chairs and Rapporteurs of Workshops	Chair Panel Session: Prof. Dr. Schulz-Nieswandt Chair of WS 1: Dr. Sylvia Sänger and Lisa Biehl Chair of WS 2: Dr. Andreas Reimann and Dr. Christine Mundlos Chair of WS 3: Prof. Dr. Erik Harms and Mirjam Mann Chair of WS 4: Dr. Christoph Vauth Rapporteur PS: Elisabeth Watermeier (ACHSE) Rapporteur WS 1: Katherine Rommel (Orphanet) Rapporteur WS 2: Jérome Ries (BKMF)

	Rapporteur WS 3 : Antje Schütt (TMF)p **Rapporteur WS 4 : Horst Ganter (DGM)**
Attachments (programme, list of participants, etc.)	**Programme** **List of Participants**

II. Main Report

The National Conference was a very lively gathering of more than 200 participants coming from different fields. The rare disease community was highly gratified to see so many so strongly engaged for patient orientated care and improvements in the quality of life for people living with a rare disease. The conference has generated many ideas for a National Plan and inspired many to continue to strive for improvements.

In March 2010 the German Ministry of Health initiated a National Committee for People living with a Rare Disease "NAMSE" (*Nationales Aktionsbündnis für Menschen mit Seltenen Erkrankungen)*. This committee, consisting of important stakeholders in the German health care system, will draft a National Action-Plan (*"nationalen Aktionsplan")* steering various activities designed to improve information, health-care, diagnosis and research related to rare diseases. NAMSE is coordinated by the Federal Ministry of Health, the Federal Ministry of Research and the German Alliance for Rare Diseases (ACHSE e.V.). As a result the German Conference fortunately did not have to convince its participants that a National Plan is necessary nor did the conference have to consider questions of procedure.

Since we have the good fortune, that the process of developing a National Plan has already been started by the Ministry of Health, the ideas discussed in the national conference organised by ACHSE will not only become part of the present report. As many of the participants are also representatives in the working groups of NAMSE, the different ideas discussed in these two days can by different spokespersons be integrated in and therewith strongly contribute to this process. We have never been as hopeful that a meaningful National Plan will improve the lives of people with a rare disease in the near future.

In his opening words of the national conference the *Patientenbeauftragter* – the Appointee of the Government for the interest of patients – Wolfgang Zöller (Member of Parliament) stressed the importance of awareness of rare diseases and he announced that he wishes the Patient Rights Act for which he is advocating, will be passed including a passage guaranteeing access to good care for people living with a rare disease.

EUROPLAN RECOMMENDATIONS

In all Workshops the EUROPLAN recommendations were considered valid recommendations to which everybody could agree in principle. The recommendations constitute a good guideline for the content of a National Plan. The recommendations do, however, still need to be translated into specific measures.

Additional work will have to be done to specify the measures necessary in the local situation. In this report many Recommendations are therefore not commented. This should not be understood as a disagreement with those recommendations.

Main Themes

Theme 1 - Methodology and Governance of a National Plan / Strategy (NP)

Sub-Themes

1. Mapping exercise before developing a National Plan
2. Development and structure of a National Plan / Strategy
3. Governance of a National Plan
4. Monitoring the National Plan
5. Sustainability of the National Plan

Introductory words on the Workshop on Monitoring and Indicators

All participants of the Workshop on Monitoring and Indicators agreed that an effective National Plan of high quality should stipulate the indicators for success and provide for a methodologically sound system of monitoring the measures provided for in the national plan. It is of utmost importance that those indicators are defined with focus on the patient interests and in a process in which patients play an active role.

The 60 indicators defined by EUROPLAN, subdivided in 10 areas, have been discussed (such as Classification, Research or Centres of Expertise). The indicators were evaluated as useful points of reference for establishing international comparisons and for the work on additional national indicators. The Workshop advises the National Committee on Rare Diseases ("NAMSE") to use the EUROPLAN-Indicators as a basis of reference for agreeing on the necessary indicators. The areas on Centres of Expertise, Diagnosis and Patient Empowerment were considered to be of the highest importance.

The Workshop advises to focus first on those results that can be achieved with the least amount of effort and/or money with the best result. Those indicators should be established first and not a theoretic systematic approach should be chosen, e.g. starting with Indicators in area 1 of EUROPLAN and then 2 etc.

The National Plan should implement a monitoring commission which defines indicators and evaluates the results on the basis of these indicators. The commission should contain sufficient patient representatives and should already start its work during the development of the national plan.

High quality monitoring is only possibly with highly qualified members, especially with respect to the patient representatives. Qualifying the patient representatives of the ACHSE member organisations is therefore necessary to help ACHSE provide for a continued high quality patient input into the monitoring process.

In order to be able to compare the results on a European level for some indicators additional information should be documented, such as the financial budget and the form of patient representation. The documentation should show the progress of the project.

From this first thorough discussion on the indicators of a national plan a number of observations emerged from the discussion.

In general the participants of this workshop felt, that in addition to the many process indicators more indicators reviewing quality or quantity should be specified. In Area 1 for example the indicators that verify whether the main criteria of National Plan are achieved – Is an expert committee established? Is there a budget allocated to the Plan? – need to be supplemented with indicators of quality such as the kind of experts in the committee or the amount of the budget.

Furthermore the following observations were made:

- An efficient monitoring process needs transparency of and access to the data on the basis whereof the evaluation of the plan is performed.
- The ICD-Code should be used to specify the diseases included into the monitoring parameters.
- The number of participants in the different registries should be another indicator in addition to the number of registries and the number of diseases covered by such registries.
- An indicator for registries to gather information on Off-Label-Use is considered useful.
- Research: additional indicators should be the number of international research projects in which German researchers are participating and the number of publications.
- For a good evaluation of the research efforts the data should be differentiated in basic research, epidemiology, clinical research, social research and public health.
- The criteria for a “Centre of Expertise” should be defined – number of patients treated, patient satisfaction, certification etc. – in order to evaluate indicators 4.1 to 4.5.
- A modus has to be found to evaluate how many diseases (ICD) and to what extend are covered by Centres of Expertise.
- Different indicators evaluating the quality of patient participation in the decision making process should be established. Whether patients are actually empowered to make their voice heard should be monitored. Where do they have the right to vote? What kind of procedural rights do the patient representatives have? What is the democratic legitimisation of the contribution of patient representatives in the different decision making processes? Etc.
- Access to information, in particular on medication, should be an indicator ofthe level of patient empowerment.
- The number of available Orphan Drugs is not the only an indicator in respect to drugs. The enormous importance of Off-Label-Use, Medicinal Products, other therapeutics and psychological treatments should be taken into account.
- A quality criterion should also be the availability of emergency guidelines.

- On diagnosis indicators were lacking on the time between symptoms and correct diagnosis and where this diagnosis is made. Also the quality of medical training and the permanent education of physicians should receive strong attention in the National Plan and in the monitoring process. The goal should be that physicians are empowered to think the uncommon at the right moment, without knowing all possible rare diseases.
- Also the number of references to rare diseases in guide lines for more common diseases could be interesting in addition to the number of guide lines available on particular rare diseases.

1. Mapping Exercise before developing a NP

1. **Is there an awareness of the situation of RD in your country (epidemiologic figures, dimension of the problem)?**
2. **Is an inventory being made or a report of the existing resources and actions on RD (or of which RD Patients can benefit) in the national health care and social system?**
3. **Are the unmet needs of RD patients being evaluated?**

The Study "Measures to improve the healthcare situation of people living with a rare disease in Germany" performed by order of the German Ministry of Health constituted a first assessment of these questions. The Working Groups of NAMSE will elaborate thereupon. The National Conference confirmed that this study gives a good overview of the current situation for people living with rare diseases in Germany.

