European Project for Rare Diseases National Plans Development (EUROPLAN)

Selecting indicators to evaluate the achievements of RD initiatives

By WP5: Manuel Posada, Manuel Hens, Maria José Carroquino and EUROPLAN Working Group on Indicators

Rare Diseases Research Institute
Instituto de Salud Carlos III

Madrid March, 29th, 2010

Table of contents

Background and aims

The European Project for Rare Diseases National Plans Development (EUROPLAN) is a three-year project of the program of Community action in the field of Public Health (2003 - 2008), which began in April 2008.

The **main goal** of the project is to develop recommendations on how to define national/regional strategies/plans for Rare Diseases. These recommendations prioritize areas and actions of intervention in the field of rare diseases and provide advice on the different steps for developing a strategy/plan

Work Package 5 (WP5) of this project entitled "**Selecting indicators to evaluate the achievements of Rare Diseases initiatives**" has a main and unique objective defined as "**to identify indicators to assess Rare Diseases initiatives (monitoring the implementation and evaluating the impact of national plans for Rare Diseases)**" Thus, the starting point for looking for and identifying a list of indicators to assess rare diseases initiatives has to be mainly based on its utility for, i) monitoring the implementation and ii) evaluating its general impact.

On the other hand, the European Commission invites to elaborate an Implementation Report of the state of art of each Member State (MS) strategy/plan in 2013. Hence, in addition to providing some tools to evaluate MS activities in a uniform manner and aid to MS in the harmonization of their activities, indicators developed in this project could also contribute to the elaboration of comprehensive information to be included in that European Implementation Report. Therefore, the indicators will be important for the MS but also for the EU.

The concept of indicators development has already a long trajectory in the public health field. Since the end of the 18th century, information on the health of communities has been gathered on a health system level, and public health indicators have become more sophisticated over the years. The development and use of indicators is an integral part of planning and designing health services, as they are management tools for health care services and health systems (20). In the process of indicators selection, the relationship between each one of the indicators selected and their real potential usefulness for achieving their final objective must be considered. However, the same indicator could be valid for more than one objective, if either some variation on its computation or type of assessment is included. Prioritisation of indicators is important for two reasons, i) the first is cost because human resources in the measurement field are extremely scarce and ii) the second is visibility because indicators drive policy attention and resources nationally and regionally. This inevitable dynamic means that health problems with priority indicators will receive more attention than those that are not measured or not measured as well. Prioritisation requires several questions to be answered (24).

- **What is the proposed indicator intended to measure?**
- **What is the public-health significance of the indicator?**
- **How well does the indicator measure the quantity of interest?**
- **Is the indicator value readily interpretable?**
- **Is there a practical measurement strategy?**
- **How should equity dimensions of an indicator be captured?**

Indicators can be classified into six categories on the basis of what it is they measure: health outcomes, risk factors, intervention coverage, structure, process, and non-health-related results. All these types of indicators have important uses in different contexts (24).

In the field of RD, two main areas from two different perspectives where indicators could be applicable have been suggested. From one side, health indicators, devoted to facilitate topics on research and surveillance which are under the scope of the Rare Diseases Task Force-Working Group on Indicators (RDTF-WG), and on the other side indicators for health and social planning monitoring that are oriented to policy makers and planners and they are under the scope of this EUROPLAN project. However, both groups have been collaborating and partners of this project are also involved of the RDTF-WG.

At the same time, the high cost involved in creating and sustaining this type of public information systems and the scarcity of valid information in the field of rare diseases strongly calls for focusing our work on the development of those indicators that can accomplish and fulfill the mentioned EUROPLAN aims. To do so, WP5 takes into account the areas of interest listed in the EU Council Recommendation and the EU Commission Communication on RD and the EUROPLAN WP7 document entitled "**Recommendations for the development of national plans for Rare Diseases Guidance Document"**

