2011

FINAL REPORT

- **EUROPLAN WP8**
- **Title:** “Promoting the recommendations for rare diseases national plans and presenting the Commission Communications on Rare Diseases”.
- **Leader:** EURORDIS

EURORDIS
Rare Diseases Europe

EUROPLAN
European Project for Rare Diseases National Plans Development

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1. MAIN RESULTS of the 15 EUROPLAN National Conferences

MAIN RESULTS of the 15 NATIONAL CONFERENCES

- 14 National Conferences in 2010
- 1 National conference in 2011
- 15 participating countries
- National events in 3 additional countries (outside the scope of EUROPLAN)
- Good geographical distribution (Northern and Southern Europe, big and small countries, new and old EU members and one candidate member)
- More than 2000 total participants
- 150 participants per National Conference on average
- 6 EURORDIS Advisors supervising the organisation of 2 or 3 Conferences each
- 7 Themes based on the Council Recommendation
    - Governance
    - Definition, coding and classification
    - Research
    - Standards of care
    - Patient empowerment
    - Sustainability
    - Pooling of expertise
- Variety of national stakeholders attended:
    - 14% health professionals
    - 20% researchers
    - 10% industry
    - 14% national public authorities and politicians
    - 40% patient representatives
- Good media coverage in some Conferences
- Common framework for all Conferences
- Great awareness-raising and momentum-building opportunity to promote National Plans and Strategies for rare diseases in all countries involved.

1.1. Background

The **EUROPLAN National Conferences were designed and organised to promote the Commission Communication on Rare Diseases and the Council Recommendation on an Action in the field of Rare Diseases, as well as to help the rare disease community to take the necessary steps towards outlining high quality National Plans or Strategies on rare diseases (RD) with concrete objectives in each field.**

When the EUROPLAN project was designed, the main concern of the project leader and partners was to support the harmonisation and integration of public health strategies on RD throughout Europe, contributing to reducing inequalities in healthcare services for EU citizens with RD and their families. In

order to achieve this goal, it was felt necessary to provide support to national authorities to develop and implement National Plans and Strategies for rare diseases, once the European Council Recommendation on an action in the field of RDs (2009/C 151/02), at the time still in preparation, would have been finally adopted. With this objective in mind, two essential documents were developed thanks to the project: a Guidance Document on recommendations for the definition and implementation of National Plans and Strategies for rare diseases, and a set of Indicators for monitoring and evaluating the implementation of national actions. Also, a Report on initiatives in the field of rare diseases in European countries was produced by the EUCERD[1] Secretariat in collaboration with EUROPLAN.

In this context, the EUROPLAN National Conferences were conceived to complement these efforts by helping to link national initiatives with a common strategy at European level. By the time the National Conferences were organised (2010-2011), a solid body of common policy guidelines[2] was built and shared everywhere in Europe. In particular, the Council Recommendation had set a desired date (2013) for all EU member countries to adopt National Plans or Strategies.

In addition to the commitment of experienced EUROPLAN partners, who worked together to assess the effectiveness of existing national policies and develop the supporting documents mentioned above, the Conferences were instrumental to gathering all relevant stakeholders at the national level in the field of RD. They encouraged consensus to advance the development or the fine-tuning of National Plans, depending on the situation of the country.

Ultimately, the EUROPLAN Conferences aimed at helping patients with RD to have a better life by promoting or improving national strategies, including those elements which may integrate with the EU policy on rare diseases. In fact, National Plans for RDs are effective instruments to improve life of people affected by RDs.

> 1. *Establish and implement plans or strategies for rare diseases …in order to aim to ensure that patients with rare diseases have access to high-quality care, including diagnostics, treatments, habilitation for those living with the disease and, if possible, effective orphan drugs.*
> (Council Communication (2009/C 151/02))

[1] Aymé S., Rodwell C., eds., "2009 Report on Initiatives and Incentives in the Field of Rare Diseases of the European Union Committee of Experts on Rare Diseases", July 2010. The EUCERD is the European Union Committee of Experts on Rare Diseases, formerly Rare Disease Task Force.

[2] The "*Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions on Rare Diseases: Europe's Challenges"*, COM (2008)679, 11 November 2008, and the "*Council Recommendation of 8 June 2009 on an action in the field of rare diseases" (2009/C 151/02). The final draft of the EUROPLAN Recommendations was available on June 2010.*

1.2. Key facts and figures

The EUROPLAN National Conferences were set to **take place in 2010**. Exceptionally, the Irish Conference, due in December 2010, was postponed to January 2011 because of extremely adverse weather conditions.

They gathered **more than 2000 participants** from a **variety of national stakeholders**. Organisers and members of the Steering Committees performed a remarkable job to gather relevant and numerous representatives of all interests at stake in the country, creating momentum on the event. From a first analysis of the participants who attended the Conferences, it is possible to have an idea of the distribution of stakeholders' groups.

The EUROPLAN Conferences attracted the interest of **healthcare professionals**, as individuals, representatives of hospitals and centres of reference or representatives of medical societies and medical associations (on average, 14% of the participants, with a peak in France, where they were representing 29% of the audience).

Almost 20% of the attendants of the Conferences were **researchers and academics** of different specialties and representatives of research centres, both public, private and foundations, with the highest percentage, 30%, recorded in Hungary.

Industry representatives were on average 10% of the audience, with important differences from country to country (22% in UK and 16% in Ireland, and only 4% in Italy, 5% in Spain and 6% in Germany).

With an average 14% of participants, **public authorities** were also well represented at different levels of government (including the regional level, in some countries like Italy and Spain). This group seemed more present in Southern countries (Spain 22%, Italy 20%). Politicians, notably members of the Parliament or of political parties, were counted with the national authorities.

Patient groups at different levels (individuals, single or multiple disease associations, National Alliances, European Federations or individuals) were of course numerous, with their presence approaching 40% of the audiences on average. Health insurers and their associations were not present in all countries, but had a good representativeness in Germany and the Netherlands.

Finally, members of the **press** attended the Conferences in some countries.

As for their geographical distribution, the 15 National Conferences were quite evenly distributed:

As it can be seen in the picture above, **both Northern and Southern countries were involved, as well as both new and old EU members, and even a candidate member to the EU, Croatia. EUROPLAN Conferences took place in countries of different sizes, from the largest EU member (Germany) to small countries like Denmark or Ireland**. Finally, **all sorts of health systems were represented: from the more centralised ones to those system with a greater degree of decentralisation (Germany, Spain, Italy and UK)**.

The Table below provides an overview of the key facts and figures related to the 15 National Conferences:

DATE	**COUNTRY**	**CITY**	**N° of Partici pants**	**ORGANISER (NA or foundation)**	**ADVISOR**
28-29-30 May	**BULGARIA**	Plovdiv	352	NAPRD National Alliance of People with RD	Dorica Dan
18-19 June	**ROMANIA**	Bucarest	178	RONARD	Dorica Dan

17-18-19 September	**CROATIA**	Dubrovnik	180	Croatian Society for RD	Christel Nourissier
30 September	**FRANCE**	Paris	153	Alliance Maladies Rares	Christel Nourissier
13-14 October	**GERMANY**	Berlin	190	ACHSE	Mirjam Mann
15-16 October	**HUNGARY**	Budapest	138	HUFERDIS	Dorica Dan
22 October	**POLAND**	Krakow	64	Foundation MATIO	Christel Nourissier
5-6 November	**SPAIN**	Burgos	116	FEDER	Simona Bellagambi
11 November	**SWEDEN**	Stockholm	84	Sällsynta diagnoser	Britta Berglund
13-14 November	**ITALY**	Florence	120	UNIAMO	Simona Bellagambi
16 November	**UNITED KINGDOM**	Manchester	86	Genetic Alliance UK - Rare Diseases UK	Avril Daly
18-19-20 November	**NETHERLANDS**	The Hague	80	VSOP	Mirjam Mann
19 November	**DENMARK**	Copenhagen	81	Rare Disorders Denmark	Britta Berglund
26-27 November	**GREECE**	Athens	199	PESPA	Simona Bellagambi
20 January 2011	**IRELAND**	Dublin	169	GRDO	Avril Daly
Total number of participants			**2190**		

The echo of the EUROPLAN National Conferences transcended the country's boundaries, with, for example, eight international visitors coming to Croatia, from five Balkan countries.

Moreover, **on the wake of the National Conferences, national events have been organised based on the approach of EUROPLAN' meetings in countries outside the scope of EUROPLAN Conferences.** This spill-over effect has produced results in Switzerland, where, on February 19th, 2011, 400 people gathered to discuss rare diseases as a public health priority. The conference was organised by the newly created Swiss Alliance ProRaris. The adoption of a National Plan on Rare Diseases is seriously considered, with a Swiss Member of the Parliament who engaged to propose a vote in Parliament on the Plan. A few months earlier (15-16 October 2010), RD stakeholders met in Austria (Mariazell) for a very successful national conference, where the proposal for a National Plan was presented and discussed. The Ministry for Health has already set up a working group in charge of it.

1.3. Methodology

While 10 Conferences were initially set out as project's deliverable, eventually 15 EUROPLAN National Conferences were organised in the framework of the project Work Package 8 (WP8), "*Promoting the recommendations for Rare Diseases national plans and presenting the Commission Communications on Rare Diseases*". WP8 was led by EURORDIS, the European Organisation for Rare Diseases. The National Conferences were conceived with this double mission:

- Presenting the aforementioned Commission Communication and Council Recommendations on RD to national audiences, so to ensure that common policy guidelines be shared everywhere in the EU;
- Promoting the EUROPLAN Recommendations on RD National Plans. The latter are intended as 'guidance' for the development of National Plans or Strategies, implementing the contents of the two main European documents on rare diseases mentioned above, in particular the Council Recommendation. As such, the EUROPLAN Recommendations are meant "to guide national efforts for rare diseases and to make them compatible with a common strategy at European level".

In order to achieve this mission, a methodology has been built up based on the following elements:

- **PATIENT-RUN AND MULTI-STAKEHOLDERS.** The EUROPLAN National Conferences have been organised in close collaboration with the EURORDIS' Council of National Alliances, patient associations at national level: 14 EURORDIS National Alliances and 1 Foundation for RD. Conference had a clear mandate to involve all relevant national stakeholders in the field of RDs. These included patients and their families, representatives of patient organisations and national alliances, public authorities, academics and scientists, healthcare professionals, medical societies, industry, carers and social workers, insurers, etc. This varied participation was reflected in the thematic Workshops of the Conferences and in the membership of the Steering Committees organising the Conferences, as it was made mandatory to have a collegial body taking the main decisions on the national event.
  This methodological choice derived from a clear goal: ***to make sure that all interests at stake in each country were closely involved in the debate that should eventually lead to advance the national policy on RD.***

- **EU AND NATIONAL LEVEL.** In order to face ***the challenge of the transferability of the EU policy recommendations***, it was felt necessary ***to maintain a supranational coordination while ensuring a close touch with the national situations***. This was made possible thanks to EURORDIS national member associations, its 'National Alliances'. In actual fact, EURORDIS, in charge of ensuring the overall coordination, worked with 6 Advisors selected among engaged patient representative active within their National Alliance:
  - Simona Bellagambi, UNIAMO, Italy
  - Britta Berglund, Rare Diseases Sweden, Sweden
  - Avril Daly, GRDO, Ireland
  - Dorica Dan, RONARD, Romania
  - Mirjam Mann, ACHSE, Germany
  - Christel Nourissier, Alliance Maladies Rares, France

Each of them was in turn responsible of supervising the organisation of 2 or 3 National Conferences. They also liaised with the Conference organisers on a regular basis, being their key contacts throughout the entire project; liaised with EURORDIS and among themselves to exchange best practices; supervised the agenda setting; contributed to develop common documents. In brief, the Advisors played an essential intermediary role between the national and the European level.

Both the National Alliances and the Advisors were selected following 'Calls for Expression of Interest', in which EURORDIS asked the candidates to demonstrate their willingness and ability to perform the tasks requested (*see above, Chapter 1.2 Key Facts & Figures, for the names of the Advisors and the National Alliances responsible of the organisation of the EUROPLAN Conferences*).

- **RESULT-ORIENTED**. It was agreed that the Conferences should have aimed at formulating concrete proposals, rather than presenting a description of the status quo. The Conference organisers, therefore, were given a proposed format (*see below*) ***conducive to deliver suggestions to improve the existing country policy on RDs, while analysing the transferability of European guidelines into the national system.*** With no doubt, the Conferences were also an important opportunity to map out the situation in the country, given the invaluable chance of having all stakeholders sitting around the same table. Nevertheless, as it shown in the second part of this report, the Conferences were above all a source of propositions covering all relevant areas of RD policy.

- **COMMON FRAMEWORK FOR ALL CONFERENCES**. The EUROPLAN Conferences proposed a harmonised model of discussion. This was made possible by developing:
    - a common format to which Conference organisers were asked to adhere;
    - common guidelines on the discussion topics and specific questions to be answered during each thematic Workshop;
    - common documents posted on EURORDIS website, EUROPLAN section: http://www.eurordis.org/content/europlan-guidance-national-plans-and-conferences
    - common presentations for each thematic Workshop, based on the Council Recommendation and the specific questions extracted from the EUROPLAN Recommendations.