2. Development and structure of a National Plan / Strategy

As NAMSE, consisting of 26 major players in the health care system, which has to agree on a National Plan for Rare Diseases, was just recently constituted, discussing the best way of developing a national plan in the workshops of the National Conference was not very useful at this time. The NAMSE participants comprise representatives from the statutory health care insurances ("Krankenkassen"), the Federation of private doctors contracting with Krankenkassen, hospital organisations, chambers of health-care professions, industry, patient organisations and the Federal Joint Committee governing the statutory health care system.

3. Governance of a National Plan

4. Monitoring of a National Plan

A Workshop of two half-days was consecrated to recommendations of Working Package 5 of EUROPLAN. The conclusions of the workshop are described above.

5. Sustainability of a National Plan

It was agreed during the National Conference in plenary session and in the workshops that Rare Diseases are not a project; the problem will never go away. Suitable care for people living with a rare disease means adapting the healthcare system to their needs. While doing so lots of costs currently incurred by wrong diagnosis and wrong treatments can be saved. Different approaches necessary for rare diseases e.g. in case management, combining care data with research data, multidisciplinary approaches, etc. will be beneficial for people living with a more common disease as well. A National Plan should therefore be well evaluated in order to have a qualified estimation of the most important measures for the second National Plan following the first plan.

EUROPLAN RECOMMENDATIONS

R 1.1 Patients with rare diseases deserve dedicated public health policies to meet their specific needs.

R 1.2 Initiatives are taken to raise awareness about the dimension of the problem and to create joint responsibility.

R 1.3 A mechanism (e.g. interdisciplinary panel, committee) including relevant stakeholders is established to assist the development and implementation of the National Plan or Strategy.

R 1.4 A situation analysis is carried out including:

- *An inventory of existing healthcare resources, services, clinical and basic research activity and policies directly addressing rare diseases as well as those from which rare disease patients may benefit .*
- *Unfulfilled needs of patients are assessed.*
- *Available resources for improving health and social care of people affected by rare diseases at national level are evaluated.*
- *European collaboration and the European documents in the field of rare diseases are taken into account in the development of the National Plan or Strategy.*

➔ The Study “Measures to improve the healthcare situation of people living with a rare disease in Germany” performed in order of the German Ministry of Health constituted a first assessment of these questions. By establishing a suitable monitoring system a continued evaluation of these data, which is necessary, would be made possible.

R 1.5 The National Plan or Strategy is elaborated with well described objectives and actions. The general objectives of a National Plan or Strategy are based on the general overarching values of universality, access to good quality care, equity and solidarity.

R 1.6 The policy decisions of the National Plan or Strategy are integrated i.e. structured maximizing synergies and avoiding duplications with existing functions and structures of the health care system of the country.

R 1.7 The policy decisions of the National Plan or Strategy are comprehensive, addressing not only health care needs, but also social needs.

R 1.8 Specific areas for action are indicated, with priority given to those of the Council Recommendations, taking into account the major needs identified in the member state.

R 1.9 Appropriate resources are allocated to ensure the feasibility of the actions in the planned time.

R 1.10 Information on the National Plan or Strategy is made accessible to the public and it is disseminated to patients' groups, health professionals' societies, general public and media, making the plan known also at European level.

R 1.11 Measures are taken to ensure the sustainability, transfer and integration of the actions foreseen by the national plan or strategy into the general health system of the country.

R 1.12 The National Plan or Strategy has a duration of three to five years. An intermediate deadline is established, after which, an evaluation process is undertaken and corrective measures are adopted. For longer time scales or no defined time frame, a 2- to 3-year cyclic evaluation and adaptation process is adopted, if needed.

R 1.13 The National Plan or Strategy is monitored and assessed at regular intervals using, as far as possible, EUROPLAN indicators.

➔ The importance of this recommendation was stressed at several instances. The Workshop on Monitoring and Indicators did conclude that the indicators needed an adaptation to the local situation.

R 1.14 The implementation of the actions and their achievements are assessed.

R 1.15 The most appropriate evaluation of a National Plan or Strategy is by an external body and takes into account also patients' and citizens' views. Patients' needs are assessed at the beginning and the end of the plan implementation using the same methodology. Evaluation Reports are made public.

➔ Especially the importance of transparency of methods and results as well as a strong contribution of patient representatives was stressed in the working group.

Theme 2 - Definition, codification and inventorying of RD

Sub-Themes

1. Definition of RD
2. Classification and traceability of RDs in the national health system
3. Inventories, registries and lists

2.1. Information and training

4. How to improve information on available care for RDs in general, for different audiences
5. How to improve access to quality information on RDs
6. How to ensure adequate training of healthcare professionals on RDs

1. Definition of RD

1. Is the EU official definition (RD are those affecting up to 5 out of 10,000 persons) used in your country. Are there alternative or more specific definitions used in addition?

- The EU Definition is adopted by the committee developing the German National Plan ("NAMSE"). In the conference no objections were put forward against the use of the European definition.
- The further use of a subdivision of ultra rare diseases was discussed, but the use was rejected to prevent disadvantages for those being affected by "ultra rare" diseases.

2. Classification and traceability of RDs in the national health system

2. What classification system is used in your country) ICD9, ICD 10, SNOMED, OMIM, Orphan..

3. For which purposes is the classification system used, e.g. surveillance, reimbursement, provision of social support etc.

- Currently the ICD-10 and the ICD-10-GM are used for the mortality statistics, the reimbursement, social services, research on health care quality etc.
- ICD-10 is for epidemiological purposes only of limited value, as most orphan diseases are not individually listed.

4. Is your country prepared to adopt the WHO-led system, the ICD-11, recommended by the EU in Council Recommendation on RD, when ready (2014)?

- The ICD-11 Coding for Germany will be accepted and is required. .

5. What level of awareness and knowledge do healthcare professionals have of the RD classification and codification? What can be done to improve it?

- In general healthcare professionals have insufficient awareness of rare diseases, the Orphanet classification and the lack of codification within the ICD-10.

3. Inventories, registries and lists

6. Are there official lists of RD in your country? Is there an official governmental RD Registry? And/or specific RD databases e.g. held by CoE? Are there RD surveillance projects or programmes (e.g. sentinel programmes, surveys)?

- There is no exhaustive and/or governmental list of RD in Germany, but there are several databases known in Germany, that give information on rare diseases with different levels of detail.
- The most comprehensive database is represented by www.orpha.net. The Orphanet encyclopaedia is funded by the *European Commission*
- The national alliance for rare diseases develops patient orientated diseases descriptions and offers the possibility of information exchange on its information portal www.achse.info. The portal is a reference database, using the Orphanet classification of rare diseases. It is funded by the Robert-Bosch-Stiftung and donations to ACHSE.
- Beside the above mentioned internet information sources for rare diseases there exist several informational websites for rare diseases run e.g. by 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: Roche Lexicon (www.tk.de/rochelexikon) private company, DermIS (www.dermis.net) an internet based information system for dermatology (recently public funded by the BMBF, now private funding by Schering AG), ONKODIN (www.onkodin.de) with focus on hematological diseases, public funding, www.patienten-information.de (www.patienten-informationen.de) of the ÄZQ (Medical Centre for Quality) – an initiative of the *Bundesärztekammer* (Federal Society of Physicians) 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.). About 100 rare diseases are described within this database from a private company (goFeminin.de GmbH) in the Onmeda database (www.onmeda.de). There is also the Rare Metabolic Diseases Database which receives Public funding from the German Federal Ministry of Education and Research. It is hosted by the Bielefeld University, Bioinformatics Department. It also represents a patient registry for rare metabolic diseases.