Methods

Previous considerations with regard the development of indicators

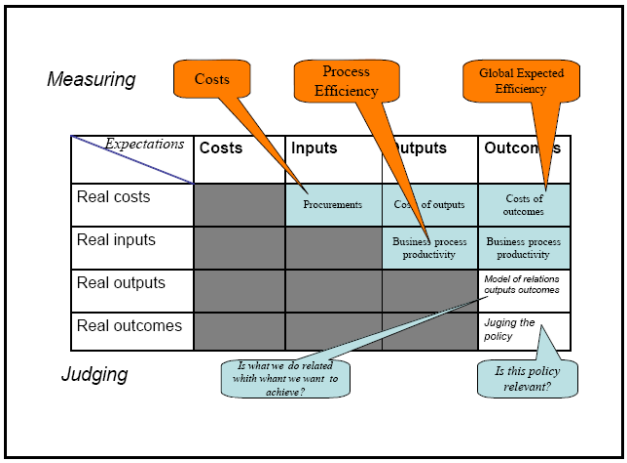
Building of a set of harmonized indicators on rare diseases strategies/plans is a complex task requiring a great consensus and also a careful analysis of its feasibility. In addition, there is little experience on this particular area because only France has finished its first national plan on RD and evaluated its impact (16, 18).

There are also thousands of diseases showing different and specific questions and necessities; there is not a universally accepted classification of rare diseases; valid information about the evaluation of the RD activities related with the health care systems is insufficient or lacking; and countries' health care systems do not always follow the same organizational scheme across Europe, among others added difficulties. Therefore, some capacity building for developing specific and new indicators useful for RD purposes needs to be developed.

On the other hand, it should be taken into account that once indicators are approved, they will require some institution to be responsible for collecting and sustaining the resulting information system. It is also well known that turning data into valid information for planning health services is a difficult matter (20). In summary, the procedure for selecting indicators developed within this WP5 has taken into account the following main items,

- The areas of the plan and their specific actions
- Well defined criteria for selecting indicators addressed to the aims of each action
- Clear definition of the sources of information available
- Preliminary considerations in the estimation of the cost of sustaining an information system (Figure 1) (33).

Figure 1. Some considerations about indicators system implementation



Areas of work for selecting indicators

EUROPLAN WP4 has been in charge of organizing the discussion and of developing the appropriate activities to reach a final consensus on the areas to be developed. One of the agreements reached in EUROPLAN was to adopt as the main references for the identification of priority areas, the two recently launched European documents related to the RD field: 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"*** (4) **and the *"COUNCIL RECOMMENDATION on an action in the field of rare Diseases"*** (5). The list of areas was taken for the latest of them. The full list of areas is:

Area 1- Plans and strategies in the field of Rare Diseases

Area 2- Adequate definition, codification and inventorying of Rare Diseases

Area 3- Research on Rare Diseases

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

Area 5- Gathering the expertise on Rare Diseases at European level

Area 6- Empowerment of patient organisations

Area 7- Sustainability

Sources of information

There are various sources of information for selecting indicators such as administrative databases, websites from other European indicator projects, national/regional health statistics, advocacy group databases, national/regional surveys, etc. The analysis of all of

these sources, allowed us to distinguish some areas for which indicators could be already available and other areas where new indicators would have to be developed.

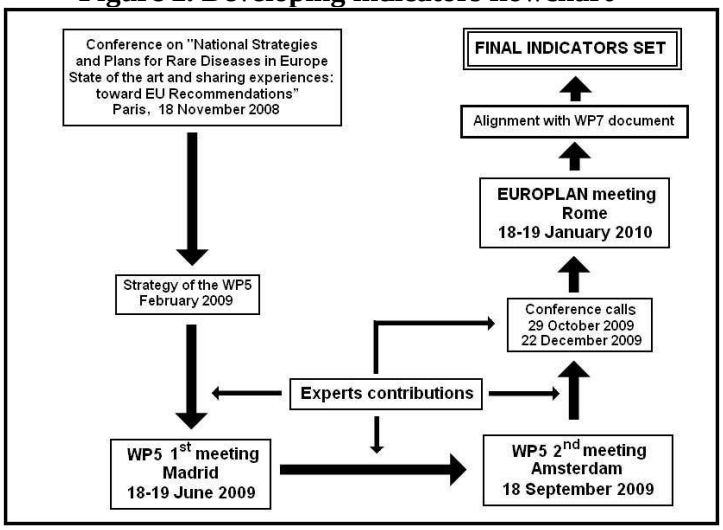
The final version of the first report of the Rare Diseases task Force Working Group edited on June, 2008 and titled ***"HEALTH INDICATORS FOR RARE DISEASES: State of the Art and Future Directions"*** (29) stated that ***"the development of relevant indicators is crucial for the monitoring of rare disease health policy and knowledge progression at the European and single member state/region levels"***. At the same time, this report emphasized that actions for developing indicators in the RD field should be based on their relevance, utility, reliability, validity, applicability, accessibility and feasibility. A new final report from the second workshop on Health Indicators for Rare Diseases belonging from the RDTF-WG on Health Indicators will be available soon. However, although results of the RDTF-WG work on indicators exceeded by far the needs of EUROPLAN, the experience of the RDTF-WG in this field is very valuable and has been considered in our work for our purposes.