As for the **common format**, it was based on the following elements:

1. A multistakeholder **Steering Committee** was set up in each country and made responsible for the preparation of the Conference. While a minimum membership of 6 people was demanded, in fact Steering Committees counted up to 19 members (Italy) or 23 (Netherlands, where the already existing 'Madurodam-group' functioned as Steering Committee). Representatives of national authorities, usually the Health Ministry, were instrumental to facilitate the dialogue with government and paved the way to their greater engagement. At least one representative of the National Alliance organising the Conference and in most cases the assigned Advisor were appointed members of the Steering Committee and attended its meetings. Other members of the Steering

Committee where appointed to ensure a balanced representation of all stakeholders, especially healthcare professionals and their societies, academics and researchers, often from Centres of Expertise, ORPHANET national representatives, industry.

In conclusion, the Steering Committee proved to be instrumental not only to the organisation of the Conference, but also to the National Strategy altogether. In the Netherlands, the so-called 'Madurodam Group', which had started the national debate on the RD policy, worked as Steering Committee of the Conference, creating a direct link to the ongoing national debate and the EUROPLAN Conference. In other countries (e.g. Ireland, Croatia), where the RD debate is at its inception, ***the Steering Committee set the basis of a working group which is bound to last beyond the Conference itself***. On the whole, ***the Steering Committee was an important testing ground for stakeholders who learnt to work together, well ahead of the Conference, and sometimes for the first time, even in countries where a policy on RD existed for a while*.**

2. Each National Conference was configured in **Plenary Session** and **Workshops**. During the Plenary Session, the EUROPLAN project and the **key EU documents (Commission Communication and Council Recommendation on RD), as well as the EUROPLAN Recommendations were introduced**. Speakers' interventions in plenary were generally limited to the essential, so to leave as much space/time as possible to the Workshops to discuss and develop in detail the proposals for their respective Themes. The **Workshops** were the real core part of the Conferences. They were set up according to specific Themes linked to the chapters of the Council Recommendation on Rare Diseases[3], with a Workshop for each Theme:

THEMES of Workshops	
MAIN THEMES	Also including:
1. Methodology and Governance of a NP	
2. Definition, codification and inventorying of RD	**Information and training**
3. Research on RD	
4. Standards of care for RDs - Centres of Expertise / European Reference Networks	**Orphan Drugs and Provision of Treatment**
5. Patient Empowerment	
HORIZONTAL THEMES	
6. Sustainability	
7. Gathering expertise at the European level	

[3] COUNCIL RECOMMENDATION of 8 June 2009 on an action in the field of rare diseases (2009/C 151/02)

Two Themes of the Council Recommendation, considered **"horizontal",** were addressed within the different Workshops from 1 to 5, even though organisers were left free to choose to set up separate Workshops: **"Sustainability"** and **"Gathering expertise at the European level"**. The two areas of "**Information and training"** and **"Orphan Drugs",** which were felt requiring a dedicated reflection, although not corresponding to a specific chapter of the Council Recommendation, were in some countries dealt with in separate Workshops, while in the remaining ones they were covered under Workshops 2 and 4, respectively.

Despite the common format, organisers were left a certain degree of flexibility to adapt the layout of the Conferences to the most pressing needs of the RD community in their respective countries. The Workshops' choice made in each country is described at the beginning of each of the Final Reports of the 15 National Conferences: http://www.eurordis.org/content/europlan-guidance-national-plans-and-conferences#EUROPLAN National Conference Final Reports

For each Theme, a number of Sub-themes were identified, and for each Sub-Theme a list of questions was suggested to assist organisers and Chairs in running the Workshop in line with the Council Recommendation/ EUROPLAN Recommendations. These questions, in fact, were formulated to a large extent using the 'EUROPLAN Recommendations'[4], the document providing practical guidelines on how to develop National Plans or Strategies on RD.

Covering the listed Themes and Sub-themes was made mandatory, as they constituted the common outline required in all EUROPLAN National Conferences. The questions were non mandatory guidelines, but highly recommended. For a full overview of Themes, Sub-themes and questions: http://download.eurordis.org/europlan/3_EURORDIS_Guidance_Documents_for_the_National_Conference/01_Content_Outline_of_EUROPLAN_National_Conferences.pdf.

3. Workshops were moderated by **Chairs**, sometimes supported by **Rapporteurs**, appointed by the Steering Committee to ensure that the conclusions of the Workshops were drawn and correctly reported. Chairs and Rapporteurs had a pivotal role and were carefully selected, often among experienced and technically prepared patients. Ahead of the Conference, Chairs and Rapporteurs prepared the discussion with the support of the PowerPoint presentations (http://www.eurordis.org/content/europlan-guidance-national-plans-and-conferences#Presentations for Working Group Chairs), based on the Sub-Themes and the guideline questions identified for each Theme. The conclusions of the Workshop discussions were eventually presented to the plenary by the Rapporteurs.
4. A **Final Report** in English was produced by each Conference organiser, based on a common template, which in turn mirrored the common outline of the Conferences. The Final Reports, as a result, largely reflect the outcomes of the discussions following the Themes and the Sub-themes of the Conferences' Workshops. All Reports are posted here: http://www.eurordis.org/content/europlan-guidance-national-plans-and-conferences#EUROPLAN National Conference Final Reports

[4] The EUROPLAN Recommendations, when the content of the Conferences were developed, were not finalised. Therefore the Workshop questions were based on a provisional draft, which was further modified. Therefore, some discrepancies with the final draft of the EUROPLAN Recommendations may be found, although they concern the structure rather than the content itself.

To conclude, the proposed common format allowed to:

- ***Set up a harmonised model of discussion***
- ***Tackle the same issues***
- ***Strengthen the unity of RDs' Community***
- ***Link up the supranational (EU) level with the national debate.***

1.4. Key messages about the EUROPLAN National Conferences

- ***The EUROPLAN Conferences introduced two essential policy reference texts into the national debate: the Commission Communication and the Council Recommendation on Rare Diseases.***

Participants familiarised with their content via the preparatory work to the Conference, the Workshop presentations, the discussion in Workshops and in plenary. This helped them to realise that a wider, European framework is being shaped which is having an impact on the advancement of the national policy on RD. While the Conferences maintained an undoubtedly national perspective, the European documents and, in particular, the consciousness of being part of a European, "global" experience proved to be instrumental in producing momentum around the debate and in raising interest of national stakeholders.

The Conferences, therefore, played an important role to let the national RD communities understand that: 1. an underlying EU strategy exists, which is supported by those two key documents and strengthened by the EUROPLAN Recommendations; and 2. national efforts are "embedded" into a more comprehensive and long-term approach which integrates the EU and the national level.

- ***The National Conferences largely "validated the EUROPLAN's tremendous work in setting the theoretical ground"[5] for the Conferences themselves.***

Whether or not the climate for development of a National Plan was set prior to the National Conferences, the latter raised great interest of patients and their families, local patient organisations, medical professionals. Overall, the EUROPLAN initiative was seen by all stakeholders as an important and successful step towards the establishment of a National Strategy for Rare Diseases in their countries by 2013.

National and regional authorities were also involved, although sometimes with greater difficulty, they became active partners of the organisation of the Conferences (via the Steering Committee) and engaged in the debate. The Workshop-based structure of the Conferences and the guideline questions helped to permeate the national debate with the specific indications of the EU Council Recommendation and of the EUROPLAN guidelines, as well as to tackle the main themes of the RD policy one by one and in great detail.

As a result, as for their ***transferability of the EUROPLAN Recommendations*** it can be concluded that they have been ***integrated into the debate and the language of stakeholders participating to the Conference,*** although sometimes referred to as "the EUROPLAN questions" (as they were presented in each Workshop as guideline questions for the debate, as explained above in *1.3 Methodology*).

[5] Final Report of the Croatian Conference.

Altogether, the EUROPLAN Recommendations were endorsed and in many cases complemented by the national audiences. **These additional remarks and proposals are collected in Part 2 of this Report, where all the EUROPLAN Recommendations are listed and commented**.

- ***There is a great variability among and within countries about the type of services provided to rare disease patients and the accessibility to these services***.

As highlighted in the Guidance document of the EUROPLAN Recommendations, this is due to the fact that in some countries the process of introducing measures dedicated to rare diseases (RD) started years ago, whereas in others it only started very recently or has not yet started. This provides a diversified landscape in terms of how patients with rare diseases can be diagnosed and followed, with great inequalities across Europe.

It should be added, however, that the different welfare traditions and the different national health systems also led or will lead to the adoption of different measures in the field of RDs. This must be added to the different governance solutions existing in the EU Member States (decentralised/ centralised systems) and to the different organisational implications deriving from the country being of small, medium or large size.

In order to reflect this wide diversification of national situations, the EUROPLAN Conferences were modulated to propose a common format, while at the same time leaving a certain degree of flexibility to the organisers to respond to the most pressing questions arising in their society. This is why –as a way of example- in Germany it was felt important to organise an entire Workshop on "Monitoring of the National Plan". The German Conference in fact was timely organised at the early stages of the nation-wide effort to outline the first Plan and the need for a monitoring system was identified since the beginning of the process. In Romania, the debate on Standards of Care focused particularly on screening policies, which are insufficiently responding to the national needs, according to stakeholders. In the Netherlands, it was necessary to organise a Workshop on early diagnosis, a hot topic in the country.

- ***EUROPLAN Conferences provided an invaluable opportunity to have the national stakeholders sitting around the same table.***

Key national stakeholders worked together, discussed and sat around the same table to tackle the main and outstanding issues, and even managed to find a common ground and compromise positions on controversial issues. The result-oriented approach and the discussion in thematic Workshops compelled stakeholders to deal with the specific topics of the RD policy and of the European guideline documents. The involvement of national authorities allowed patients, scientific, medical and industry representatives, who have often been working closely on the rare disease agenda for a long time, to engage with relevant state agencies in a coordinated and productive way. Altogether, the Conferences and their preparation proved to be an extremely useful exercise to listen to other points of view beyond each group's specific standpoints.

- ***The whole experience of EUROPLAN proved to be an outstanding awareness-raising exercise in the field of rare diseases at the national level and created momentum on Rare Disease National Plans in Europe.***

Since the adoption of the key European policy documents in this sector, the EUROPLAN Conferences were, together with the patient-led initiative "Rare Disease Day", one of the most remarkable cross-country awareness raising opportunities in Europe. National Conferences helped to create a grassroots movement demanding National Plans for RD. Even in France, the only country as far as discussing the Second Plan, the EUROPLAN Conference in September last year was a timely event, since the announcement of the Second Plan was delayed until 2011.

Efforts have been made in all countries to ensure a significant media outreach, hence to raise awareness with the public at large.

The awareness-raising experience has been confirmed by the attendance in some cases of participants from other countries (notably, eight Balkan countries' participants attended the Croatian Conference) and the requests from countries who did not organise a EUROPLAN Conference to have one organised in their country as well (Slovakia, Austria, Estonia, for example).

- ***Momentum should not be lost: the results of the EUROPLAN Conference should converge into the work carried out in the country and serve as a "roadmap" to develop/implement the NP.***

The organisation of the EUROPLAN Conferences demanded important efforts to involve as many national stakeholders as possible. The Conferences also helped to make theoretical progress in all key issues related to RD. These efforts went as far as the organisation of a public consultation in Italy, and the creation of a virtual office where participants to Workshops could elaborate the discussion documents ahead of the Conference.

Such endeavours and outcomes should not be wasted, but should constitute the starting point for the next phase of work at the national level, whatever that level may be in each country. Mechanisms should be designed that ensure the continuation of the debate which was initiated or moved forward thanks to the EUROPLAN Conferences. "We need to consolidate what has been created, which is strong", pointed out Antoni Montserrat, from the European Commission.

- ***Finally, the WP8 National Conferences proved instrumental to achieve the expected outputs of the EUROPLAN project:***
  - "to stimulate a discussion and reach a consensus on the importance of national plans for structuring all relevant actions in the field of rare diseases;
  - to promote the development of National Plans or Strategies for rare diseases within EU Member States;
  - to provide instruments to support countries in designing National Plans or Strategies for rare diseases accordingly to the Commission Communication on Rare Diseases and Council Recommendation on an Action in the field of Rare Diseases" (www.europlanproject.eu).

"***EUROPLAN is more than a project. The Conference are in fact a practical instrument to support countries in designing their National Plans for Rare Diseases***" (Dr. Domenica Taruscio, EUROPLAN project leader, Head of the Italian Centre for Rare Diseases, Istituto Superiore di Sanità, ISS)

1.5. Key outcome messages by area

Note: The following key messages result from the discussion of the Workshops of the National Conferences. However, for the purpose of this Report, in the following section they are presented following the structure of the EUROPLAN Recommendations, which in the final version have a slightly different structure, although covering basically the same topics.

Area 1. Methodology and Governance

- ***It is essential to concentrate policy actions on RDs around a Plan or a Strategy at national level.*** This is a recurring and consistent message throughout all National Conferences: there is an urgent need to improve the living conditions of RD patients by developing a comprehensive legislative framework, as a necessity to restore basic human rights recognition and protection for the RD patients and make room for progress. "Our country is wealthy enough to be able to take care of the most vulnerable", said Ivo Josipovič, President of the Republic of Croatia, intervening at the EUROPLAN Conference in his country.