- The Kindernetzwerk, a network for chronically ill or disabled children, young people and (young) adults maintain a data base on more than 2,000 diseases - among them also many rare diseases. Furthermore the data base contains over 225.000 addresses, for example from parents, groups of patients /patient organisations, clinics / hospitals, federal associations or internet addresses.
- As of today about 80 patient registries for rare diseases/group of diseases in Germany are known (source: Orphanet). Almost all of them are hosted by an institutional organisation/ university with public funding. Some of them are organized within international structures (Networks).
- A special situation exists for the hematologic and oncologic diseases. All federal states are forced to register cancer based diseases in the existing population based cancer registries. They are not exclusively dedicated to rare diseases but capable to give insight about rare oncological disease epidemiologics in Germany as well.
- Guidelines for diseases are available by the Guidelines International Network (www.g-i-n.net) offering the largest international guideline library. The German AWMF (Association of the Scientific Medical Societies in Germany) is one of the founding members. The AWMF is offering "Science-based Guidelines for Diagnostics and Therapy" in German on their website (www.uni-duesseldorf.de/AWMF)
- Other sources of information are International Publications in Journals (PubMed), Books, Brochures (health assurances, associations), Scientific meetings and conferences, Medical seminar, Counselling (especially in terms of genetic counselling), Television, Telephone, Tell-it-everybody, further training, lectures at universities and educational institutions, award ceremonies.
- In general rare diseases are not subdivided from frequent diseases, but information on rare diseases are implemented as well. It is important to extract the already established information hidden under the global information and to make use of this existent information.
- In general there are many information sources, but it is very difficult to establish for which information the quality is ensured by a process of evaluation, based on the right expertise etc.

7. What kind of initiatives should be taken or reinforced in your country?

- One of the results during the workshop was the fact that existing resources are not used in an adequate manner or are not known. There is an enormous fragmentation of information, many databases are not known. This means concentration of given resources should be pushed and also the information politics should focus more on existent knowledge.
- Efforts should be made to have reliable up-to-date patient orientated disease descriptions in the German language for most rare diseases available. A strong support of Orphanet and ACHSE for a joined effort on systematic improvement is necessary.

- Registries should set up cooperation with patient registries in other countries, if existent. Moreover the establishment of international networks is a essential tool to exchange existing knowledge. Establishment of competence and reference centres is mandatory.

8. Do these registries and programmes receive government support?

- The majority of registries are supported by governmental or institutional funding. The 16 Rare Disease Networks for particular (groups of) rare diseases are funded by the Ministry of Research.

9. How to ensure, through appropriate funding mechanisms, the long-term sustainability of registries and databases?

- Governmental funding of registries and databases is essential to ensure long term sustainability.
- Governmental funding of Orphanet and ACHSE is lacking. Funding of the work of Orphanet in the national context and in the local language is essential for reliable up-to-date and accessible information.

10. Does your country participate to the development of a EU inventory of RD as recommended in the Council Recommendation on RD?

This has not been discussed.

4. How to improve information on available care for RDs in general, for different audiences

11. What are the existing information sources in the country? Are they of good quality?

- See also Question 3.
- Orphanet Germany should be considered the national official website for Rare Diseases in Germany; there is no need for an additional website by the government.
- The associations feel a self-commitment to inform physicians and the general public. This work increases the capacity of private persons, so the funding for them should be appropriate. The Patient Organisations are often the thriving force behind the gathering and reviewing of information on “their” disease. The work of the patient organisations on improving information on rare diseases should also be supported.
- Patients’ experiences should be systematically documented and analysed. This should be done with a standardised questionnaire in order to ensure comparability of the results.
- Patient organisation meetings and scientific conferences should take place in cooperation to exchange knowledge.

- ACHSE offers a help line for patients and family member (ACHSE Betroffeneberatung), that is so well known by patients and family members, that ACHSE does not have enough resources for responding as fully and as quickly as it considers necessary. The help line is only funded by donations and should be funded with public means.
- The ACHSE help line for health care professionals (ACHSE Lotse an der Charité) is starting to become equally well known. As asking for help conflicts with the myth of the omniscient doctors a stronger effort to have the service known and accepted was and is necessary.

13. How are these information resources and initiatives publicised?

This Question has not been discussed.

14. How to make sure that they reach out to the target audiences?

- All information sites, even Orphanet, are not known or used enough by medical practitioners or patients. A large part of the older generation of medical professionals is not sufficiently inclined to use the internet at all; other practitioners are of the opinion that their time budget does not allow for searches o the internet.
- Medical professionals are not sufficiently aware of the expertise of patient organisations; neither do they always know, that patient organisations often have a network of medical experts in respect of their diseas(es) nor that they can be a strong sparring partner on an expert level, where questions are unresolved.

5. How to improve access to quality information on RDs

This Question has not been discussed

6. How to ensure adequate training of healthcare professionals on RD?

15. How to ensure adequate training of healthcare professionals on RD?

- Improvement of knowledge on rare diseases by the experts could be mediated by different efforts, especially the further- and specific education should be improved. Rare diseases should be implemented in the current medical subject catalogue for students and also the training of health care professionals should be reformed.
- Rare Diseases should be a meta-issue in the obligatory curriculum of the medicine studies and should be part of the continued education of physicians. Not knowledge on all the rare diseases, but awareness of the existence of more than 5.000 rare diseases as well as methodology to deal with the diagnosis of rare diseases should be learned. Part of this should be the acceptance of and a strategy for the fact that a physician cannot diagnose on his own all

or many rare diseases. The right diagnosis of a rare disease is often the result of team work and real expertise can only for a small group of diseases

- It is of great interest to enhance the cooperation between patient organisations and health professionals. There should be appropriate materials (brochures, movies..) available to inform the experts about rare diseases and the specialised health care situations. The establishment of workshops for physicians together with patient organisations was requested. The development of a specific diagnosis tool usable by experts and non-professional was addressed.
- Learning Partnerships between patient and physician should be established. Particularly for specialists for their disease and council on how to deal with day-to-day practicalities of living with this disease, patient organisations are the strongest and often the only experts
- Quality of training should be improved by cooperation with patient organisations and offering financial support therefore. Patient organisations should work together hereto.

16. How to ensure that existing and validated international guidelines are use at national level to guide diagnosis and treatment of RD?

- The AWMF – the Association of Learned Societies - is offering "Science-based Guidelines for Diagnostics and Therapy" in German on their website. The AWMF is a founding member of the Guidelines International Network. The TMF (Technology and Methods Plattform for interconnected medical research) offers an evidence based guideline database [was beinhaltet dieses Angebot genau?]. The ÄZQ – Medical Centre of Quality – has gathered enormous expertise on the development of treatment guidelines and patient versions of those guidelines for more common diseases. These efforts should be combined in a systematic approach to develop guidelines for rare diseases and foster the knowledge about and application of those guidelines. The future Centres of Expertise should be part of that effort. Patient experience and expertise should be systematically documented.

EUROPLAN RECOMMENDATIONS

R 2.1 The European definition of rare diseases is adopted in order to facilitate transnational cooperation and community level actions (e.g.: collaboration in diagnosis and health care; registry activities).

➔ Fully agreed – one European definition is useful for facilitating cooperation and community actions. All participants expressed the necessity and expectation, that Germany will (continue to) use the European definition also when more legally binding documentation is set up.

R 2.2 The use of a common EU inventory of rare diseases (Orphanet) is promoted in the national health care services and collaboration is carried out to keep it updated.

➔ This should be part of the National Plan.

R 2.3 Coding of rare diseases is promoted, encouraging their traceability in the national health system.

➔ This should be part of the National Plan.

R 2.4 Cross-referencing rare diseases is carried out across the different classification systems in use in the country, ensuring coordination and coherence with European initiatives, such as reference to the Orpha-code.

➔ Cross-referencing is useful and should be provided, however to date it is not in use

R 2.5 Collaboration with the ICD10 revision process is ensured and ICD-11 is adopted as soon as possible.

➔ The ICD-10 review process is underway and experts from Germany are involved. ICD-11 is foreseen to be adopted in Germany.

R 2.6 Healthcare professionals are appropriately trained in recognizing and coding rare diseases.

R 2.7 Initiatives are promoted at national level for the integrated use of administrative, demographic and health care data sources to improve the management of rare diseases.