EUROPLAN-WP5 work flowchart on Indicators Developing

On the basis of the strategy commented above, we delivered the first draft report in Feb, 2009. The second version was in April, 2009 and a comprehensive document was discussed during the meeting held in Madrid in June, 2009. After the Madrid meeting, some amendments were added, and a third version, was discussed in meeting held in September 2009 in Amsterdam. Finally, after the meeting held in January 2010 in Rome an alignment with the WP7 document was made (Figure 2).

This process has been always fitted with patient demands, MS possibilities and EU requirements. In this way, EURORDIS has always been involved not only as an associated EUROPLAN partner but as patient representative.

Figure 2. Developing indicators flowchart



More than an hundred amendments to the initial draft coming from partners, external experts and policy–makers were taken into account. After discussing and reaching a

consensus through lengthy and rigorous discussions, the final document includes 7 **different areas, 14 aims, 27 actions and 59 indicators (Table 1).**

Table 1.- Summary of results

Area no.	Aims	Actions	Indicators
1	1	5	7
2	3	3	5
3	3	3	10
4	1	1	5
5	3	6	13
6	2	7	16
7	1	2	3

TOTAL			
Areas	**Aims**	**Actions**	**Indicators**
7	14	27	59

Indicators are presented in this report in tables by specific areas preceded by some general comments about the following items: Background, Key Message, Rationale, and Health context. Each table area includes aims, actions, indicators associated to them, type of indicator (process, outcomes) and methods for computation[1].

Basic Criteria for Selection of Indicators and their assessment

It is clear that, in order to optimize efforts and resources, we have only utilised those indicators that have the capacity of pointing out changes in the trend of actions implemented, enabling comparison of the current period (the time when an evaluation is needed) with a previous period (the time where the plan had not been yet implemented). If this is not possible, the system at least has to provide accurate information about the current state of the actions and activities implemented in order to consider if planned resources are sufficient, assess their efficiency and/or allow us to make valid comparisons between geographical areas and MS.

In the same way as other public health tools, indicators must be evaluated. In the initial phases of the design of a monitoring system, indicators are roughly set up, so there is the need to evaluate them. However, at present it was not possible to perform a deep evaluation of this set of indicators due to the time limitation of the EUROPLAN project. Because of these limitations, it was considered that the consensus reached by an expert panel was an acceptable criterium for the inclusion or exclusion of an indicator from the list (33).

Thus, we have developed an evaluation procedure based on a set of properties containing general criteria and on a set of specific issues suggested by several stakeholders. Definitions of each one of those properties and issues were taken from different standardized sources and they are based on following principles, A) the right indicator is

[1] Note that code numbers preceding each one of the indicators do not necessarily are coincided with the order of recommendations included in the WP7 document

essential for effectively evaluating your progress and B) the right indicator should: 1. Be relevant; 2. Be easily understandable to everyone interested in the analysis of the situation; 3. Be easily measured; 4. Provide reliable information (3).

These criteria fit very well with the basic criteria of the EC for defining health indicators in the ECHI program (34), which state that indicators for Europe have to be,

- Easy to read and understand
- Policy relevant
- Mutually consistent
- Available in a timely fashion
- Available for most, if not all Member States, Acceding and Candidate countries
- Comparable between these countries and, as far as possible, with other countries
- Selected from reliable sources
- Not impose too large a burden to Statistical Institutes, Ministries of Health and other respondents

However, some refining of these properties led us to categorize EUROPLAN indicators according to three criteria, namely, ***intrinsic properties; resources demand and decision making.***

The list of indicators properties and their standardized definitions are included in the Annex1.

In addition we provide an evaluation table for each group of indicators, based on the scoring of each of the indicator properties considered. A simple score system - **High, Medium, Low and non-applicable** (see legend at the top of each table) – as interpreted by the expert panel has been used for filling out these tables. These tables provide a visual overall impression of the strengths and weaknesses of the indicators proposed, and can orient directions for further work on the development of indicators.