  The findings of the Conferences confirmed what already highlighted in the EUROPLAN Recommendations, "*EU member states have in place genetic services and health policies for disability and for the medical and social need of children. Patients with rare diseases may have in some cases the characteristics (e.g. severity, clinical complexity) to benefit from the provisions by these services and policies*". Nevertheless, "*the lack of initiatives and health policies specifically targeted at rare diseases result in delayed diagnosis and difficult access to treatment and care. This leads to additional physical, psychological and intellectual impairment, lack of prevention and inadequate social services or even harmful treatment*".

  NPs for RD will serve as the basis for intensified efforts on behalf of citizens suffering from rare disorders, who should have the same rights and access to treatment and social support as everyone else. A legislative framework is the only way to give RD patients their voices back as equal citizens in their own country.

  In conclusion, this message echoes the European guidelines, which are thoroughly supported, and could be condensed in a key sentence of the Impact Assessment Working Staff Document accompanying the Council Recommendation document: '***within the member states, there is fragmentation of the limited resources available for rare diseases, thus it is essential to have a specific plan to concentrate and make efficient use of these resources'*** (SEC(2008) 2713 final, 11.11.2008 - http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=SEC:2008:2713:FIN:EN:DOC).

  To be successful, National Plans or Strategies are to be based on the following common principles across the EU.

- ***Integration of the measures of the NP into the national health system is crucial, as rare disease patients need to be included in the health and social system planning.*** "There are good practices, but they are isolated. We need a National Plan to streamline policy and create a common structure", said Simona Bellagambi, EURORDIS Advisor and representative of the Italian National Alliance UNIAMO. This concept is particularly important in countries where the national health system globally covers all citizens in need of healthcare. In UK, for instance, the idea itself of a NP was put into questions by a minority of participants because conflicting with a healthcare system comprehensive in its principles. However, it emerged that different approaches necessary for RDs (e.g. care management, combining care data with research data, multidisciplinary approaches, etc.), may be beneficial for people living with more common diseases as well.

- ***Mapping existing resources is a process necessary virtually in all countries. Situation analyses have been carried or planned in almost all countries. In some cases, the EUROPLAN C***onference constituted the first opportunity to globally consider the national RD policy. In addition to the EUROPLAN Recommendation R 1.4 (carrying out national situation analyses), a useful proposal came out of the Conferences whereby this exercise could be demanded to a Working Group to be set up within the mechanisms or coordinating function (see below, next message) responsible to draw up the National Plan.

- ***Drawing up a national plan should be an inclusive process***. The EUROPLAN Recommendation calling for the establishment of a mechanism responsible for the development and the implementation of the NP is fully supported. All stakeholders must commit and be given the chance to provide inputs. It should work with the ambition to leverage all the resources existing in the society.

  In addition, most Conferences insisted on the role of patients. The national coordinating function must work starting from the patients' needs with a lifelong perspective. Patients should be involved in the management, their role should be institutionalised, hence training, coverage of their expenses or other financial support should be considered.

- ***Work on a national plan should transcend sectors****.* National Plans must be ***comprehensive***. They should not only lay out healthcare-related provisions, but they should leverage and integrate resources available more generally in the welfare system (education and labour market related measures, for example). Ultimately, National Plans should aim to improve not only health conditions, but also the quality of life of patients and their families.

- ***A Plan or Strategy on RDs cannot be functioning without resources attached to it****,* even though coordination of funding is an issue because different actions under the plan depend on different administration departments. ***Sustaining the Rare Disease Strategy will be very important, particularly in terms of embedding the strategy into everyday healthcare services.*** It is important to set out the requirements for services provided based on the needs of patients and not dictated by current rationing of resources in the health services, which is a recurring concern throughout

Europe. Also, it is anecdotal evidence that patients with rare diseases take up a significant proportion of hospital beds and money. Developing, implementing and sustaining a rare disease strategy will help the national healthcare system to deal with these patients far more appropriately and cost effectively. "By diagnosing patients earlier and having care pathways and channels for them to be supported, the Rare Disease Strategy is anticipated to be self sufficient" (UK Final Report).

Moreover, RD sustainability needs to be taken into consideration not only from an economic but also from a social point of view. "As for the rare disease sustainability, the new horizon for the near future shall be closely connected to the creation of a social value. It is necessary to plan, project, implement, monitor and assess policies that permit a clear definition of tasks, assessment criteria and consequent responsibilities. Focusing the attention on such element means acknowledging the global needs of rare disease patients and developing an integrated approach that may guarantee an added value both for the individual and the society"[6].

- ***A monitoring system must be integrated into the Plan with a suitable representation of qualified patients***. The National Conferences emphasised the importance of monitoring the Plan. Conferences' organisers decided on their own initiative to 1. use the EUROPLAN Indicators as an instrument to do a reality check of the country's current situation (e.g. Poland, Greece and Bulgaria); 2. set up a full Workshop dedicated to Monitoring the forthcoming Plan (Germany).

  An effective, high-quality NP should set up indicators to measure its success and a methodologically sound system for monitoring the measures in the Plan itself. It is especially important that process indicators are defined with focus on patient interests, and that in the monitoring phase the regular and strong contribution of patient representatives is ensured, together with the greatest transparency of methods and results. Qualifying patient representatives who are members of this WG is necessary to help patient organisations to provide for a continued high quality patient inputs into the monitoring process.

  A Monitoring Working Group should be established that defines the national process indicators, using as a reference the EUROPLAN Indicators; monitors on a regular basis the performance of the actions envisaged in the Plan on the basis of the Indicators; holds regular meetings; and is composed of a sufficient number of patient representatives.

Area 2. Adequate definition, coding and inventorying of rare diseases

- ***The EU definition on RDs is supported.*** It is generally agreed that one European definition is useful for facilitating cooperation and community actions. Conferences' participants broadly expressed the necessity and expectation to (continue to) use the European definition, especially in view of laying down legally binding legislation, as required by European policy documents. Nevertheless, voices of

[6] Final Report of the Italian Conference, page 22. A study was outsourced by the Italian Natioal Alliance UNIAMO to

disagreement have been recorded, in Denmark and Sweden, in particular, and in the Netherlands to a certain extent.

- The ***swift adoption of ICD-11 classification system*** is unanimously supported in all countries when ready (2014), because of the specific arrangements for rare diseases envisaged therein and unfortunately lacking in ICD-10. While waiting for the release of the ICD11, ***it is suggested to introduce existing coding systems such as the ICD10 or the Orphanet code, possibly with cross-referring across systems*** to account for and overcome the respective shortcomings of the two different systems.

  An early introduction of a RD-oriented coding system is necessary not only for inventorying purposes, but also to raise greater awareness and knowledge on RDs with healthcare professionals.

- ***Day-to-day registration of rare diseases should be organised in such a way that the workflow, as far as possible, is integrated into existing administrative systems,*** possibly by laying down the legal framework necessary, defining competences and establishing the coordination mechanisms among public institutions, administrations and/or private centres. Coordination purposes may be better achieved by creating a (nation-wide) epidemiological portal defining a minimum data set for the existing databases and registries and supporting the interoperability of their content (see, as an example, the 2nd French NP).

- ***Registries sustainability must be achieved by optimising resources and reducing fragmentation and overlapping.*** In each country, this should be the preliminary step, before developing or advancing any policy actions on registries. Focus should be on a better use and better information on existing knowledge and existing information sources. Government resources are generally considered indispensable by all Conferences' participants to sustain the functioning of RD registries. National quality standards, integrity issues, privacy requirements and networking efforts with other (EU) countries were demanded by many Conferences. Specific proposals for the sustainability of registries included the preferential creation of registries which fulfil multiple purposes (from epidemiological studies to the feeding into clinical trials) and are supported by a variety of stakeholders. Sustainable funding at EU level was also considered essential.

Area 3. Research on rare diseases

- ***RDs must be a priority in medical research in the country and* ad hoc *national research measures should be dedicated to RDs.*** This call for the creation of a specific programme for RD research emerged from all Conferences but the German one, and it was supported in countries with either a tradition of non-thematic approach to research or countries where the absence of dedicated RD funds results rather from limited resources, lack of funds or lack of political willingness.

A body should be created at national level which steers and advises on RD research; develops public private partnerships with industry and associations; create close links with centres of expertise; and acts as a one-stop shop for all information on RD research and potential incubator for enterprises.

- ***RD research programmes must be supported by adequate public funds***, even though public-private partnerships were not excluded. Dedicated research programmes for rare diseases would help to streamline scarce and scattered resources.

- National programmes should especially encourage an approach to RD research which is ***multidisciplinary*** (with more professionals involved, from different scientific backgrounds) and ***covers all research areas, but chiefly focus on translational research.*** However, ***basic research*** needs to be reinforced for many diseases (or groups of diseases) for which it is scarce or inexistent, and its outcomes need to be made available.

- ***Socio-economic research (i.e. research on quality of life, living conditions, etc.) is extremely important and should become a national priority***, not only for public health planning, but also for provision of services which help to provide an answer to the needs of patients in their daily life and empower them. This message resonated strongly in very many EUROPLAN Conferences (Italy, Denmark, Sweden, Romania, France, Spain, Germany...).

- ***Qualified patients must become fully-fledged research partners.*** Patients association should take and should be recognised a more proactive role as research partners. For an optimal support by patient organisations, qualifying training of patient representatives and financial support to patient representatives should be ensured. In the case of rare diseases with genetic risk of recurrence, the family should be involved. Also, family doctors must be trained in the field of rare diseases (*see further in Area 5*).

- ***Centres of Expertise must play a pivotal role in closing the gap between research and care***. Centres of Expertise are crucial for researchers and patients: good healthcare infrastructures, where patients meet, provide significant possibilities to research. Appropriate legal and financial frameworks should support this role of Centres of Expertise. For the Centres of Expertise to play this role, it is important to establish mechanisms allowing a tight exchange of outcomes and needs between the two expertises in order to speed up the translation.

  At the Centre level, clinical and basic science could be connected with social and political sciences in order to optimise the provision of patient care and of those services which go beyond healthcare.

- ***The creation of quality patient registries should be a primary objective and a basic requirement to develop RD research.*** Quality registers for rare diagnoses are needed: structure needs to be clarified, as well as long-term funding. Clearer definitions of rules on the storage of data, the definition of quality standards to ensure trustworthiness, the development of uniform data structure and software platforms are required.

- ***Multi-centre national and international studies are an absolute necessity for the organisation of clinical trials*** to address the limited number of patients and the scarcity of expertise. This Recommendation of EUROPLAN is fully supported, with the addition that it is essential to promote clinical and preclinical testing in cooperation with the pharmaceutical industry.

Area 4. Centres of Expertise and European Reference Networks for Rare Diseases

- Prior to any planning on CoE, ***mapping out CoE (Centres of Expertise) in a Directory is a necessary exercise, which should acknowledge the different role and competences of CoEs and Centres (e.g. Centres of Reference), providing care at local level***. This is to recognise that in basically all countries expertise on rare diseases does exist. It is important to underline the existence of different kinds of Centres in order to set up the national network of care, which are complementary and not subordinated to each other. This expertise is, however, not always easy to find, not systematically and sufficiently funded and neither officially defined or identified as a Centre of Expertise hence not accessible to patients.

- ***The EUROPLAN National Conferences called uniformly for common quality standards for the designation and the accreditation of CoE***. The Rare Disease Task Force recommendations on CoE (2006) were evoked, as well as the EURORDIS Declaration (2008). Amongst the criteria suggested at the Conferences, recurring ones are:
    - multidisciplinarity;
    - training and education of medical and paramedical specialists; specialised information for both professionals and patients/families;
    - transition from paediatric to adult age;
    - contribution to patient registries (or management of registries);
    - facilitation of research activities;
    - validation of performance based on clinical results but also on patient satisfaction;
    - participation to the Centre to European Reference Networks and other forms of international exposure and projects, including EC-funded Networks of Excellence.

- ***Proximity of care is a recurring theme with answers modulated according to the size of the country and the healthcare system existing therein.*** The attribution of competences between the more specialist centre (often far from the patient's domicile) and the local level of care, is debated everywhere.

  In ***smaller countries***, where the establishment of CoE for all diseases would be too complex and expensive, networks of medical experts could be established dealing with RDs, while promoting cross-border cooperation at the same time. All-disease centres are not the most popular solution**.**

  In ***decentralised systems or in larger countries***, systems of 'vertical referrals' (local/regional/national) are often in place or recommended. From the regional/national centres or hospital, patients are referred to central/national CoEs where diagnostic test are performed,

specialised treatment is offered, whereas the daily care is left with the centres in the proximity of the place of living. Sometimes (e.g. the French Competence Centres) intermediary levels are introduced e.g. hospitals able to ensure some of the main tasks of a CoE. Referral to a CoE in another EU country could be the ultimate step of the vertical referral system, when the necessary expertise is not found in the country of origin.

Particularly in bigger countries, the creation of ***networks of CoEs*** is also supported, which reflects the needs to cover the largest possible number of diseases and share scattered information and expertise throughout the countries. A system based on networks of CoEs also helps to optimise resources by reducing redundancies or filling gaps.

Finally, in response to the need for proximity of care, it is suggested that ***information platforms, case managers or tools such as telemedicine, protocols and guidelines, able to functionally connect the CoE with the other structures involved in the continuity of patients' care, be developed***. This coordination structures should coordinate day-to-day care within an acceptable travel distance and expert care (diagnosis, establishing a care plan, regular check-up, certain emergencies, etc.) provided in CoE.