R 2.8 International, national and regional registries for specific rare diseases or groups of rare diseases are promoted and supported for research and public health purposes, including those held by academic researchers.

R 2.9 Collection and sharing of data from any valid sources, including Centres of Expertise, and their availability for public health purposes is promoted by public health authorities, in compliance with national laws.

R 2.10 Participation of existing national registries in European/International registries is fostered.

R 2.11 Instruments are identified for combining EU and national funding for registries.

Theme 3 - Research on RD

Sub-Themes

1. Mapping of existing research resources, infrastructures and programmes for RDs
2. Needs and priorities for research in the field of RDs
3. Fostering interest and participation of national laboratories and researchers, patients and patient organisations in RD research projects
4. Sustainability of research on RD
5. EU collaboration on research on RD

1. Mapping of existing research resources, infrastructures and programmes for RDs

1. Evaluation of RD Research resources and infrastructures across different disciplines and source of funds, both public and private. Considering whether a combination of private and public support is feasible.

A full overview of the German research efforts in the field of rare diseases cannot be given:

- Most research programs are open for all diseases, the number of grants given for projects relevant to rare diseases is not documented.
- The German contribution to ERA-Net und E-Rare is strong. The scientific society shows a strong interest in international networking.
- Although funds for research will never be enough to deal with the 5.000 to 8.000 rare diseases the general feeling in the conference was that the German Ministry of Research makes a strong serious effort in supporting research for Rare Diseases.

2. Does a specific national RD research programme with dedicated funds exist? Is there a scope for such a programme?

- The German Federal Ministry of Research funds 16 Networks for Rare Diseases. The Volume of research aid for these networks amounts to 7.5 Million per year in total for a further period of 3 years. Each Network may apply for a prolongation for another 3 years. The networks also have a network among them, which will likely be supported with a specially staffed office for coordination and identifying common problems.
- The Federal Ministry of Research considers a Bottom-Up approach as the way for obtaining the best results. Apart from the abovementioned program no particular rare disease calls are envisaged.

3. What is the scope of patient driven research?

- Patient driven research is considered of great importance, a major goal of most patient organisations and done by many with enormous differences in financial means and professional approach.
- Participants agree that for an optimal support by patient organisations qualifying training of the patient representatives and the support of a scientific board for the selection of projects is necessary in order to make a good assessment of the needs for research in a particular field and to identify the most promising projects to achieve results for the patients.
- The contribution of patient organisations to research should be strengthened, also with financial support for the infrastructure of the patient organisations. Often patient organisations are the knot in the web of researchers. A networking effort that is relevant to success and is hardly ever funded.

Specific Areas: Biobanks and Databases

A section of the workshop was devoted solely to **"Patient Registries".** The conclusions of this part are described herein.

Goals of Patient Registries

Patient Registries can fulfill different objects, e.g. gathering of epidemiological correlations and differences in order to research the prevalence, causes and changes over time in the occurrence of diseases. Registries assist in describing the health care situation and to improve it. Analysis of data can demonstrate the quality of health care and allow for comparison between institutions or groups of institutions. Essential is the support to clinical studies. The effectiveness of interventions can be evaluated or hypothesis generated.

Registries embedded in clinical studies constitute a special case. Herewith it is possible to combine an observing and interventional research form. Evidence can be generated on the effectiveness of intervention under clinical conditions as well thereafter during every-day life. By extending the research group beyond the patients that are part of the clinical study the gap between optimal and routine conditions can be closed. The day-to-day effectiveness of the drug can be better evaluated.

Another important goal of patient registries is the evaluation and monitoring of patient security, particularly for those groups who generally do not take part in clinical studies (children, old people, too ill or not ill enough, multi-morbidity, additional medication etc.) As many cases as possible for as long as possible allow for statistical sound evidence on complications and interaction between medication.

Problems and hurdles

- The current spread and quality of registries for the different rare diseases is unclear. Most registries are held by the academic community; it is to be reviewed whether that is the best solution.
- Most registries are merely epidemiological designed.
- Most registries are not used enough.
- There is no common documentation.
- The financing is insufficient.
- Access is limited. Rules are necessary to stipulate access to registered data, ownership of data and who decides on the use of data.
- Registries are very heterogeneous. As a result transparency is unsatisfactory and trust is lacking. As patients fear a misuse of data, a technically sound storage and safe-guarding of anonymity is a prerequisite for trust.
- Data can only be gathered with permission of the patient. The patient data protection implications are not trivial.
- Recruitment of patients for clinical studies for rare diseases is difficult. Gathering sufficient evidence is a real challenge, which could be mitigated by centralized study management.
- High quality registries can only be made with a strong cooperation with the relevant patient organisations. Also the goals of the registry and what would be considered success is to be defined in cooperation with patient organisations.

Measures

- Systematic development of registries.
- Linking of European registries per disease.
- Ensure strong cooperation and information transfer between research and care.
- Obligatory documentation of treatment progress and a registration of such data in clinical registries also.
- Introduce a documentation fee (reimbursement of efforts!).
- Public financing of registries (national and EU).
- Clearer definition of rules and regulation concerning storage of data.
- Define and ensure standards of quality (see existing checklist of TMF) to establish best possible validity and trustworthiness.
- Analysis of data by experts, preferably from centres of expertise.
- Develop a uniform data structure and software platform.

- Establish a register for register and develop a national best practice guideline for registries.
- Acknowledge the importance of patient organisations to motivate and inform patients to contribute to the registry. The registry does not only need their data or material, but also their opinion on registry design, organisational and financial support as well their view on the analysis of the data summarised in registry reports.
- Different ideas are currently in discussion, like a registry for registries and generic software for patient registries for rare diseases. TMF, the German Network for Health Services Research (DNVF, www.dnvf.de), the Institute for Research in Operative Medicine of the University Witten/Herdecke (www.uni-wh.de/ifom) and ACHSE cooperate in the application procedure for funding by the research ministry. Such calls should continue and be part of the national plan.
- Sustainability of registries needs to be ensured.

2. Needs and priorities for research in the field of RD

4. Assessing need and priorities for basic, clinical and translational research, as well as priorities for social research

- There is a strong need for all these forms of research but particularly for translational and social research. Needs differ, however, depending on the disease. Patient organisations can give a strong input on questions to be addressed and prioritising them.
- A major obstacle for research about rare diseases is the strong separation between research and care. The time pressure for clinical work and the lack of reimbursement for documentation, gathering of data etc. relevant for research, hinder research.
- Generally the lack of "protected time", time for researchers to think and develop ideas, is identified as an impediment to successful research.

3. Fostering interest and participation of national laboratories and researchers, patients and patient organisations in RD research projects

5. How to make the link between basic and translation research and Centres of Expertise?

- The 16 research networks funded by the research ministry are good start for a link between research and care. The same doctors that are in those networks are often the specialists for these diseases also in care. A structural approach, in which research by specialist care takers is furthered, is lacking in Germany. Future Centres of Expertise should be given the right framework for research efforts.

6. Promoting interdisciplinary approaches to research

- An interdisciplinary approach is essential. The networks are a good example.

7. Strengthening the exchange among patient organisations

- Cooperation between patient organisations of diseases that are similar or have common issues is a way of dealing with the lack of resources in research and may often lead to better ideas and hypothesis' as it strengthens the scientific exchange.

8. Specific programmes for funding or recruiting young scientists on RD research

This has not been discussed.

4. Sustainability of research on RD

9. How to ensure, through appropriate funding mechanisms, structural and long-term sustainability of research projects and research infrastructures in the field of RDs? In particular in respect to public health and social research, as well as transversal infrastructures.

- It was generally agreed that the clinical constraints of researchers should be addressed. A combination of clinical and research work in respect to a specific disease is in the case of rare diseases by most considered to be important to further the best possible research as well the best possible care. Time constraints and difficulties of reimbursement hamper this combination in practice and make it very unattractive if not plainly impossible for the physicians.