Given the large number of indicators proposed, and the large number of properties considered. It would be difficult to make an overall assessment of each group of indicators (for each priority area) on the basis of this table. The table is offered as a way to illustrate a preliminary qualitative assessment method that can be refined in the future for the assessment of the indicator system.

A table of summary of indicators is also shown in Annex 2.

Area 1.- Plans and strategies in the field of Rare Diseases

Background: A Rare Diseases Plan or Strategy is now considered as one of the priority topics by the Commission Communication on Rare Diseases approved on November, 11, 2008 (4-5). Rare Diseases have become the area where a better coordination of all actions is really needed. Patients and families come across and endure difficulties resulting directly from the diseases they suffer, as well as a result of the needs of services and resources they have.

Key Message: It is important that MS develop some RD coordinated actions, RD strategy/plan in advance, according to the principles of the Commission Communications.

Rationale: These seven indicators serve as for **a** global follow up of this main action, and it is important that MS include these indicators in their own aims as a way for comparison with other countries. MS regularly elaborate some type law or regulation when they need to implement some policy actions that they foresee to have major effects on the population. That is why, the first of these indicators checks if this type of normative has been established in a country. Along these types of actions, some other indicators may explore how the plan will be coordinated and whether there is an Advisory Committee in charge of maintaining appropriated surveillance and correct defects when needed. Finally, it is important to know the temporal and geographical setting of this plan. Some MS may decide to develop plans limited to some geographical regions. At the same time, it is a common way of work that plans have a limited duration and appropriate budget. Therefore, a plan should be dynamic, because ideally it should be assessed, modified and/or adapted according to the new knowledge regularly.

Health context: It is obvious that most of difficulties and needs suffered by the RD patients are related to lack of accessibility of appropriate health services. Thus, indicators are very important from the health perspective because plans have to be oriented to solve some of these problems (29).

Area 1.- Plans and strategies in the field of Rare Diseases

Area to be explored	Aims	Actions	Indicators		Type of indicator	Answers
Plans and strategies in the field of Rare Diseases	To establish National/Regional plans and/or strategies on RD	Development of Regulations/Laws	1.1.	Existence of regulations/laws that support the creation and development of a RD plan	Process	• *Not existing, not clearly stated* • *Existing, clearly stated, partly implemented and enforced* • *Existing, clearly stated and substantially implemented and enforced*
			1.2.	National/regional (percentage of regions)	Process	*Index based on the number of regions with a plan divided by total number of regions. A national plan will account for this index equal 100%*
		Establishment of Coordination mechanisms	1.3.	Existence of a coordination mechanism	Process	• *Not existing, not clearly stated* • *Existing, clearly stated, partly implemented and enforced* • *Existing, clearly stated and substantially implemented and enforced*
			1.4.	Existence of an expert advisory committee	Process	• *Exiting and meets regularly* • *Exists but partly functioning* • *Does not exist*
		Establishment of an external evaluation of the plan/strategy procedure	1.5.	Existence of an external evaluation body/procedure	Process	• *Number of meetings held by year*
		Degree of comprehensiveness	1.6.	Number of priority areas included in the plan	Process	• *Number ranging from 0 to 10*
		Establishing of a budget for developing the plan/strategy	1.7.	Budget of plan/strategy	Process	• *Overall budget allocated*

High ☐ Medium ■ Low ■ ☐ non-applicable

List of Indicators		Intrinsic properties							Resource demand					Decision making			
		Understandability	Reliability	Validity	Consistency	Sensitivity	Specificity	Feasibility	Availability	Sustainability	Implementability	Workload demand	Timeliness	Applicability	Coherence	Comprehensiveness	Relevance
1.1.	Existence of regulations/laws that support the creation and development of a RD plan		■	■	■	■	■										
1.2.	National/regional (percentage of regions)																
1.3.	Existence of a coordination mechanism																
1.4.	Existence of an expert advisory committee																
1.5	Existence of an external evaluation body/procedure		■	■	■	■	■										
1.6.	Number of priority areas included in the plan																
1.7.	Budget of plan/strategy		■	■	■	■	■	■									

Area 2.- Adequate definition, codification and inventorying of rare diseases

Background: One of the major problems in the RD field is the lack of an inventory of diseases with unique codes. WHO International Classification of the Diseases and other systems that allow either cataloguing or classifying diseases are not universally adopted and/or they are insufficient for thousand of RD diseases currently known. To develop adequate mechanisms for definition, codification and inventory of rare diseases, in order to provide a framework for recognition of rare diseases, and facilitate the sharing of knowledge and expertise is an essential task to be developed in a RD plan (4, 31-32).