- ***Integration between medical and social levels must be strengthened further, with a necessary reinforcement of the social level*.** Social counselling and information about available social services should be provided at the CoE. Social support should be ensured as much as possible in the proximity of the place of living. The involvement of patient organisations in social counselling is essential and they should be systematically involved.

  ***Services acknowledged as fundamental for Centres of Expertise to provide should be recognised and properly reimbursed, such as complex consultations, coordination of multidisciplinary care*.** A promising example will be the allocation in France, under the Second NP, of special funding for multidisciplinary consultations, and also for activities performed by the CoE, recognised as "missions of general interest". Those activities, such as clinical research, second opinions, production of guidelines for diagnosis and care, in-depth clinical and biological investigations, coordination of international networks, etc, are currently underperformed due to the lack of reimbursement, human resources or time.

  Rehabilitation and social aspects should be considered in the CoE. In some countries there is a distinction between social and medical assistance, but both are important in the rehabilitation process. Rehabilitation is important because develops compensatory mechanisms for patients. The patient's rehabilitation depends on multidisciplinary teamwork. Untreated or inadequately treated symptoms can reduce the quality of life (e.g. problem dressing in Epidermolysis bullosa, special diets).

- ***Healthcare pathways are defined and adopted, based on best practices and expertise at national and international level***. This EUROPLAN Recommendation is entirely supported, with the addition of the proposal for the simplification and acceleration of procedures for the production of protocols for diagnosis and care.

- ***"Case managers" should dedicate their attention to individual cases and follow them all along the healthcare pathway including the transition from the paediatric to adult age*.** These would be coordinators and/or mediators who assist patients facing complex situations from a medical, social and/or administrative point of view. Their role would be helping to secure a coordinated and coherent coverage by available medical and social services, providing also assistance to get patients acquainted with their rights and get them through the administrative hurdles. Such initiatives are aimed to fulfil the urging needs of patients and families in their daily lives, which is often the most difficult part of living with a rare disease.

- ***Mechanisms should be found to recognise and reimburse the interventions of paramedical and other specialist professionals involved in the care of RD patients*.** Taking charge of rare pathologies implies sometimes the involvement of health professionals whose outclinic acts are not covered by the sickness insurance. Such is the case, for example, with dieticians, psychologists, physiotherapists, etc. In order to better value the work of these professional specialties, their interventions should be integrated into the reimbursement schemes, provided that they are prescribed by the CoE. Procedures for reimbursement should be accelerated and simplified.

- ***Promoting the participation of CoEs in European Reference Networks (ERN) should be integrated in the NP and become a quality criterion of the performance of each CoE.*** This was a recurring message of the National Conferences, to the extent that in many cases it was specified that the participation to European-level networks is the only way forward to assure sustainable progress in the RD field. In order to attract CoEs, ERN should provide resources, such as biobanks or registries, which demand strong networking. It was also underlined, however, how time-consuming (and resource consuming) are the international networking activities. European funding should be considered to finance them.

- While the mobility of expertise is a primary objective, and strong international network exchanges of know-how are of the utmost importance for all diseases, ***cross-border healthcare should be promoted***, especially for very rare diseases, for any situation in which there is no sufficient expertise in the country or whether particular expertise has been developed in certain countries. **Mobility of patients appears a concern everywhere, because existing resources cannot cover all RDs, and principally in small countries**. With the new EU Directive on cross-border healthcare under way to adoption, RD patients, healthcare professionals and national health authorities will have to explore the new rights and opportunities.

- ***Screening policies must be supported by solid legal frameworks and by reliable implementation and evaluation policies.*** The case of Romania, where a dedicated session of the Workshop focused on screening, showed how in actual fact the lack of resources such as appropriate screening centres, or the lack of consistent application of the policy, create important gaps in detection of RDs and

delays/mistakes in diagnosis. Screening policies should be therefore accompanied by evaluation procedures to assess the quality and performance of the programmes.

- ***Current neonatal screening programmes should be extended, with the help of international exchanges on the effectiveness and regulations***. This recommendation stemmed from some of the National Conferences where the issue was debated. Outcomes of the EC-funded project on neonatal screening of RD in Europe, which aims at issuing recommendations for good practices, is awaited.

Area 5. Gathering expertise at the European level

(This Area of the EUROPLAN Recommendations include, in particular Information and Training on rare diseases and Orphan Drugs)

- ***Activities to promote information and increase awareness on rare diseases with the public at large must be boosted.*** Access to both national and international information websites is widely promoted and their financial support encouraged. Also, national awareness raising initiatives are urged in many countries which aim to increase knowledge and raise awareness among the general public on RDs and on the existence of sources of information, which are crucial for patients and families.

- ***Information sources for patients and professionals should be updated and validated to ensure a consistent quality level***. Mechanisms of control and evaluation of the information provided should be set up.

- ***In order to make healthcare professionals acquainted with rare diseases, training of professional doctors should start during the medical degree course and continue during their careers, with different degrees of specialisation.***

  Firstly, it is considered hugely important by basically all Conferences that an education package on rare disease be introduced in medical and paramedical degree courses. In order to facilitate the task, innovative approaches may be found, such as virtual trainings or channels.

  In the course of their careers, trainings of professionals should be systematically organised. Specifically targeted trainings should be provided, with different degrees of knowledge, depending on whether addressed to specialists or to general practitioners and paediatricians (for the latter, general training, broadly encompassing all disease areas). This general type of training for family doctors is necessary to create awareness on possible rare diagnoses and to prepare them to deal on a day-to-day basis with rare patients.

  Postgraduate trainings should bring a more in-depth knowledge of RDs, with an additional component of management, so to move "from the knowledge of the disease to the knowledge of the patient"[7].

[7] Final Report of the Spanish Conference.

Training opportunities should be equally envisaged for paramedical professionals within the Centres of Expertise.

- ***Guidelines should be developed to align actions performed at different levels of care and by different healthcare professionals, with specific information for patients, families, caregivers and teachers.*** A network coordinated by the centre of expertise, gathering available scientific evidence at national and international level, should be in charge of defining principles of best practice in clinical and laboratory diagnosis, as well as therapeutic protocols for each disease. This network should include all expert doctors and scientists and patient associations, like in Denmark, France and the UK Patient involvement in the definition of such guidelines has been called for during the National Conferences.

- ***Collaboration among EU countries and EU authorities is necessary to overcome the bottlenecks created by the scarce and fragmented expertise on orphan drugs at national level***. An ***EMEA Working Party for the assessment of the clinical added value of OD*** could be the right mechanisms to make this cooperation work in practice. National authorities should engage into this EU-level cooperation activity. Gathering expertise at EU level for the assessment of the clinical added value of orphan drugs and the definition of post-marketing studies would allow timely production of well-informed opinions which would lead to non-binding Common Assessment Reports on the clinical added value of orphan drugs based on enhanced information and would reduce the information deficit, thus speeding up national pricing and reimbursement decisions.

- ***In order to manage compassionate provision of orphan drugs, systems of 'temporary authorisations' could be granted under certain conditions***. For instance, temporary authorisation could be granted to drugs used to treat cohorts of individuals before they obtain market authorisation (see French Final Report). The application of temporary protocols to cohorts rather than individual patients avoids cumbersome procedures to obtain ad hoc individual authorisations. Protocols for therapeutic use and information collection clearly must be followed. The advantage of such an approach would be the possibility of organising with the concerned industry the follow-up of treated patients, of collecting data on the tolerance and efficacy in real life of drugs, and thus improving knowledge on these products.

  It is important to make compulsory at the national level the collection of data on the efficiency and tolerance of treatments under compassionate or off-label use of drugs. Lack of scientific evidence and strict conditions for reimbursement may deter physicians from prescribing drugs off-label, even when these are the only alternative available to treat the disease. A suggested solution (Germany and France) to the above-mentioned problem is the reimbursement of off-label drugs, as long as the prescribing physician engages to systematically record effects and side-effects in a centralised database, thus gathering better evidence of the potential benefits and risks of the off-label drug.

Area 6. Patient Empowerment

- ***Patient empowerment is achieved firstly with a holistic approach to each individual citizen*.** It is important that everyone masters the daily situation. In order to overcome the fact the RD are often "invisible" to social services, consistent, validated and evidence based healthcare pathways (see Area 4) designed to cover a spectrum of conditions and symptoms would benefit RD patient and would be particularly beneficial for those with a progressive or chronic condition. Continuity of care should be guaranteed; in particular the transition from childhood to adult age should become smoother.

- ***Involvement of patient groups in decision-making processes can be only achieved when patients are really enabled to participate to such processes.*** In practice, this means that patients need to be qualified to become fully-fledged partners in decision-making debates which affect them directly. It should be also recognised that education leads to virtuous circles that cascade down to patients and associations and eventually to the entire system. Training is extremely important to allow patients to understand the scientific landscape and to discuss with researchers, medical staff and industry on equal foot.

- ***The importance of specialised services for RD patients for patients and families must be recognised.*** It is also demanded that their support through public money becomes a priority for the whole community. Evaluation of the services provided should be carried, quality systems should be adopted as well as guidelines, staff should receive adequate professional training. Guidelines and best practices developed at the EU level within and beyond the Rapsody project, coordinated by EURORDIS, should be used and supported further.

- ***Mechanisms need to be devised to recognise and integrate RD patients into existing social services (rehabilitation, integration into school and workplaces, recreation and respite services), while recognising their specificities and providing quality services in response to their needs***. For instance, in order to address to specific evaluation of disability in RD patients, it would be useful to modify the disability evaluation procedures so to consider other factors apart from the functional character of the disorder, and to include chronic character, degenerative processes, behaviour related problems and outbreaks. Peer to peer discussions and social studies would be useful to assess existing needs for specialised social services and describe how to better use and save resources in this field.

- ***Help lines as well as other interactive information and support services for patients should be included in the provisions of a NP on RD*.** National help lines should be created which are based on toll free numbers and linked to the European free-toll number, once it will be set up. Setting up ***quality help lines*** is essential for the patients benefiting from the service and for the credibility of the service itself. Quality criteria for Help Lines are established in the framework and in the follow-up of the Rapsody project led by EURORDIS. Prior and regular monitoring of the information needs

of patients and their families should be carried out. The national umbrella organisation may be useful in consolidating helpline services and acting as a signposting service. The need for further support for patients representing those affected by very rare conditions was stressed; even though support does exist through the umbrella organisation, there are little supports for these groups or people individually. It was also suggested that information on help lines could be given to patients as part of their 'healthcare pathway', by clinicians/staff that patients come into contact with.

2. Detailed comments and additions to the EUROPLAN Recommendations

Note: In this final section of the Report, account is given of the remarks, comments and additional propositions which could be gathered having attended the National Conferences and from their Final Reports. The selected propositions or comments to each Recommendation reflect, as far as possible, the prevailing point of view emerged from the Conferences. When important minority positions came forward, they are reported herein. However, not all topics were dealt with the same level of detail in all countries; hence the reported comments or suggestions may be coming from a smaller group of countries or even a single country, if considered deserving particular attention. As much as possible, it is explained how broadly the comments to the Recommendations are supported.

In the following tables, the left column lists the EUROPLAN Recommendations, whereas the comments or the additions resulting from the Conferences are in the right column. The comments reported in the right column are always meant to provide something in addition to Recommendation they refer to. The arrows (➔) refer to specific additional recommended actions or suggestions on the topic addressed by the Recommendation in the left column. When no remarks are found in the right column, this means that the related Recommendation was endorsed with no further comments (or, in a few cases, it was not discussed in detail).

From the explained Methodology and from what said above, it is obvious that these conclusions are in no way intended to have a statistical value, as they are the outcomes of a debate, even though framed into a common format.