5. EU collaboration on research on RD

10. How to foster and support the participation of national researchers and laboratories, patients and patients organisations in EU-wide projects?

- Networks only work if they are well coordinated. The coordination of networks is often either not arranged or not sufficiently funded.
- Considering the disproportionately strong contribution of German Researches in ERA-Net there obviously is a strong interest in international networking. This should be continually furthered by continuing these programmes and by continuingly raising awareness of the variety of interesting scientific questions and the possibilities of international networking in respect of rare diseases.

EUROPLAN RECOMMENDATIONS

R 3.1 Dedicated national research programs for rare diseases (basic, translational, clinical, public health and social research) are established and supported with dedicated funds, preferably for a long period. Research projects on rare diseases should be made identifiable and traceable within broader national research programs.

➔ Funding for research about rare diseases is necessary, long term is also necessary. Considering the success of bottom-up approaches and the presumption that rare diseases become a considerable amount of funding out of the general research budgets a special research fund for rare diseases has – apart from the necessity of strongly supporting networks for rare diseases – not been advocated. A discussion on the allocation of funds between rare and more common diseases is not necessarily beneficial for rare diseases.

R 3.2 Specific provisions are included in the National Plans or Strategies to promote appropriate collaborations between Centres of Expertise and/or other structures of the health system and health and research authorities in order to improve knowledge on different aspects of rare diseases.

➔ This collaboration is extremely important.

R 3.3 National networks are promoted to foster research on rare diseases. Special attention is given to clinical and translational research in order to facilitate the application of new knowledge into rare disease treatment. Compilation and updating of a directory of teams carrying out research on rare diseases should be endorsed when feasible.

➔ Very important issue that should be addressed.

R 3.4 Proper initiatives are developed to foster participation in cooperative international research initiatives on rare diseases, including the EU framework program and E-RARE. The national funding of these initiatives should be increased considerably.

➔ The EU-Framework program and E-Rare are strongly supported and should receive continued and substantial funding.

R 3.5 Specific technological platforms and infrastructures for rare disease research, including clinical research, are established and supported and the creation of public-private partnership is explored.

➔ Participants were in Agreement to this recommendation. Different ideas are currently in discussion, like a registry for registries and generic software for patient registries for rare diseases. TMF , the German Network for Health Services Research (DNVF, www.dnvf.de) , the Institute for Research in Operative Medicine of the University Witten/Herdecke (www.uni-wh.de/ifom) and ACHSE cooperate in the application procedure for funding by the research ministry. Such calls should continue and be part of the national plan.

R 3.6 Multi-centre national and trans-national studies are promoted, in order to reach a critical mass of patients for clinical trials and to exploit international expertise.

➔ The participants agreed that this is important.

R 3.7 Specific programs are launched for funding and/or recruitment of young scientists on rare diseases research projects.

➔ As it is difficult to get "new blood" in the rare disease community measures in order to prevent the loss of knowledge as well to ensure the levels of care that have been achieved, when doctors retire, are very important. Efforts need to be made to inspire young doctors and arouse their interest in rare diseases. The fact that health care for rare diseases is mostly not sufficiently reimbursed ensures that an interest for rare disease is actively discouraged by clinic directors and others who are responsible for return on investment.

R 3.8 The assessment of already existing drugs in new combinations and in new indications is supported since it may be a cost-effective way to improve treatment for patients with rare diseases.

➔ Research on drugs that are prescribed off-label can improve treatment of rare diseases with less cost than the development of totally new drugs. It is necessary that the results of off-label treatment are better documented. A liberal regime for reimbursement in combination with an obligation for documentation could contribute to better evidence on effectiveness and consequently be a basis for reassessing the off-label-reimbursement.

Theme 4 - Standards of care for RDs - Centres of Expertise (CoE)/ European Reference Networks (ERN)

Sub-Themes

1. Identification of national or regional CoE all through the national territory by 2013
2. Sustainability of CoE
3. Participation in ERN
4. How to shorten the route to diagnosis
5. How to offer suitable care and organise adequate healthcare pathways for RD patients
6. How to ensure in CoE multidisciplinary approaches and integration between medical and social levels
7. How to evaluate CoE

4.1. Orphan Drugs (OD)

8. Future of OD
9. Access of RD patients to orphan drugs Pricing and Reimbursement
10. Compassionate use and temporary approval of orphan drugs. Off label use

Remark: Even though the Rare Disease Task Force has defined the concept of a reference centre (currently referred to as a "centre of expertise") as well as that of European Reference Networks, and Eurordis has developed a Charter on Reference Centres there still is a strong need for a clear definition that is easy to explain and identical in all European countries. Likewise, the German terminology needs to be defined. The workshop concluded that the terms "Kompetenzzentrum" for a European Centre of Expertise and "Fachzentrum" for a national/regional Centre of Expertise may be the most appropriate translations. More importantly, the Workshop on care summarised the main criteria and functions of such Centres of Expertise:

- Multidisciplinary – Interdisciplinary – Case Meetings;
- Strong focus on communication and coordination;
- Systematic national and international networking;
- Contribution to patient registries (for research, documentation of care and epidemiological purposes);
- Participation t
- Contribution to research efforts;
- Appropriate capacities for diagnostic, documentation of disease progression and long term care;

- Quality Management (also outcome), development of guide lines, implementation of standards of care;
- Telemedicine where it improves the standard of care otherwise possible;
- Suitable qualification of specialists and continued education;
- Holistic approach, including the family unit and environment of patient in the care process, for example by offering suitable social counselling.
- Strong cooperation with the patient organisations, representing the diseases that are treated in a particular Centre of Expertise, in particular to aspects of social counselling.
- Facilitation of cross border care.
- Case Management in the process of finding a diagnosis as well as after diagnosis, i.e. during treatment.

1. Identification of national or regional CoE all through the national territory by 2013

1. How to ensure that all patients living with a rare disease have access to a CoE in your country or abroad, and support the creation of CoE where necessary?

- The German health care system offers expertise to many rare diseases. This expertise is, however, not easy to find, not systematically and sufficiently funded and neither officially defined or identified as a Centre of Expertise (as referred to the European context).
- A mapping exercise of existing expertise should be part of a National Plan.
- Also the criteria for Centres of Expertise should be defined and verified by an independent governmental body. Evaluation of structure and process to establish the continued expertise and standard of care should be performed regularly. Part of such an audit should be whether guidelines are adhered to and the patient satisfaction should be assessed.
- The research networks that are established in Germany constitute a good starting point for developing centres of expertise.
- It was stressed in the plenary session that the existing of qualified Centres of Expertise does not suffice. Measures have to be taken, that general practitioners, paediatricians, physicians with other expertise, refer their patients to their colleagues. Accepting your own limitations, accepting that there are unusual cases, for which not every doctor can have an answer, should become normal. Centres of Expertise can only be such if the cases are sent there. Not every doctor should (have the right to) do everything.
- It is generally accepted that expert care for rare diseases will in general not also be close to home. Methods have to be developed for general practitioners to recognize the uncommon soon enough. Also structures have to be developed to ensure day to day care in an acceptable travel distance, while ensuring expert care for diagnosis, establishing a care plan, regular check-up, certain emergencies etc...

- The existing Social Paediatric Centres ("SPZ") were generally considered to offer a high quality of interdisciplinary care, which constitutes a good starting point for how Centres of Expertise could be developed in Germany.

2. How to best apply in your country the criteria identified in the report of the Rare Disease Task Force, which will possibly become part of the EC Cross-Border-Healthcare Directive, art. 15, for designation of CoE

- There was a strong consensus that consistent criteria need to be applied by a public authorisation body rather than allowing a policy of self-designation as a CoE. Preferably, that public body should be on a national rather than on a Länder (regional/federal states)-Level.
- Learned societies and patient organisations are best positioned to define the specific capabilities, resources and processes to be performed by CoEs.