Key Message: Adopting the strategy of incorporating the most updated classification of rare diseases is the best way for improving RD knowledge and patients quality of life.

Rationale: Most of RD are not so well recognized because they are not included in any list of diseases. International classifications are good instruments for developing health and social services but at the same time, they require a long and complicated process where an international consensus has to be reached. That is the reason why, updating these type of classification requires and lengthy discussions and time, while the scientific knowledge is quickly growing. These difficulties negatively impact on RD knowledge and recognition. At the same time, information on several other activities such as information systems on RD, and registering issues is going to be collected under this area.

Health context: Health Care Systems use some list of diseases – generally some WHO ICD version – for monitoring activities, costs and health care burden. Updating these classification systems is always problematic because the relationships between versions are not simple and this produces some break in the series of several indicators used by the policy makers. However, RD necessarily involve these type of transformation and system adaptability. Patient outcome registries are wonderful tools for collecting cases for clinical trials and observational studies.

Area 2.- Adequate definition, codification and inventorying of rare diseases

Area to be explored	Aims	Actions	Indicators		Type of indicator	Answers
Adequate definition, codification and inventorying of rare diseases	Use a common definition	To officially adopt the EC RD definition (No more than 5 cases / 10,000 inhabitants)	2.1.	Adoption of the EC RD definition	Process	• *Yes* • *not* • *EU definition modified with an additional definition*
	Ensure that RD are adequately coded and traceable in the health care information system	To include the best RD diseases classification currently existing into the public health care related services	2.2.	Type of classification used by the health care system	Process	• *ICD-9* • *ICD-10* • *OMIM* • *SNOMED* • *ORPHAN* • *MESH* • *Others*
			2.3.	Developing policies for recognising RD by the care information systems	Process	• *Not existing, not clearly stated* • *Existing, clearly stated, partly implemented and enforced* • *Existing, clearly stated and substantially implemented and enforced*
	Support registries for better epidemiological knowledge	Defining a surveillance system based on a patient outcomes registry	2.4.	Registering activity	Process	• *Centralized RD registry* • *Multiple RD registries but well coordinated and standardized* • *Multiple RD registries not standardized* • *No registry at all*
			2.5.	Number of diseases included	Outcomes	*Number ranging from 1 to 20*

High □ Medium ■ Low ■ non-applicable □

List of Indicators		Intrinsic properties							Resource demand					Decision making			
		Understandability	Reliability	Validity	Consistency	Sensitivity	Specificity	Feasibility	Availability	Sustainability	Implementability	Workload demand	Timeliness	Applicability	Coherence	Comprehensiveness	Relevance
2.1.	Adoption of the EC RD definition																
2.2.	Type of classification used by the health care system																
2.3.	Developing policies for recognising RD by the care information systems																
2.4.	Registering activity																
2.5.	Number of diseases included																

Area 3.- Research on Rare Diseases

Background: The term "Rare Diseases" was born from the lack of research on new drugs by the pharmaceutical industry. Research gaps were first detected among low prevalence diseases together with some other difficulties associated to the lack of information. Research is the underlying way for acquiring new knowledge and providing information that can be used for policy makers when they need to plan for resources and other social and health issues.

Key Message: It is important to define research priorities oriented to improving the knowledge of RD ethiology, mechanisms, treatment and prevention.

Rationale: Research is one of the major tasks demanded by RD patients and families (8). Research is always the main gap detected when RD patient needs are faced and have to be addressed. Improving RD knowledge is the only way to ameliorate patients suffering.

Health context: Health and social research should be closely joined to a better health services provision. In addition, health research is the best method to address knowledge gaps and deficiencies in the health care system.