Area 1. Methodology and Governance

R 1.1 Patients with RDs deserve dedicated public health policies to meet their specific needs.	Most countries where a EUROPLAN Conference was organised do not yet have a NP or Strategy. In those countries, as a result of the Conferences, it is has been consistently concluded that a National Plan is needed and competent authorities are urged to do so. Given the presence of many stakeholders, including public authorities, engagements were often taken to step up the process. In two countries, the process has just started (early 2010) with the creation of national bodies in charge of developing a NP (Germany, Croatia, see R.1.3.) and was further consolidated with the momentum created around the EUROPLAN Conferences. In Spain, the final report of the Conference will be the "Roadmap" to improve the extent and the implementation of the National Strategy for RD. ➔ **Consistently, the conclusions of the EUROPLAN Conferences reported that there is an imperative need to better structure the situation of RD patients within a comprehensive legislative framework as a necessity to restore the recognition of basic human rights and the protection of RD patients. NPs for RD will serve as the basis for intensified efforts on behalf of citizens suffering from rare disorders, who should have the same rights, access to treatment and social support as everyone else. A legislative framework is the only way to give RD patients their voices back as equal citizens in their own country.** ➔ **Given the efforts made to involve as many national stakeholders as possible, and the theoretical progress made in all key issues related to RD, the results of the EUROPLAN Conference should converge into the work carried out in the country and serve as a "roadmap" to develop/implement the NP.**
*R 1.2 Initiatives are taken to **raise awareness** about the dimension of the problem and to create **joint responsibility**.*	**The whole experience of EUROPLAN proved to be an outstanding awareness-raising exercise in the field of rare diseases at the national level. Since the adoption of the key European policy documents in this sector*, the EUROPLAN Conferences certainly were (coupled with the patient-led initiative of the Rare Disease Day, at is third edition in 2010) the most remarkable cross-country awareness raising opportunity on RD for the public at large in Europe, thus creating a grassroots movement demanding National Plans for RD. The EUROPLAN Conference in September 2010 was a timely event also in France, the only country as far along the process to discuss the Second Plan (the announcement of the 2nd French NP was delayed until 2011, due to government changes and budget constraints).** **Efforts have been made in all countries to ensure a significant media outreach, hence helping to raise awareness with the public at large** (This proved particularly successful in Spain, Ireland, Greece). **The awareness-raising experience has been confirmed by the attendance in some cases of participants from other**

	countries (notably, 8 Balkan countries' participants attended the Croatian Conference) and the recurring requests from countries that did not organise a EUROPLAN Conference to have a EUROPLAN Conference organised in their country as well (Slovakia, Cyprus, Estonia, for example).
*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.*	Generally speaking, great expectations are raised in respect of this national coordinating body or function. All Conferences acknowledge the importance of this centralised mechanism, whether it does exist or is meant to be set up. In early 2010, Germany a Commission consisting of 26 major players in the health care system, named 'NAMSE', was constituted to agree on a NP. Participants comprise representatives from statutory health care insurances, or "Krankenkassen", the Federation of private doctors contracting with Krankenkassen, hospital organisations, chambers of healthcare professions, industry, POs and the Federal Joint Committee governing the statutory healthcare system. In Croatia, a National Commission has been established by the Minister of Health and Social in February 2010 with the mission to develop a NP, which has already identified the priority areas of the NP. The EUROPLAN Conference recommended making it into a multi-stakeholder platform, a "Partnership for RD" between patient organisations, Ministry of Health and Social Welfare and the Croatian Institute for Health Insurance in order to achieve better coordination in preparing the Plan. In Spain, work is divided between a Technical Committee and an Institutional Committee, the latter in charge of assessing the relevance and feasibility of proposed objectives. Working Groups are developing specific aspects of the implementation of the Strategy. Seven Working Groups were established in France to develop a Second Plan for RD, all composed with representatives of main stakeholders. In France, under the Second Plan, a Committee for Orientation, Monitoring and Accreditation will provide opinions, monitor the Plan and advise on the accreditation of reference and competence centres; while an inter-ministerial coordinator, together with an operational project leader, will be responsible for the implementation of actions envisaged in the NP. ➔ **Drawing up a national plan should be an inclusive process. All stakeholders must commit and be given the chance to provide inputs if the process and the implementation of the national plan are to succeed. A NP should be developed with the ambition to leverage all the resources existing in the society.** ➔ **The national coordinating function must work starting from the patients' needs with a lifelong perspective. Patients should be involved in the management, their role should be institutionalised, hence their remuneration should be considered.** ➔ **Working Groups may be composed to focus on specific aspects of the Plan or Strategy, with balanced**

	representation of all stakeholders.
*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 RDs as well as those from which RD patients may benefit .* • *Unfulfilled needs of patients are assessed.* • *Available resources for improving health and social care of people affected by RDs at national level are evaluated.* • *European collaboration and the European documents in the field of RDs are taken into account in the development of the National Plan or Strategy.*	Situation analyses are ongoing at different level in the 15 countries concerned. This may be as systematised as in Germany, where a study "*Measures to improve the healthcare situation of people living with a RD in Germany*", mandated by the German Ministry of Health, was also a first assessment of the situation of RD patients and their needs, as well as of the resources available to face these needs. In other countries, the EUROPLAN Conference was the first opportunity to instigate a mapping exercise which was sometimes performed or sketched at the Conference itself, as it was the case in Croatia. In many cases, the Conference acknowledged the lack of a comprehensive, accurate and systematic analysis of the current situation in terms of epidemiological figures (fragmented information depending on the disease or the group of diseases, the region, the presence of health centres or scientific societies, etc.), available resources and unmet needs of patients. ➔ **A Working Group of the specific body in charge of developing the NP could be formed to carry out the specific situation analysis as per Recommendation R 1.4, including mapping out the national situation and proposing guidelines on: how to unify epidemiological data on RD (registries); information systems on RD resources; validation methods of such resources, etc. Such Working Group must take into account the work already done (for ex. patient-run surveys on unmet needs, outcomes of previous relevant workshops, results of the EUROPLAN Conference, etc.) and should have patients represented in their membership.**
*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.*	In all Conferences, although spelled out in different ways, it emerged the urge to ensure that patients with RDs have the right to the same healthcare quality, regardless of their diagnosis and of where they live. It also emerged that in all NPs, both existing and in development, actions are articulated along priorities or specific areas (see Recommendation R 1.8). The Second French Plan, in particular, provides a practical model for structuring the NP: provided that each area (or broader 'objective') is composed of more actions, a **basic template for each proposed action** includes: context, rationale, objective, description, timeline for implementation, process/result indicators, links with actions in other public health plans, European/international dimension, financial table (costs are identified for action and not for area).
*R 1.6 The policy decisions of the National Plan or Strategy are integrated i.e. structured **maximising 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.*	➔ **Work on a national plan should transcend sectors. It is not only health conditions that are of major importance, but also about quality of life of patients and families, hence NPs should not only be about healthcare, but resources available more generally in the welfare system of the country (social services, education, labour market related measures, etc.) should be considered and integrated.**
*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.*	In each country, the specific priority areas have been identified in existing or forthcoming national plans.
*R 1.9 Appropriate **resources** are allocated to ensure the feasibility of the actions in the planned time.*	The discussion on the allocation of appropriate resources was integrated into the thematic Workshops, depending on the choice of the organisers. The greatest difficulties encountered concerned how to earmark dedicated resources to a variety of activities which, at national level, frequently depend on the budgets of different administrations (research, centres of expertise, orphan drugs...) or of different sub-regional entities. ➔ **However, in the Workshops on the Governance it was consistently argued that a Plan or Strategy on RDs cannot be functioning without resources attached to it.** ➔ **Sustaining the Rare Disease Strategy will be very important, particularly in terms of embedding the Strategy into everyday healthcare services. It is important to set out the requirements for services provided based on the needs of patients and not dictated by current rationing of resources in the health services, which is a recurring concern throughout Europe.** Also, it is anecdotal evidence that patients with rare diseases take up a significant proportion of hospital beds and money. ➔ **Developing, implementing and sustaining a rare disease strategy will help the national healthcare system to deal with these patients far more appropriately and cost effectively. As matter of fact, the sustainability of a rare disease NP could be well achieved by spending resources effectively and not wasting them where they are not needed: "by diagnosing patients earlier and having care pathways and channels for them to be supported, the Rare Disease Strategy is anticipated to be self sufficient" (UK Final Report).** A study on the sustainability of a NP on RD has been outsourced by the Italian National Alliance UNIAMO to the Università Cattolica, Milan. Their findings would deserve a thorough analysis, as they are of relevance of all counties. However, in short it was found that: ➔ **RD sustainability needs to be taken into consideration not only from an economic but also from a social point of view. "As for the rare disease sustainability, the new horizon for the near future shall be closely connected**

	to the creation of a social value. It is necessary to plan, project, implement, monitor and assess policies that permit a clear definition of tasks, assessment criteria and consequent responsibilities. Focusing the attention on such element means acknowledging the global needs of rare disease patients and developing an integrated approach that, in terms of sustainability, in its widest meaning, may guarantee an added value both for the individual and the society."[8] *Note: The discussion on sustainability was spread throughout the Workshops in basically all Conferences. Therefore, remarks on sustainability of policy actions have been made area by area. For more details, please see Areas from 3 to 6.*
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.*	The integration of the NP into the national health system was debated at length especially in countries where the national health system globally covers all citizens in need of healthcare. In UK, for instance, the idea itself of a NP was put into questions by a minority of participants because conflicting with the comprehensive healthcare system. ➔ **Integrating the measures of the NP into the national health system is crucial as patients need to become part of the health and social system planning.** ➔ **Different approaches necessary for RDs, such as e.g. care management, combining care data with research data, multidisciplinary approaches, etc., may be beneficial for people living with more common diseases as well. Such an assessment may be performed in the evaluation phase of the NP, when the actions specific to RDs could be identified and distinguished from the rest. The former would become the object of the NP while the latter would come under the general HC system. It is therefore important that, in the evaluation of the NP, that a NP be evaluated to have a qualified estimation of the most important and specific measures for RD.**

[8] Final Report of the Italian Conference, page 22 in particular. Additional important remarks: "With respect to priorities regarding the system sustainability and financing, it is evident the need for a future plan and a better coordination of the sources (at least in the public context), regarding the RD field in order to develop an homogeneous and coordinated policy, regarding RD priority policies (expertise centres, socio-health networks, research, registries, orphan drugs, etc.). A technical economic coordination to support the policies implementation, priority investment guidelines, identification of the proper periods to develop investments and financing policies at every institutional level is essential. Such context should represent all the people involved in the rare disease system and should be on equal terms, advisory and proactive. It is desirable that the shared and financed contexts and projects be transversally systematic with the focus on the rare disease patient in order to generate an immediate and desirable organizational and health care effect to give real assistance and economic and social benefits to the rare disease patients".

*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 these recommendations was stressed at several instances. In France, this reflection was the result of the assessment of the first NP, which showed the need to reinforce the monitoring process. This resulted in clearly defined actions (82 for the whole Plan), each of them with process indicators and results indicators attached to them, as well as an impact measurement performed through 5 survey (ante and post Plan). In four countries, a dedicated work on the EUROPLAN Indicators was carried out during the Conference. In Germany, a specific Workshop on Indicators analysed in detail the Indicators developed in the EUROPLAN project. The Workshop agreed to advise the National Committee for the NP, NAMSE, to use them as the basis of reference to develop the indicators of the German NP, while concluding that the indicators needed an adaptation to the local situation. In Poland, Greece and Bulgaria, each of the thematic Conference Workshops worked specifically on the Indicators relevant to its Theme, using them as a tool to assess the provisions of the existing NP.
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.*	➔ **A suitable monitoring system must not be overlooked and must be integrated into the Plan. An effective, high-quality NP should set up indicators to measure its success and a methodologically sound system of monitoring the measures provided for in the Plan itself.** ➔ **As a methodological suggestion, it would be useful –when developing the NP- to attach to each identified action one or more process indicators to monitor its implementation in respect of the scheduled phasing of the action itself (see 2nd French Plan).** ➔ **It is especially important that process indicators are defined with focus on patient interests, and in a process where patients play an active role.** ➔ **It is equally important that the monitoring phase is carried out ensuring the greatest transparency of methods and results, as well as regular and strong contribution of patient representatives.** ➔ **Within the body in charge of steering the NP, a Monitoring Working Group could be established that defines the national process indicators, using EUROPLAN Indicators as a reference. The Monitor WG would also be in charge of monitoring on a regular basis the performance of the actions envisaged in the Plan on the basis of the Indicators. In order to ensure such a continuation of monitoring process, regular meetings should be scheduled and/or regular (yearly, for instance) reports could be scheduled.** ➔ **The Monitoring Working Group should contain a sufficient number of patient representatives. Qualifying the patient representatives who are members of this WG is necessary to help patient to organisations provide for a continued high quality patient inputs into the monitoring process.** ➔ **In addition to the use and integration of process indicators, surveys could be organised to measure the impact**

	of the actions outlined in the NP at the beginning and at the end of NP.