3. In particular, how to make sure that CoE are – as much as possible – expert of the specific RD in both the clinical and the research field?

- Combined care and research projects should be furthered. However, it may be possible to differentiate between CoEs providing clinical care and undertaking basic, pre-clinical and clinical research and those centres providing predominantly clinical care and participating in clinical trials.
- Infrastructure should strengthen research and the possibilities to optimise care, in particular patient registries and biobanks should be systematically funded and administered.
- Clustering diseases will be necessary to develop centres of expertise also for the very or ultra rare diseases.

4. What are the best structures and solutions suitable to be a CoE in your country? Do they depend on the disease (or group of diseases) Are they regional or national?

- Unlike the majority of EU member states, Germany is a Federal country with the "Länder" (federal states) having the main responsibility for organising health-care. However, the participants of the workshop strongly preferred a national over a regional accreditation system for CoEs.
- Both combinations of a group of diseases as well as single diseases – in case the prevalence allows singling out these diseases – are possible structures.
- The authorisation body should certify not only structures but also processes and parameters of patient satisfaction. Likewise, participation in research projects may become criteria for accreditation of CoEs.

- The "market share", i.e. the coverage of patients with a given disease taken by the CoE, may become a useful evaluation parameter.

2. Sustainability of CoE

5. How to ensure, through appropriate funding mechanisms, the long-term sustainability of healthcare infrastructures, in particular CoE?

- Unlike the structures in most of the EU member states, specialised out-patient care in Germany is mainly provided by privately organised specialists rather than by hospitals. However, this particular system does not work well for many rare diseases mandating interdisciplinary care and strong connection with research facilities. Therefore, rare-disease health care in Germany today is frequently provided by hospital-based out-patient clinics which in turn, however, are underfunded because appropriate funding schemes are either lacking or not well designed for these particular structures.
- The extraordinary effort for the treatment of rare diseases and the provision of a CoE should be reimbursed. Sufficient reimbursement could be ensured by fees for coordination, continued education, contribution to registries, documentation and the like. However, the statutory health-care insurance is aware of the potential double-funding of structures and processes. Therefore, an appropriate way of recognising the health-care services and their reimbursement in CoEs must be defined.
- Possible reimbursement schemes could include (1) a premium for successful referral by a general practitioner to a specialist; (2) a lump-sum or general fee for the holistic care of a particular rare disease associated with clearly defined quality criteria or special contracts between Health Care Insurers and selected providers for the care of a given disease or a group of diseases.
- Not one kind of reimbursement should be developed, but a set of tools that could be applied in different situations.
- Particularly interesting could be a model in which the current centres of social paediatric care ("sozialpädiatrische Zentren") according to § 119 Social Code of Law, Book 5). are extended to adult patients. This clause stipulates for a comprehensive care including psychosocial services and interdisciplinary efforts designed around the needs of the patients. Unfortunately, however, it is so far available for paediatric and adolescent patients only.

3. Participation in ERN

6. How to foster the participation of CoE to European Reference Networks?

- CoEs recognized in Germany should be particularly encouraged to participate in European research networks (e.g. those funded within the EU-framework research programs).

- By providing resources demanding strong networking (such as patient-registries or biobanks), European Reference Networks will facilitate participation of national CoEs.

7. How to support the mobility of patients and/or professionals beyond the national borders?

- In general, interest of German rare disease patients in cross-border care is rather low as Germany is already providing excellent, yet difficult to find, services for rare-disease patients. It was agreed that the upcoming directive on cross-border care may be helpful to facilitate mobility of patients also in Germany.

4. How to shorten the route to diagnosis

8. How to support the mobility of expertise and knowledge to facilitate the treatment of patients in their proximity (including mobility of information through ICT)?

- Patients should be given appropriate sources of information allowing them to identify acknowledged CoEs within their vicinity where possible.
- Health-care providers, in particular general practitioners, may become an important source of information if trained to identify and to communicate CoEs appropriate for a given patient.

9. How to map, network and support the laboratories at national level?

- By law, genetic labs have to be acknowledged by a public body. All labs participating in diagnostic services reimbursed by the statutory health-care insurances have to provide evidence of this acknowledgement.

Screening and genetic testing

Has not been discussed.

10. How to organise DNA and samples exchanges and reimbursement at European and international level?

- Has not been discussed.

11. How to support the development of European guidelines on diagnostic tests and population screening?

- Population screening aiming at identification of heterozygotes is prohibited by law in Germany. Post-natal screening programs covering a list of defined diseases are available and fully reimbursed.

12. What mechanisms to develop in order to support common protocols and recommendations such as European reference opinions on diagnostic tools, medical care, education and social care??

- Has not been discussed.

5. How to offer suitable care and organise adequate healthcare pathways for RD patients

13. How to develop a system based on the adoption of clinical pathways for the provision of care for RD patients: provide funding for multidisciplinary consultations, cover Patient and families transportation costs?

See above

14. How to link medical expertise of the specialised centres to local medical, paramedical and social care?

- See above

15. How to establish good cooperation with relevant experts within the country or from abroad when necessary through European reference networks, with the aim to adopt common healthcare pathways based on the best evidence and expertise?

- See above

6. How to ensure in CoE multidisciplinary approaches and integration between medical and social levels

- Social counselling should not be provided by CoE only. A network of social counselling that can provide a continued counselling within the proximity of the place of living should be established.
- The counselling services of hospitals could be a knot of this network. The cooperation with patient organisations is the only way to ensure adequate counselling. If possible, i.e. depending on the strengths of the particular patient organisations the provision of social counselling should be within the responsibility of the patient organisation (obviously on the assumption that specific and sufficient funding is provided here for.)
- If no specific patient organisation is active for a specific disease, e.g. because of the very low prevalence, ACHSE should be involved.

7. How to evaluate CoE?

16. How to envisage a system for the evaluation of CoE? Would it be based on clinical outcomes or patient satisfaction or both?

- All participants agreed that the establishment of CoE should not occur by self appointment.
- Different approaches to CoE should be possible: with a full service approach, i.e. also with a strong emphasis on research on the one hand and units that are more focused on care, but which do still contribute to registries or clinical studies on the other hand.
- Criteria should be established by the learned societies in cooperation with the patient organisations.
- The fulfilment of criteria should be reviewed by an external body;
- CoE should be established by the granting of an official seal by a governmental body; such seal to be regularly reapplied.

8. Future of Orphan Drugs?

17. Number of OD on the market and number of patients treated

- All OD centrally approved by EMA are available and fully reimbursed by the statutory health-care insurances.

18. Obstacles to the availability of OD approved in the EU within the timeframe requested by the regulations (180 days)

- Question 17 and 18 have not been discussed within the German context. Obstacles to availability of OD only occur in cases where physicians fear that the extraordinary expenditure draws attention to their praxis in general or when they are not aware that OD are available. Theoretically all OD admitted in the EU are immediately available in Germany.
- Obstacles in performing clinical studies for orphan drugs should be removed. Many obstacles of a bureaucratic nature could be decreased. Accepted standards in biometry in order to deal with low numbers of subjects (Probanden?) should be established. The fact that common statistical numbers can never be achieved should be a reason for different standards, not for the exclusion of clinical studies.
- A separate list of OD available in Germany was considered to be superfluous as a list of all drugs is available already. There is no value of an extra list. A list of clinical studies recruiting patients with rare-diseases in Germany should be available online. That list can be based on the EUDRACT database
- The EU-legislation on Paediatric-Use-Marketing-Authorisations (PUMA) is unfortunately yet without value because companies developing an extended indication based on PUMA are left without any protection for their investment as current social law provides for the same

reimbursement level as for products without a PUMA extension. Hence, reimbursement schemes must take into account PUMAs. A major obstacle for the development of orphan-drugs can be the enormous investment needed. Public-private-partnerships including public guarantees and/or loans combined with a pricing agreement for the post-marketing-authorisation phase may become useful instruments in fostering clinical development.