Area 2. Adequate definition, coding and inventorying of rare diseases

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).	➔ **It is generally agreed that one European definition is useful for facilitating cooperation and community actions. Conferences' participants broadly expressed the necessity and expectation to (continue to) use the European definition, especially in view of laying down legally binding legislation, as required by European policy documents.** Nevertheless, in two Nordic countries, Denmark and Sweden, the Conferences did not support the adoption of the RD definition as recommended by the Council. While they are currently adopting a more restrictive definition (less than 1 or 2 in 10 000), the problem related rather to the inadequacy of the prevalence criterion as the only parameter to define rare diseases. In Sweden, the incidence figures were proposed as an additional criterion. The complexity of the diseases (severity of disease, genetic nature in particular) was referred to in Denmark. In some cases, a further subdivision of ultra rare diseases was discussed, with diverging results: rejected to prevent disadvantages for those being affected by "ultra rare" diseases (Germany, for instance); or supported to protect the voice of persons with ultra RD which would become comparatively smaller in the RD community (Sweden).
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.	*See below*
R 2.3 Coding of rare diseases is promoted, encouraging their traceability in the national health system.	All Conferences supported the necessity of having a functioning coding system to ensure traceability of RDs at the national level. ➔ **It is recommended, while awaiting the release of ICD11 (expected in 2014/2015), to introduce existing coding systems: ICD10 is the most commonly used system, but it is deemed not satisfactory for the coverage of RDs. The ORPHANET classification (Orpha code) is largely in line with the future ICD11, which will not be finalised before a few years, and is used to a certain extent is some countries (Spain, France, for example). It is nevertheless sometimes criticised for lacking stability.** ➔ **This is why cross-referring across different classification systems is supported, as in the Spanish experience,**

	where a combined system is being developed based on ICD10, to which 2 digits are added, and on the Orpha Code; or the work of the Italian Working Group for Coding and Classification of RDs.
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.	When discussed, it was found that cross-referencing is useful and should be provided, however to date it is generally not in use. This recommendation should be made stronger in the NPs (see above, Recommendation R 2.3).
R 2.5 Collaboration with the ICD10 revision process is ensured and ICD11 is adopted as soon as possible.	It was unanimously agreed that the ICD11 should be adopted when ready. However, in many countries it was pointed out how the slow introduction of ICD10 is being in relevant areas, where it would be useful to have an international-agreed classification system. On the other side, it was also stressed how ineffective in almost all countries is ICD10 when it comes to classifying RDs. ➔ **National Conferences unanimously supported the swift adoption of ICD11 after its release.** ➔ **A more flexible system should be envisaged to allow for new diagnoses to be added also following the entry into force of ICD11.**
R 2.6 Healthcare professionals are appropriately trained in recognising and coding rare diseases.	In general, healthcare professionals do not have sufficient awareness of RDs in general, of the ORPHANET classification, nor are they aware of the lack of a proper codification of RDs within the ICD10. It was stressed in more than one country (e.g. Bulgaria, Greece, Spain) that the problem lies with the lack of familiarity with RDs by general practitioners or family doctors. ➔ **A change in attitude vis-à-vis disease inventorying is demanded, as the foundation for ICD11 acceptance. This is why it is recommended, while awaiting the release of ICD11, to introduce existing coding systems into clinical practice: Orpha Code, preferably, as ICD10 is deemed not satisfactory as for the coverage of RDs, or jointly, as in Spanish case, where a combined system is being developed. Such an early introduction would also help to promote a higher level of awareness and knowledge of RDs by healthcare professionals (in addition to the more obvious inventorying purposes).** ➔ **The introduction and the use of appropriate IT tools may support these efforts. An example is the protocol developed in Spain that allows family doctors to check if a disease is rare or not and provide support to identify criteria for decision-making.** ➔ **Undergraduate and postgraduate courses are proposed for improving RD knowledge among professionals, which include opportunities to familiarise with the coding systems (Spain).** ➔ **Workshops for similar purposes have been also proposed (Bulgaria) to be organised at the local level to make**

	RDs a more tangible experience.
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.	➔ **In order to guarantee the sustainability of registries, ongoing registration of rare diseases should be organised in such a way that the workflow, as far as possible, is integrated into existing administrative systems. As a preliminary step, it is, of course, essential that a consistent, unique coding system is used at national and ideally at internationally level (*see above Recommendations*).** ➔ **In addition to ORPHANET, which often is the only information source on RD registries in the country, an epidemiological portal, such as the one to be set up in France under the Second NP, could be a useful tool to describe the content of existing databases on health and cohorts, whether private of public (type of data, coordinators contact details, condition of access, etc.).** ➔ **Associating patients to the collection of data may become a valuable approach: this is already is being tested at the international (Rett syndrome database) and national level (France, leukodystrophy).** ➔ **In some countries an explicit call has been made for laying down the legal framework necessary to define competences and establish the coordination mechanisms among public institutions and administrations and/or private centres, especially when it is required that delocalised registries feed into central registries or databases. Such a legal structure is clearly important for countries where the healthcare system is decentralised.**
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.	➔ **In order to ensure registries sustainability, another challenge to face is the availability of resources. One first recommended step is to optimise resources by reducing fragmentation and overlapping. Focus should be on a better use and better information on existing knowledge and information sources. ORPHANET could be instrumental in doing this. Optimisation of resources may include adopting mechanisms to extract the already established information hidden under the global (all diseases) information.** ➔ **Government resources are generally considered indispensable by all Conferences' participants to sustain the functioning of RD registries, even though in some countries this is current practice (Germany, Sweden, Italy, for instance) and in others this is not happening (Greece).** ➔ **In two projects run in Bulgaria, the involvement of all stakeholders proved to be key to the success and to the long-term duration of RD registries. This is especially recommended as it offers diversification of funding sources (government, academia, industry, patient organisations, ...).** ➔ **The differentiation of registries' outcomes also emerged as a decisive factor: as far as possible, registries should be "multi-purposes", i.e. used for public health planning, research and international cooperation...** ➔ **Integrity issues and privacy requirements must be integrated into the regulatory frameworks governing**

	patient registries, whether publicly or privately funded. ➔ **Quality requirements for registries have been demanded in many Conferences (Germany, Italy, Sweden, for ex.) and exist in France. It is recommended that national quality standards are applied even when registers are locally managed. Monitoring bodies and process could be envisaged, coupled with sanctions for not compliant registries (Italian proposal).** ➔ **Efforts should be made to establish cooperation and exchanges with patient registries in other (EU) countries, where existing. Setting up international networks is essential to exchange existing knowledge and optimise resources. The long-term sustainability of these networks should be also supported with adequate public funding.**

Area 3. <u>Research on rare diseases</u>

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.*	EUROPLAN Conferences were an important opportunity throughout Europe to sketch out and discuss the state of the art of research on rare diseases. National Conferences' Reports account in detail for the outcomes of such discussions. From these national 'mappings' it appeared that in most countries there are no dedicated national research programmes or funds for RD research. This is sometimes due to different approaches or traditions in research funding. For instance, in some countries (Sweden, Denmark, Germany, UK) no thematic approach is adopted, research being funded through bottom-up procedures, whereby the best application gets funded, whatever the theme may be. ➔ **It was generally recommended, as Conference conclusions, that RDs be considered as a priority in medical research in the country and ad hoc national research measures be dedicated to RDs. With the exception of Germany, this conclusion concerned both those countries where traditionally a non-thematic approach is adopted and those countries where the absence of dedicated RD funds results rather from limited resources, lack of funds or lack of political willingness.** ➔ **It was equally stressed in basically all countries that it is crucial to support dedicated RD research programmes with appropriate funding, in order to ensure the longevity of research projects and their sustainability. Dedicated programmes would also help optimise scattered resources by improving knowledge on existing research activities and better coordinating them. Although the majority of Conferences clearly called for public funding, proposals were made to also consider private-public partnerships. In Bulgaria, it was proposed to create an industry-based fund, earmarking 5% of drugs' marketing funds. Similarly, in Italy, a fund is available**

	each year for independent research, which results from the legal requirement upon the pharmaceutical industry to pay their trade association (AIFA) 5% of money committed to their advertising campaigns. ➔ As far as the management of RD research is concerned and its sustainability, interesting proposals concern the establishment of **a body to be created at national level which steers and advises on RD research, develops public private partnerships with industry and associations, create close links with centres of expertise and acts as a one-stop shop for all information on RD research and/or potential incubator for enterprises** (see, by way of example, the "Foundation for scientific cooperation", supported in France by the Second NP, or the proposed extended role of the Spanish CIBERER, Centre for Biomedical Network Research on RD). **A centralised database on research projects and research teams would be also handled at central level. Such a system of central coordination would also favour the establishment of a continuous funding scheme (and not only based on call for proposals).** ➔ **Research on RDs should range from basic to clinical research, with most of Conferences insisting on how crucial is developing further translational research.** ➔ **Moreover, RD research has to be carried out with a multidisciplinary approach, involving professionals from different backgrounds, as it was pointed out in most Conferences.** ➔ **Many Conferences (Italy, Denmark, Sweden, Romania, France, Spain, Germany...) highlighted the importance of public health and socio-economic research. Research into quality of life, living conditions are extremely important not only for public health planning, but also for provision of services which help to provide an answer to the needs of patients in their daily life and to empower them.** The concept of patients and patient groups as real partners in research has been supported in various conferences. Patients and their associations are essential to foster knowledge sharing; identify research topics; promote and help maintain patient registries and cohorts; involve patients in clinical trials. Patients also fund research. ➔ **Patients associations should take and should be recognised a more proactive role as research partners. For an optimal support by patient organisations, qualifying training for patient representatives and financial support to patient representatives should be ensured.**
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*	➔ **National Centres of Expertise are important for researchers and patients. A good infrastructure in healthcare where patients meet, gives significant possibilities to research. Currently, a major obstacle for research is the separation between research and care.** ➔ **The centres should have an independent board that cooperates with patient organisations.** Patients **are good resources as well, also as mediators to facilitate contacts among their primary care physicians, specialised**

diseases.	**clinics and researchers. Patient organisations can give strong inputs on questions to be addressed and prioritising them.** ➔ **Mechanisms could be established to allow 1) researchers to fully integrate within clinical services; and 2) clinicians to devote time to research without compromising care.** ➔ **By establishing translational centres, clinical and basic science could be connected with social sciences and political sciences in order to optimise the provision of both patient care and services which go beyond healthcare.**
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.*	➔ **Research networks where researchers are also the specialists for these diseases in care** (see the example of the 16 networks funded in Germany)**, help to link research and care. Such networks need to be developed further through the Centres of Expertise, which should be supported by the right legal and financial framework to carry out research activities.** o In this context, due account should be taken of the fact that time pressure for clinical work and the lack of reimbursement for activities which are relevant to research (documentation, gathering of data, etc....), hinder research. ➔ **Better coordination of national resources on research on RDs would be facilitated by the creation of databases or directories of all ongoing research projects or under development, including and beyond ORPHANET (Croatia, Sweden, Romania).** ➔ **Better dissemination of research results to practitioners, patient groups, as well as on leading scientific journals and even media coverage were also proposed as a way to profile RD research and increase awareness on RDs in general.**
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.*	➔ **Participation in E-RARE was recognised and supported as an important form of international cooperative research initiative (Denmark, Romania, Greece, Germany, France...).** ➔ **As in E-RARE projects, which are good examples of well managed international cooperation, data on patient cohorts and on biological collections should be shared in order to set up smoothly functioning international cooperation initiatives.**
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*	➔ **The creation of patient registries was consistently supported by EUROPLAN Conferences. It should be a primary objective and a basic requirement to develop RD research. Moreover, it is necessary that such registries be of high level quality: their structure needs to be clarified and their funding in the long-term ensured.**

explored.	The Bulgarian Conference, in particular, based on the national experience with two specific RD registries, advised that the best way to ensure sustainability of registries is involving all RD stakeholders and designing registries which fulfil different purposes, from the support to epidemiological studies to the feeding into clinical trials. By extending the research group beyond the patient group which is part of the clinical study, the gap between optimal and routine conditions can be closed. ➔ **Clearer definition of rules and regulations concerning the storage of data, quality standards to ensure trustworthiness, the development of uniform data structures and software platforms** were recommendations which emerged in more than one Conferences, but were explicitly spelled out at the German Conferences, where a dedicated Workshop on Patient Registries was organised. ➔ To complement the general recommendation that research and care should be better coupled together, it was proposed to introduce the **obligation to document the treatment progress and to register such data in clinical registries.** ➔ **Ideas such as the creation of a "registry of registries" (Germany) or an "epidemiological platform" (France) were also considered carefully. Such centrally-managed infrastructures would describe the contents of existing databases, registries and cohorts, whether private or public.** (*see also Recommendations on Registries under Area 2)*
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.*	➔ **National and/or international networks are an absolute necessity when it comes to the organisation of clinical trials to address the limited number of patients and the scarcity of expertise. It is essential to promote clinical and preclinical testing in cooperation with the pharmaceutical industry.**
R 3.7 Specific programs are launched for funding and/or recruitment of ***young scientists*** *on rare diseases research projects.*	➔ **Incentives for young scientists should be created through career training resources. However, better recruitment rates of young scientists can be only assured if attractive career perspectives do exist and appropriate funding for RD research is put in place.**
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 medicinal products 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 treatments are better documented. A liberal regime for reimbursement in combination with an obligation for documentation could contribute to gather better evidence on effectiveness and consequently be a basis for reassessing off-label-reimbursement.** (*see also Recommendations on Orphan Drugs under Area 5)*

Area 4. Centres of Expertise and European Reference Networks

*R 4.1 Well defined mechanisms of **designation** of centres of expertise are established and their quality is assured, efficiency and long term sustainability.*	➔ **As a preliminary exercise to any planning on Centres of Expertise, a mapping of Centres of Expertise (CoEs) is demanded by the Conferences where this does not exist or has not yet been done** (see also R 4.4). This is to recognise that in basically all countries expertise on rare diseases does exist. This expertise is, however, not always easy to find, not systematically and sufficiently funded and neither officially defined or identified in Centres of Expertise. In order to set up the national network of care, it is also important to underline the existence of different kinds of Centres (e.g. in some countries, like Italy, Centres of Reference providing care at local level), which are complementary and not subordinated to each other. Their different role and competences should be acknowledged. Where CoEs exist, **designation and accreditation** procedures vary significantly (see, in addition to the National Reports of France, Spain, UK, Italy and Denmark, in particular, also par. 4.3. of the Guidance Document on the EUROPLAN Recommendation). ➔ **Consistently, the National EUROPLAN Conferences called for common quality standards for the designation and the accreditation of CoEs. It has been recalled that the Rare Diseases Task Force recommended in 2006 the criteria for the accreditation of CoEs, which should constitute the basis for defining common quality parameters. Similarly, the 2008 EURORDIS Declaration was also mentioned. Amongst the criteria evoked at the Conferences, these are the recurring ones:** o **multidisciplinarity;** o **training and education of medical and paramedical specialists; specialised information for both professionals and patients/families;** o **transition from paediatric to adult age;** o **contribution to patient registries (or management of registries);** o **facilitation of research activities;** o **validation of performance based on clinical results but also on patient satisfaction;** o **participation of the Centre to European Reference Networks and other forms of international exposure and projects, including EC-funded Networks of Excellence (NoE).**
	As for the **structuring and the organisation of CoEs**, differences may be important depending on the size of the country concerned and on the governance of the national health system. Decentralised systems, with significant

	decision and financial power lying with the regional (or assimilated) authorities, differ from the centralised ones. Nevertheless, the proximity of care is a recurring theme. The attribution of competences between the more specialist centre (often far from the patient's domicile) and the local level of care, is debated everywhere. ➔ **Structures have to be developed to coordinate day-to-day care within an acceptable travel distance, and expert care in Centres of Expertise (diagnosis, establishing a care plan, regular check-up, certain emergencies, etc.). These structures may be information platforms or tools able to functionally connect the centres with the other structures involved in the continuity of patients' care.** The organisation of CoEs diverges also insofar as diseases are grouped by homogeneous groups of diseases (as in the RDTF recommendations) or whether diseases are all grouped at the central level. This is the option in certain countries like, for instance, Bulgaria, where 5 or 6 national all-disease centres are established, or the situation (existing or envisaged) in smaller countries, where the limited territory and population does not justify a complex network of (regional/local) CoEs. ➔ **In smaller countries, where the establishment of CoE for all diseases would be too complex and expensive, networks of medical experts dealing with RDs could be established, while promoting cross-border cooperation at the same time. All-disease centres are also a solution, even though experience shows (see the Danish situation, where 2 all-disease centres has been set up) that such centres may be overburdened and under-resourced to fulfil all the tasks they are assigned, especially in relation to the global management of patients' care.** ➔ **In larger countries solutions are found to introduce intermediary levels, such as the 'competence centres' in France or in Romania, i.e. hospitals able to ensure three main tasks of a CoE: referral, data collection and research. Generally speaking, in large countries, systems of 'vertical referrals' (local/regional/national) are often in place or recommended. From the regional/national centres or hospitals, patients are referred to central/national CoEs where diagnostic test are performed, specialised treatment is offered, whereas the daily care is left with the centres in the proximity of the place of living. Referral to a CoE in another EU country could be the ultimate step of the vertical referral system, when the necessary expertise is not found in the country of origin** (see also R 4.3)**.** ➔ **In bigger countries the creation of networks of CoEs is also supported, which reflects the needs to share scattered information and expertise throughout the national territory, where more poles of expertise are susceptible of being created. A system based on networks of CoEs also helps to optimise resources by reducing redundancies or filling gaps. These remarks on networks of CoEs within the country may be similarly applied to European Reference Networks of Centres of Expertise (ERN).**

	➔ **In decentralised systems, where the regional authorities hold the most prominent decision-making power on budget and health policy, decisions on accreditation and evaluation of CoEs are taken at the regional level (Italy, where this concerns, in fact, 'Centres of References'), although this approach is not supported everywhere (Germany prefers to keep this task at Federal level).** ➔ **As to whether new centres or existing ones should be created, it is commonly agreed that existing resources and centres should be used, with many country referring to, in particular, university hospitals. Having demonstrated experience and produced results in the care of RDs should become a criterion for accreditation. However, a rationalisation of existing resources should be performed, and the compliance with quality standards should be ensured (both in the accreditation and in the monitoring process).** ➔ **As for the integration between medical and social levels, at the National Conferences it was repeatedly recommended to strengthen it further, with a necessary reinforcement of the social level. Social counselling and social services should be provided at the CoE, although, as it was pointed out in some occasions, not only there. Social support in the proximity of the place of living should be equally ensured. The involvement of patient organisations in social counselling is essential and they should be systematically involved.** ➔ **Also, the evaluation of Centres of Expertise should be defined and verified by an independent body, where the patient participation is requested. The evaluation of the structure and of the process to establish the continued expertise and standards of care should be performed regularly. Part of such an audit should be whether guidelines are adhered to and patient satisfaction attained.** As for the **sustainability of CoEs**, part of the debate concerned the extraordinary efforts for the treatment of RDs and the provision of care, how this is reimbursed or funded. ➔ **The healthcare services provided by the Centres of Expertise should be recognised and their reimbursement needs to be defined.** Suggestions include: a premium for successful referrals from GP to specialists; lump-sum fees for the holistic care of a specific RD associated with clearly defined quality criteria; or "special contracts" with healthcare insurers and selected providers of care for given RDs (Germany). ➔ **Solutions should be found for the performance of activities which go beyond the treatment (purely healthcare services), recognised as fundamental for CoEs, yet often underperformed due to the lack of fund, reimbursement provisions, human resources or time**. In France, the Second NP allocates funds for "Missions d'intérêt générale" to CoEs and introduces a system of funding based not on the single centre, but on funds dedicated to certain activities recognised as "missions of general interest". This allows creating resources for activities not strictly related to patient treatment, such as

	clinical research, production of guidelines for diagnosis and care; in-depth clinical and biological investigations; coordination of international networks, etc. ➔ **Finally, it has been raised (Spain) that in countries qualifying for it, RDs should be included in the "Cohesion budget" also available for health objectives, usually managed by the Ministry for Health.**
R 4.2 ***Healthcare pathways*** *are defined and adopted, based on best practices and expertise at national and international level.*	➔ **This Recommendation is broadly supported. It was also added (France) that procedures for the production of protocols for diagnosis and care should be simplified and accelerated at the national level.** ➔ **In various Conferences (e.g. France, Spain), it was recommended that coordinators and/or mediators support patients who usually face complex situation from a medical, social and/or administrative point of view. These would be "case managers" who dedicate their attention to individual cases and follow them all along the healthcare pathway. Their role would be helping to secure a coordinated and coherent coverage by available medical and social services, providing also assistance to get patients acquainted with their rights and get them through the administrative hurdles. Such initiatives are aimed to fulfil the urging needs of patients and families in their daily lives, which is often the most difficult part of living with a rare disease.** Experiments in this sense are being carried out by the AFM, the French Association for Myopathies, who has put in place a network of social coordinators. Ideally, a feasibility study could assess whether this practice could be extended to other RDs. ➔ **Given the importance of daily care in patients' life, medical knowledge and expertise of specialised centres should be structurally fed into primary care clinics, family doctors and socio-sanitary professionals. This may happen though onsite meetings and opportunities, virtual and telemedicine tools.** ➔ **Continuity of care should be guaranteed; in particular the transition from childhood to adult age should become smoother. The latter concern, in particular, involves training and education of GPs and healthcare professionals in non paediatric hospitals, not used to treat RD. It is necessary that this task is taken over by Centres of Expertise.**
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.*	➔ **Promotion of the participation of CoEs in European Reference Networks (ERN) should be integrated in the NP and integrated as a quality criterion of the performance of each CoE. This was a recurring message of the National Conferences, to the extent that is many cases it was specified that the participation to European-level networks is the only way forward to assure sustainable progress in the RD field. In order to attract CoEs, ERN should provide resources, such as biobanks or registries, which demand strong networking.** ➔ **It was also underlined, however, that international networking activities are time-consuming (and resource consuming). European funding should be considered in order to finance them. Guidelines should be practical**

	and exhaustive, concern diagnosis, treatment and social aspects altogether. ➔ **Providing contributions to European recommendations or guidelines should be also an activity performed by CoEs.** ➔ **Provided that strong international network exchanges and exchanges of know-how are of the utmost importance, cross-border healthcare should be promoted, especially for very rare diseases, or for any situation in which there is no sufficient expertise in the country or when a specific expertise has been developed in certain countries.** ➔ **The National Conferences stressed the importance of mobility of expertise and data. Mobility of patients appears a concern everywhere, because knowledge and expertise on RDs are generally scarce, and principally in smaller countries where the existing resources cannot cover all RDs.** Interestingly, in large countries like Spain or Germany, with decentralised healthcare systems, similar issues have been raised as in intra-European cross-border healthcare. These primarily concern the slowness of procedures to obtain prior authorisation and the differences in legal provisions across regions. *Note: the approval of the long-awaited EU Cross-Border Healthcare Directive was on its way when the National Conferences took place. Clearly, the specific provisions envisaged for RDs in the latest version of the text adopted by the EU legislator will lead to further reflections in due time.*
*R 4.4 A national **directory of Centres of expertise** is compiled and made publicly available.*	• **This Recommendation was reinforced in basically all Conferences. As said, mapping CoEs is a preliminary exercise to any planning on CoEs. This exercise is equally important to make the expertise available in the country known, hence more accessible, to patients.**
*R 4.5 **Travelling of biological samples, radiologic images, other diagnostic materials**, and e-tools for tele-expertise are promoted.*	➔ **Travelling of data and biological samples is generally supported insofar as it allows for greater mobility of expertise and creates the basis for exchanging scattered information and knowledge. However, it was also emphasised the importance of data protection and patient consent, which must be preserved under all circumstances.** ➔ **Best practices defined at European level should be applied.**
*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. The healthcare system should better value the work of therapists other than doctors** (See also Recommendation 4.12). ➔ **Information, training and statutory recognition of a number of professions related to the healthcare sector, as well as to the social services that needs to be provided to RD patients, must be ensured.**
R 4.7 A national framework is ensured on rare	➔ **A good legal basis is essential to frame RD screening policies. Also, running common surveys to assess the**

*diseases **screening options and policies**.*	**feedback of RD stakeholders on these topics may be of great value.** ➔ **Implementation is also essential. The case of Romania, where a dedicate session of the workshop focused on screening, shows how in actual fact the lack of resources or of appropriate screening centres, or the lack of consistent application of the existing policy create important gaps in detection of RDs and delays/mistakes in diagnosis. Screening policies should be therefore accompanied by evaluation procedures to assess the quality and performance of the programmes.** ➔ **Last but not least, it should be stressed that certain types of screening may be prohibited by national law. This is the case of population screening aiming at identification of heterozygotes in Germany.**
*R 4.8 Proper performance of **newborn screenings** prescribed in the country is monitored with appropriate indicators.*	➔ **Extension of the current neonatal screening programmes is demanded by many Conferences, as they are considered relatively limited. At present, more diseases can be reliably diagnosed (not too many false positives or negatives), for which early treatment would be beneficial.** ➔ **An international exchange on the effectiveness and regulations of newborn screening should be promoted further. The outcomes of the EC-funded project on neonatal screening of RD in Europe, EPIRARE, which aims at issuing recommendations for good practices, is awaited.**
*R 4.9 Accessibility to **genetic counselling** is promoted.*	➔ **Competent genetic counselling should be made easily accessible and provided before and after genetic testing, in regional centres or CoEs (Romania).** ➔ **In some countries, it was pointed out, the medical speciality of "Clinical genetics" does not exist. It is recommended that it be introduced as soon as possible in the university system.**
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.	➔ **Strict quality control and evaluation of genetic testing should be fulfilled. External quality controls programmes should be also implemented.**
*R 4.11 A national **inventory of medical laboratories** providing testing for rare disease is compiled and made publicly available.*	➔ **From the National Conferences, it was frequently demanded that an inventory of medical laboratories providing testing for RDs be compiled. This was sometimes supported by the request for accreditation of such laboratories (e.g. Romania, France).** In France, in particular, the Second NP, in addition to CoE and their networks, introduces the 'reference laboratories' and the networks of such laboratories, in order to have dedicated infrastructures (and resources) for the biological component, often neglected in CoEs, where treatment and care are usually provided as a priority.