- More research on the use of known drug-substances for OD- indications should be furthered. A high potential for cost effective treatment is neglected, because the pharmaceutical industry is more interested in developing products with new drug-substances that come with a more complete IP-protection package.

9. Access of RD Patients to orphan drugs – Pricing and Reimbursement?

19. How to improve and speed up national procedures for pricing and reimbursement of OD?

20. In particular, what mechanisms to put in place to use the "clinical added value of orphan drugs" report developed at the EU Level (EMEA) to base the national decision on pricing and reimbursement in order to minimise delays in access to OD?

21. **How to promote a national policy on conditional pricing and reimbursement, based on the EU Pharma Recommendation "Improving access to orphan drugs"?**

- Question 19 to 21 have not been discussed as such, as the German context is for the lack of fourth hurdle still quite different from most of the European countries. Until December 31, 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 therapeutical group could be subject to maximum reimbursement prices that eventually set the retail-price of the manufacturer. Effective January 1st, 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 drugs 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. .
- Access to OD can be factually limited as for many diseases there are no centres of expertise. The risk of not being treated with the best available medication is higher in such cases.

10. Compassionate use and temporary approval of orphan drugs. Off label use

23. How to foster access to OD through compassionate use?

- The general obligation of pharmaceutical companies to provide compassionate-use-medication without reimbursement of costs as set by the drug act was controversially debated. More use

should be made and more awareness should be developed on the possibilities of authorisation "under exceptional circumstances" or with a "conditional approval"

24. Can drugs be prescribed off-label and reimbursed when the evidence of a benefit for the patients exist?

- Based on jurisprudence of the supreme court on social affairs, reimbursed prescription of off-label-medication is possible when (1) a disease is life threatening or debilitating, (2) sufficient evidence exists that the use of the product is likely to be effective and safe and (3) no labelled alternatives are available in Germany. The problem is, that it is difficult to prove such benefit, especially if a certain ~~is~~ drug is not often prescribed as a result. The financial risk of denied reimbursement is then with the physician prescribing the product. As a consequence, patients may find it very difficult to obtain such prescriptions. Alternatively, the Federal Joint Committee can put a product on an exemption list that grants reimbursement despite of off-label use. As a precondition, an expert-committee has to favour such decision. However, this procedure is time-consuming and applicable only to very few products.
- A suggested solution to the above mentioned problem is liberalising the right to prescribe and a concurring obligation to reimburse such medication while at the same time obliging the prescribing physician to document effects and side effects systematically in a centralised data bank. Hereby a better evidence of the potential benefits and risks of off-label medication can be achieved, while at the same time providing patients with the only available care. If the evidence disproves the assumed positive effect, a certain drug can be put on a negative list.

25. What measures can be studied and put in place to provide treatment other than medicinal products when the evidence of a benefit for the patients exists?

- Has not been addressed during workshop.

EUROPLAN RECOMMENDATIONS

R 4.1 Well defined mechanisms of designation of centres of expertise are established and their quality is assured, efficiency and long term sustainability.

➔ This is very important (see above "identification of national CoE)

R 4.2 Healthcare pathways are defined and adopted, based on best practices and expertise at national and international level.

➔ Workshop agrees to this recommendation as well.

R 4.3 Cross-border healthcare should be promoted, where appropriate. In that case, centres able to provide quality diagnosis and care are identified in neighbouring or other countries, where patients or biological samples can be referred to, and cooperation and networking is promoted.

➔ Cross-border healthcare should be promoted especially for very rare diseases or where particular expertise has been developed in certain countries. For all diseases a strong international network and exchange of knowhow is of utmost importance.

R 4.4 A national directory of Centres of expertise is compiled and made publicly available.

➔ Good health care is only good if it is accessible for patients and known by health-care providers. . The current situation, that there is not an even overview of the few centres of expertise for rare diseases established in accordance with article 116b Social Code of Law, Book 5 is inacceptable and easy to rectify.

R 4.5 Travelling of biological samples, radiologic images, other diagnostic materials, and e-tools for tele-expertise are promoted.

➔ Even though the importance of this recommendation was agreed, the participants of the workshop feared problems with data protection.

R 4.6 Centres of expertise provide proper training to paramedical specialists; paramedical good practices are coordinated, in order to serve the specific rehabilitation needs of rare diseases patients.

➔ The importance of paramedic training was underlined. Difficulties of funding would arise in the current reimbursement system. The health care system should better value the work of therapists other than doctors.

R 4.7 A national framework is ensured on rare diseases screening options and policies.

➔ The current NAMSE-process aims exactly at developing such framework.

R 4.8 Proper performance of newborn screenings prescribed in the country is monitored with appropriate indicators.

➔ This recommendation was supported in the workshop. An extension of the current relatively limited neonatal screening program is necessary, as there are currently more diseases that can be reliably diagnosed (not to many false positives or negatives) and for which early treatment would be beneficial. An international exchange on the effectiveness and regulations of screening should be furthered

R 4.9 Accessibility to genetic counselling is promoted.

➔ Competent genetic counselling is important.

R 4.10 The quality of genetic testing and other diagnostic tests is ensured, including participation in external quality control schemes at national and international level.

➔ This recommendation was supported by the workshop. In actual fact, it is already implemented into German law.

R 4.11 A national inventory of medical laboratories providing testing for rare disease is compiled and made publicly available.

➔ Accepted as well, see above.

R 4.12 The adoption of an ad hoc coding is promoted, when appropriate, to recognise and appropriately resource and reimburse the special rehabilitation treatments necessary for rare diseases.

➔ Not discussed in detail.

Horizontal Themes

Theme 5 - Patient Empowerment and Specialised Services

Sub-Themes

1. Involvement of patients and their representatives in decision-making processes in the field of RDs
2. Support to the activities performed by patient organisations
3. Specialised social services: Respite Care Services; Therapeutic Recreational Programmes; Services aimed at the integration of patients in daily life
4. Help Lines

1. Involvement of patients and their representatives in decision-making processes in the field of RDs

1. How to involve and empower patients, e.g. in the elaboration of national plans, in the provision of information, in the establishment and management of CoE/ERN, in the definition of research policy and other areas such as the establishment and management of registries, clinical trials, therapeutic education programmes, medical training etc. etc.?

- ACHSE and the umbrella organisation for all patient organisations (also for disabilities and more common diseases) BAG SELBSTHILFE are part of NAMSE. ACHSE coordinates NAMSE together with the Federal Ministry of Health and the Federal Ministry of Research. Patient representatives take part in all working groups of NAMSE. The patients are an integrated part of this process.
- The *Patientenbeauftragter* – the Appointee of the Government for the interest of patients – Wolfgang Zöller (Member of Parliament) stated in his opening words of the national conference that he wishes that the Patient Rights Act, for which he is advocating, will be passed including a passage on a right of access to good care for people living with a rare disease.
- Effective patient participation differs depending on the kind of measures or decisions that are to be taken. In certain instances a right to consultation or a right to object suffices, in others consent should be a requirement. Ideally patient organisations are included in the preparation of all important decisions as early as possible.
- Patient should not only be given the right to participate, there should be a real commitment to foster patient participation. Different indicators evaluating the quality of patient participation in the decision making process should be established, monitored and evaluated on a regular basis.

- In particular when "benefit" is to be assessed patients should be heart. Patients know what the consequences of non-treatment are, what kind of treatment they experience as beneficial etc.. They should be part of the evaluation of the opportunity costs etc.
- It is considered important that patient representatives are involved in the development and the operation of patient registries (kind of data gathered, rules and regulations for access, ownership of data, sustainability etc.).

2. How to ensure, through appropriate funding mechanisms, patient representativeness in decision-making-processes relevant to RDs?