	➔ **Such directories should be made public in order to facilitate access to patients.** ➔ **Where not existing in the country, partnerships should be arranged with other laboratories in the EU.**
*R 4.12 The adoption of an **ad hoc coding is promoted**, when appropriate, to recognize and appropriately **resource and reimburse the special rehabilitation treatments** necessary for rare diseases.*	Taking charge of rare pathologies implies sometimes the involvement of health professionals whose outclinic acts are not covered by sickness insurance. Such is the case, for example, with dieticians, psychologists, physiotherapists, etc. Hence, difficulties of funding would arise in many national reimbursement systems. ➔ **In order to better value the work of paramedical or other professional specialties, mechanisms should be found to recognise their interventions (provided that they are prescribed by CoEs), to integrate them into the reimbursement schemes and to simplify the procedures for reimbursement.** In France, special fees for complex acts are proposed under the second NP, to be handled in connection with RD networks. *(See also R 4.6)*

Area 5. Gathering expertise on rare diseases at the EU level

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.*	➔ **This Recommendation was supported throughout all Conferences. Access to both national and international information websites and data repositories is widely promoted and their financial support encouraged. The unique role of ORPHANET has been highlighted everywhere, as well as the necessity to increase knowledge and awareness among the general public on this and other data repositories, which are crucial for patients and families.** ➔ **Government-supported campaigns have been mentioned as a solution (e.g. France, Bulgaria) to raise public awareness on RDs in general, and to make information services and repositories available at national level better known by the public at large.** ➔ **National awareness-raising initiatives are called for in many countries. Apart from the consolidated Rare Disease Day, proposals include organisation and participation to events, seminars and conferences, better media coverage on generic press, targeted articles on specialised press and medical journals, dissemination of information through professional societies and patients associations, informative brochures and leaflets to distribute locally (centres of primary care, pharmacies, etc.).** ➔ **Regarding the information sources available to both patients and professionals, it has been pointed out in more than one Conference that the information provided is not homogeneous (it varies depending on the region, on the disease or the group of diseases) and that quality is not always validated. Proposals include mapping out available information country-wide; the introduction of validation/verification systems; identifying control mechanisms for information provided on the web. It could be the responsibility of the committee in charge of the NP to assess the evaluation needs and the standardisation mechanisms of information sources.**
R 5.3 Information on how to establish or join a European Reference Network is made available for to health professionals.	*(See Recommendations on ERN in Area 4)*
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 broadly considered a Recommendation of enormous importance. Largely inspired by the two-hour module included in the French undergraduate medical courses, it is demanded that it be implemented as quickly as possible in other European countries.** ➔ **In two countries, Spain and Greece, there was a specific demand for creating a specialisation in the medical career in Clinical Genetics, which is currently inexistent.**

	➔ **Specific proposals include innovative trainings using virtual universities (see www.edubolirare.ro), online trainings and virtual channels. Virtual programmes would have to be approved by expert centres and other institutions involved in RDs. A public policy support and adequate IT platforms and tools are, of course, preliminary steps to the implementation of such training modalities.** ➔ **Systems to evaluate the quality and effectiveness of trainings should be set up, supported by outcome indicators (Italy).**
R 5.5 Training of medical doctors (general practitioners and specialists), scientists and new healthcare professionals in the field of rare diseases is supported.	➔ **Trainings of professionals should be systematically introduced and organised. Specifically targeted trainings should be provided, with different degrees of knowledge, depending on whether addressed to family doctors or specialists.** ➔ **In particular, it is widely recognised that a general training, broadly encompassing all disease areas, should be assured for general practitioners and paediatricians. This is necessary to create awareness on possible rare diagnoses and to train them to deal on a day-to-day basis with rare patients** *(see in particular, in the Report of the Italian National Conference, the reference to the project "Knowing to assist")***.** ➔ **Postgraduate training is required to bring a more in-depth knowledge of RDs to specialists, with an additional component of management, so to move from the knowledge of the disease to the knowledge of the patient** *(see, in particular, the Report of the Spanish National Conference)***.** ➔ **Training is necessary for paramedical professionals as well. Centres of Expertise should be the elective places where such training is provided, according to the outcomes of many Conferences, or at least where it is coordinated. Sharing experiences and resources by creating exchanges among Centres of Expertise would help to maximise the efforts.** ➔ **Training opportunities need to be developed for professional figures, such as the assistant of persons with severe disabilities, or other professional profiles whose role contributes to improve the quality of life of people living with RDs.** ➔ **Information and training resources should be made available on a widely accessible directory possibly validated and/or managed by a competent body. They could be supported by the ORPHANET portal.**
R 5.6 Continuing education programmes on rare diseases are made available for health professionals.	➔ **This Recommendation is supported and strengthened by the conclusions of the National Conferences. Adequate competence on RDs (general, for GPs, and more targeted for specialists) should be achieved by guaranteeing *lifelong* training of medical doctors and other healthcare professionals, including paramedical specialists. Continuing education initiatives are essential for primary care providers. Continuous training modules should aim at providing comprehensive care to people affected by RDs and should include specific**

	protocols for paediatricians to recognise relevant symptoms of RDs. ➔ **Cooperation with patient organisations is desirable. This involves encouraging cooperation and information exchanges between health professionals and patient associations, so to enhance patient-doctor communication (Spain, Italy).**
R 5.7 The exchange and sharing of expertise and knowledge between centres within the country and abroad is promoted.	*(See Recommendations on ERN in Area 4)*
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.	➔ **Guidelines should be developed to align actions performed at different levels of care and by different healthcare professionals, with specific information for patients, families, caregivers and teachers.** ➔ **One proposed solution to develop such guidelines is the creation of networks coordinated by Centres of Expertise, gathering available scientific evidence at national and international level and include all expert doctors, scientists and patient associations (see the experiences of Denmark, France and the UK). These networks should be in charge of defining principles of best practice in clinical and laboratory diagnosis, as well as therapeutic protocols for each disease.** ➔ **Patient involvement in the definition of such guidelines has been called for during a number of National Conferences (Bulgaria, France, Greece, for instance).**
*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.*	➔ **Consistently, the National Conferences called for the improvement and simplification of the procedures for off-label use of approved medicinal products. Such procedures are usually cumbersome and often do not lead to the reimbursement of the drugs.** ➔ **In order to manage compassionate provision of orphan drugs, systems of 'temporary authorisations' exist or are evoked by National Conferences, which are or could be granted to drugs used to treat cohorts of individuals before they obtain market authorisation. The application of temporary protocols to cohorts rather than individual patients avoids cumbersome procedures to obtain ad hoc individual authorisations. Protocols**

	for therapeutic use and information collection must be followed. In such cases (see the Second French NP, for example), it is possible to take advantage of marketing under temporary authorisations to organise the follow up of treated patients with the concerned industry, to collect data on the tolerance and efficacy of drugs in real life, and thus improve knowledge on these products. ➔ **Self-declaration of side effects by patients and their families should be also considered: several pilot experiments of pharmacovigilance in France have demonstrated its merits, for both drugs with or without a specific marketing authorisation. If such experiments were carried out at the European level, the information base could be broadened.** ➔ **Nevertheless, in many countries, including France, the importance of compulsory collection of data on the efficiency and tolerance of treatments (under compassionate or off-label use) has been stressed.** ➔ **In fact, strict conditions for reimbursement may deter physicians from prescribing drugs off-label, even when they are the only alternative available to treat the disease. A suggested solution (Germany) to the above-mentioned problem is liberalising the right to prescribe, imposing a concurring obligation to reimburse the medication, and at the same time obliging the prescribing physician to systematically record effects and side-effects in a centralised database. 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.**
*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.	
	In addition to the Recommendations of EUROPLAN, the Conferences insisted on the importance to **improve access to orphan drugs (OD).** Equitable and timely access to approved OD for rare diseases patients remains an issue. "Effective market access and utilisation vary strongly between and within Member States", as already underlined by the final conclusions and recommendations on Pricing & Reimbursement of the EU High Level Pharmaceutical Forum. It was also recognised during some EUROPLAN Conferences (Hungary and Ireland, for example) that some of the bottlenecks could be solved by acting at the EU level. ➔ **The creation at the EMEA of a Working Party for the assessment of the clinical added value of OD is instrumental to increase collaboration between Member States and EU-level authorities. This collaboration is**

	needed to overcome the specific bottlenecks created by scarce, uneven and fragmented expertise on orphan drugs at national level. ➔ **Gathering expertise at EU level for the assessment of the clinical added value of orphan drugs would allow timely production of well-informed opinions which would lead to non-binding Common Assessment Reports on the clinical added value of orphan drugs based on enhanced information and would reduce the information deficit, thus speeding up national pricing and reimbursement decisions.**

Area 6. <u>Patient Empowerment</u>

Note: Patient empowerment in the governance of the plan, in RD research in the management of registries, of Centres of Expertise, defining guidelines, etc., has been mentioned in the previous Areas. Therefore what follows adds up to what has not been previously covered.	
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.*	*"It is precisely because the associations possess knowledge about rare disorders and disabilities that it is imperative that they are involved in policy-making and structural development"* (Final Report of the Danish Conference). ➔ **Support to patient groups –at all levels- is essential to make their activities sustainable. Their education role to patients, medical professionals and the community at large needs to be recognised and funded or otherwise supported. Because of their competence and expertise they must have say in all decisions which affect them. Necessary mechanisms need to be put in place to ensure their participation. Trainings, financial support, official recognition, etc.** ➔ **Support to patients is particularly important, considering how difficult it is to manage an illness (whether as a patient or carer) and to dedicate time to the decision-making process. Patient and carers face hard times managing their treatments, being hospitalised, etc. Ways enabling these patients to have a voice must be employed.**
R 6.2 The patients' organisations are ***involved in decisions making processes*** *in the field of rare*	➔ **Involvement of patient groups in decision-making processes can be only achieved when patients are really**

diseases.	**enabled to participate to such processes. This implies a "transition from patients as people who are consulted to people who are actively collaborating"[9]. To do so, it also important to improve public perception of the role of patients in the decision-making processes**. ➔ **Patients need to be qualified to become fully-fledged partners in decision-making debates which affect them directly. It should be also recognised that education of patients leads to virtuous circles that cascade down to patients and associations and eventually to the entire system.** The above recommendation is shared by all the National Conferences, regardless of the political culture of the country. It must be said, however, that patient advocacy is more accepted and often integrated into the decision-making system in certain countries (Nordic countries, UK, Ireland...), whereas in other parts of Europe (Southern Europe, in particular), it recognised that it is still theoretically difficult to endorse. ➔ **Training is extremely important to allow patients to understand the scientific landscape and to discuss with researchers, medical staff and industry on equal footing.** ➔ **In particular, patients should be part of the evaluation of the opportunity costs of policy planning on RD. When "benefit" is to be assessed, patients should be heard. Patients know what the consequences of non-treatment are, what kind of treatment they experience as beneficial, etc.** ➔ **Indicators to assess the quality of patient participation in the decision-making process could be established, monitored and evaluated on a regular basis.**
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.*	➔ **Help lines as well as other interactive information and support services for patients should be included in the provisions of a NP on RD.** ➔ **National help lines should be created which are based on toll free numbers and linked to the European free-toll number, when the latter is set up.** ➔ **Setting up quality help lines is essential for the patients benefiting from the service and for the credibility of the service itself. Quality criteria for help lines are established in the framework and in the follow-up of the EC-funded Rapsody project, led by EURORDIS. It was recalled that, amongst other, an important requirement for creating a help line is the prior and regular monitoring of the information needs of patients and their families.** ➔ **It was suggested that, where this is not the case yet, the country's umbrella organisation such the country's National Alliance of RD associations may be useful in consolidating help line services and perhaps acting as a signposting service.**

[9] Final Report of the Spanish Conference.

	➔ **The need for further support for patients representing those affected by an ultra rare condition was highlighted; even though support does exist through the umbrella organisation, there are little supports for these groups individually.** ➔ **It was suggested that this information on help lines could be given to patients as part of their 'healthcare pathway', by the professional managing their individual case or other clinicians/staff that patients come into contact with.**
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.*	In a number of countries existing programmes are unevenly distributed, not appropriate because either not targeted to RD, old fashioned or hardly accessible due to the bureaucratic hurdles necessary to receive an official acknowledgement. ➔ **Mechanisms need to be devised to recognise and integrate RD patients into existing social services (rehabilitation, integration into school and workplaces, recreation and respite services), while recognising their specificities and providing quality services in response to their needs. For instance, in order to address the specific evaluation of disability in RD patients, it is important modifying the disability evaluation procedures to consider other factors apart from the functional character of the disorder, such as its chronic character, degenerative processes, behavioural aspects and outbreaks.** ➔ **It is important that NPs include such provisions and envisage concrete actions to turn them into reality. For instance, improving the legal framework could be part of the solution to speed up procedures. Financial support for such services to ensure their long-term sustainability is also requested, as well as ad hoc training for staff involved in the care of RD patients.** ➔ **It is necessary that the importance of specialised services for RD patients for patients and families is recognised. It is also demanded that their support through public money becomes a priority for the whole community. Evaluation of the services provided should be carried, quality systems should be adopted as well as guidelines, staff should receive adequate professional training. Guidelines and best practices developed at the EU level within and beyond the EC-funded Rapsody project, coordinated by EURORDIS, should be used and supported further.** ➔ **Generally speaking, existing needs for specialised social services should be identified by means of a peer-to-peer discussion. Also, social studies have been mentioned as a tool to describe how to better use and save**

	resources in this field.
*R 6.6 Specialised social services are established to facilitate **integration of patients at schools and workplaces**.*	This Recommendation hints to the need of patients living with rare conditions to integrate into social life. This includes integration at school and workplaces, but extends to social life in general. ➔ **There is a strong need to adopt a holistic approach to each individual citizen. It is important that everyone masters the daily situation. Continuity of care should be guaranteed. In particular the transition from childhood to adult age should become smoother. The latter concern, in particular, involves training and education of GPs and healthcare professionals in non paediatric hospitals, not used to treat RD. It is necessary that this task is taken over by Centres of Expertise.** However quite a number of concerns were also raised particularly around the lack of funding for social care services, especially in the current economic climate, as cutbacks are expected. ➔ **In order to overcome the fact the RD are often "invisible" to social services, it would be beneficial for RD patients to design for them consistent, validated and evidence based healthcare pathways** (see Area 4), **covering a spectrum of conditions and symptoms. This would be particularly beneficial for those with a progressive or chronic condition. Coordinating information and outlining what a "good" pathway should look like could help to provide a more consistent service across the country, thus potentially decreasing the disparity of services that patients and families currently receive.** ➔ **Again, the proposals of "case managers"** (see Area 4) **or a "clinical liaison nurse specialist[10] was proposed also in Workshops of Area 6. The case manager would be the professional in the most suitable position to address the specific range of needs of the RD patient. S/he would also have a sound knowledge of the welfare system, so to be able to signpost appropriately.**
*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-***	*See above R 6.3*

[10] UK Final Report

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.).*	*See above Recommendations from R 6.1 to R 6.5, in particular.*
R 6.10 The activities aiming at patients' empowerment carried out by patients' associations are facilitated.	