- Unfortunately, NAMSE does, apart from travelling expenses, not provide for funding of the efforts of the patient organisations.
- Networking is everything. Patient organisations can only gather knowhow if they can meet each other, talk to experts; meet with sister organisations abroad etc. Funding for travelling expenses is very important. Especially for rare diseases a sustainable funding is necessary, because there are only few people affected by the disease. As a result it is difficult to find enough volunteers and to ensure sufficient donations for the work. To ensure the professionalism needed in the exchange with other players in health care, sufficient funds for adequate training are needed. Finally many services of patient organisations, in particular counselling, cannot be done without staff support. Not only can paid staff contribute capacities not otherwise available to the organisation, the amount of work to be done is often not manageable with volunteer work only.
- The lack of reliability of funding hampers patient organisations in the planning of their activities. The continuity of their work is permanently at risk, even though many of the activities save money for the health care system, in particular counselling and information services.

2. Support to the activities performed by patient organisations

3. How to support activities performed by patient organisations, such as awareness-raising, capacity-building and training, exchange of information and best practices, networking, outreach to very isolated patients?

- Participants agree that in order for patient organisations to further research (patient driven research) qualifying training of the patient representatives is necessary to be able to understand the scientific landscape and to be able to discuss with researchers on equal footing.
- The contribution of patient organisations to research should be strengthened, also with financial support for the infrastructure of the patient organisations. Often patient

organisations are the knot in the web of researchers. A networking effort that is relevant to success and is hardly ever funded.

- Cooperation between patient organisations for establishing registries or furthering research should be supported by strengthening the networking structures of those patient organisations.
- The study performed for the Federal Health Ministry concludes that the expertise of patient organisations is not used and taken seriously enough by other parties. As a very important source of information the patient organisation should be systematically included in all developments.
- Patient organisations should be supported in their efforts to create awareness on rare diseases, particularly with doctors.
- The shared-decision-making patient organisations are striving for should be supported by the system. A change of culture, accepting that doctors have limitations like the rest of us, should be fostered and understood by doctors and patients alike.

4. What mechanisms can be put in place to support patients' empowerment activities and their representativeness in EU-wide instances?

- International exchange is very important for patient organisations of people living with rare diseases. Real Knowhow cannot be found nationally only. EU or national funding for such activities is necessary.

3. Specialised social services: Respite Care Services; Therapeutic Recreational Programmes; Services aimed at the integration of patients in daily life

5. What kind of programmes should be supported or developed? What can be done to improve their availability and accessibility of such services, including public funding?

- Even though it is considered of enormous importance by patient organisations, for lack of time this has not been discussed.

4. Help Lines

6. What kind of programmes should be supported or developed? What can be done to improve their availability, accessibility, quality, visibility of such services? Should/will there be a 116 European Number for this help line in your country? How are the help lines financed? How to ensure long term sustainability?

- ACHSE offers the only help line specifically for people affected by a rare disease (patients and family). With only one counsellor this help line is enormously understaffed. Financing the help line with private donations only is very difficult. With the current means it is impossible to

offer a sufficient and sustainable service. The help line services financed by the public health insurance neither have – from the point of view of ACHSE - any knowhow on rare diseases nor the particular expertise of patient organisations (since they are offered by a consumer organisation). Fortunately, they refer patients to ACHSE. Long term sustainability of the ACHSE help line could – again from an ACHSE point of view - be ensured by also referring funds of the public health insurance or other public funds to ACHSE for this effort.

EUROPLAN RECOMMENDATIONS

R 6.1 Advocacy of patients' needs by patients' associations is recognised as an important element in defining policies on rare diseases; the organisation of a national umbrella organisation that represents the interests of all rare diseases patients is encouraged.

R 6.2 The patients' organisations are involved in decision making processes in the field of rare diseases.

R 6.3 Valid information on rare diseases is produced and made available at national level in a format adapted to the needs of patients and their families.

R 6.4 National information of interest to patients is communicated to EURORDIS for publication in its website.

R 6.5 Specialised social services are supported for people living with a chronically debilitating rare disease and their family carers.

R 6.6 Specialised social services are established to facilitate integration of patients at schools and workplaces.

R 6.7 A directory of centres providing specialised social services, including those offered by patients' associations, is compiled, kept updated and communicated to national, regional and patients' websites and included in the Rapsody network.

R 6.8 Interactive information and support services for patients are promoted (such as help lines, e-tools etc)

R 6.9 Information and education material is developed for specific professional groups dealing with rare diseases patients (e.g. teachers, social workers, etc.).

R 6.10 The activities aiming at patients' empowerment carried out by patients' associations are facilitated.

Theme 6 – Sustainability

EUROPLAN RECOMMENDATIONS

R 7.1 The National Plan or Strategy on rare diseases is supported combining national (regular and ad hoc) and European funds, according to the country health system and decision-making processes.

R 7.2 Possibilities for European funding are exploited for those parts of National Plans or Strategies which are in the scope of the European Social Fund and European Regional Development Fund.

R 7.3 The cooperation with other member states is envisaged when cross-border health care is needed, in order to address the need for sustainability of common European infrastructures, share costs and maximise the efficacy of initiatives.

R 7.4 Participation in the debate on enhanced EU governance is ensured, in order to find agreed and improved mechanisms for the governance of the healthcare, information and research initiatives requiring transnational collaboration.

R 7.5 Agreements for coordinated projects, including long-term sustainability of common infrastructures, are pursued

Theme 7 - Gathering expertise at the EU level

EUROPLAN RECOMMENDATIONS

R 5.1 The use of international global information websites and data repositories for rare diseases is promoted.

R 5.2 Access to knowledge repositories and to expert advice for health professionals is established.

R 5.3 Information on how to establish or join a European reference Network is made available to health professionals.

R 5.4 The curriculum of the medical degree course includes an education package on rare diseases and on the relevant, specific provisions in the healthcare services.

➔ This is considered of enormous importance and is needs to be implemented in Germany as quickly as possible.

R 5.5 Training of medical doctors (general practitioners and specialists), scientists and new healthcare professionals in the field of rare diseases is supported.

➔ A systematic approach to the training in respect of rare diseases is necessary.

R 5.6 Continuing education programmes on rare diseases are made available for health professionals.

➔ Continue education programmes are of utmost importance. A cooperation with patient organisations is desirable.

R 5.7 The exchange and sharing of expertise and knowledge between centres within the country and abroad is promoted.

R 5.8 Collaboration is ensured in the European evaluation of the existing screening programs.

R 5.9 The development and adoption of good practice guidelines for rare diseases is promoted. The guidelines are made publicly available and disseminated as of the reach targeted health professionals.

R 5.10 Dissemination of the information about treatment for rare diseases is ensured in the most effective way, to avoid delays of treatment accessibility.

R 5.11 Participation is ensured in common mechanisms, when available, defining conditions for the off-label use of approved medicinal products for application to rare diseases; for facilitating the use of drugs still under clinical trial; for compassionate provision of orphan drugs.

R 5.12 An inventory of orphan drugs accessible at national level, including reimbursement status, is compiled and made publicly available.

R 5.13 Patients' access to authorised treatment for rare disease, including reimbursement status, is recorded at national and/or EU level.

R 5.14 The list of on-going clinical trials on Orphan Medicinal Products included in the European database for clinical trials on Orphan Medicinal Products (EUDRA) is made public at national level.

R 5.15 All information on centres of expertise, good practice guidelines, medical laboratory activities, clinical trials, registries and availability of drugs, collected at national level, is also published on Orphanet as planned in the Joint Action.

III. Document history

History	**101206 first confidential draft Report German Conference** **101231 second confidential draft Report German Conference** **110103 third confidential draft report German Conference**
Version n°	**Fourth and final version**
Author(s)	**Mirjam Mann (on the basis of German reports of th Rapporteurs – see above)**
Reviewer	**Kathrin Rommel, Andreas Reimann, Lisa Biehl, Christoph Vauth, Elisabeth Watermeier and others**
File name (Final Version)	**110104 Report German National Conference**