Area 3.- Research on Rare Diseases

Area to be explored	Aims	Actions	Indicators		Type of indicator	Answers
Research on Rare Diseases	Support research programmes for RD	Building a research programmes for RD	3.1.	Existing a RD National/Regional research programmes	Process	• *Specific research programme for RD* • *RD research programme included in the general research programme as a priority* • *Not RD research programme*
			3.2.	RD research programme monitoring	Process	• *Not existing, not clearly stated* • *Existing, clearly stated, partly implemented* • *Existing, clearly stated and substantially implemented*
			3.3.	Number of RD research projects approved by year (if possible yearly starting the year before plan commencement)	Outcomes	*Percentage of RD projects by the total of projects approved*
			3.4.	Clinical trials funded by public bodies	Outcomes	• *Yes, action implemented* • *No actions have been taken* • *Under discussion*
			3.5.	E-RARE joining	Process	• *On going* • *In process* • *not considered*
			3.6.	Including public health and social research, in the field of rare diseases	Process	• *Yes* • *No* • *Under discussion*
			3.7.	Research platforms and other infrastructures are also funded by the research programme	Process	• *Yes* • *No* • *Under discussion*

	Recruitment of young scientists	Existence of national policy in support of the recruitment of young researchers/scientists specifically for rare diseases	3.8.	Number of young scientists recruited every year to work specifically on rare diseases	Process	• *Number great equal zero*
	Ensure funds for the research programme	Allocate funds for the RD research programme	3.9.	There are specific public funds allocated for RD research	Process	• *Yes* • *No* • *Under discussion*
			3.10.	Funds specifically allocated for RD research actions/projects per year since the plan started	Outcomes	• *Million Euros allocated to RD research projects* • *Percentage of funds allocated for RD projects by the total funds allocated for projects*

High Medium Low non-applicable

List of Indicators		Intrinsic properties							Resource demand					Decision making			
		Understandability	Reliability	Validity	Consistency	Sensitivity	Specificity	Feasibility	Availability	Sustainability	Implementability	Workload demand	Timeliness	Applicability	Coherence	Comprehensiveness	Relevance
3.1.	Existing a RD National/Regional research programmes																
3.2.	RD research programme monitoring																
3.3.	Number of RD research projects approved by year (if possible yearly starting the year before plan commencement)																
3.4.	Clinical trials funded by public bodies																
3.5.	E-RARE joining																
3.6.	Including public health and social research, in the field of rare diseases																
3.7.	Research platforms and other infrastructures are also funded by the research																
3.8.	Number of young scientists recruited every year to work specifically on rare diseases																
3.9.	There are specific public funds allocated for RD research																
3.10.	Funds specifically allocated for RD research actions/projects per year since the plan started																

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

Background: One of the problems in the management of RD is the diagnosis delay. This problem is due to several factors such as lack of knowledge but also to the lack of coordination between the primary health care barrier and specialized hospital centres. Care and services for families and patients with rare disease are currently patchy and fragmented. A centre of expertise is a natural way of thinking of patients and families when they have a disease for which they do not receive diagnosis and neither appropriated treatment nor follow up.

Key Message: Ensuring access to high-quality healthcare, in particular through identifying national and regional centres of expertise. Their participation in European Reference Networks should be then welcome.

Rationale: Centres of expertise that are able to reach and join high level of expertise are strategies within health care systems that are capable to provide the best of options for patients care. Research can also benefit from centres of expertise because they have the possibility of providing subject cases for research and improve the knowledge and expertise of their own and other health professionals.

Health context: Creating a network of centres of expertise is challenging for national health care systems that need to provide many other health resources and have to care to the whole population. However reference centres have always been a demand by patients and professionals and they have been shown to be highly beneficial for the system (11, 15, 30). A clear definition of the care pathway* - the way must be followed by the patients from the primary care until the centre of expertise - is also important and necessary.

***Care Pathway**

The European Pathway Association defines a clinical/care pathway as:

Care pathways are a methodology for the mutual decision making and organization of care for a well-defined group of patients during a well-defined period.

Defining characteristics of care pathways includes:

An explicit statement of the goals and key elements of care based on evidence, best practice, and patient expectations;

The facilitation of the communication, coordination of roles, and sequencing the activities of the multidisciplinary care team, patients and their relatives;

The documentation, monitoring, and evaluation of variances and outcomes; and

The identification of the appropriate resources.

The aim of a care pathway is to enhance the quality of care by improving patient outcomes, promoting patient safety, increasing patient satisfaction, and optimizing the use of resources.

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

Area to be explored	Aims	Actions	Indicators		Type of indicator	Answers
Centres of Expertise and European Reference Networks for Rare Diseases	Identify and/or establish national/regional centres of expertise and European reference network of centres	Improve the quality of health care by defining appropriate centres with experience on RD as well as pathways* (*see operative definition above*) that reduce the diagnosis delay and facilitate the best both cares and treatments to patients	4.1.	Existence of a policy for establishing centres of expertise at the national/regional level	Process	• *Not existing, not clearly stated* • *Existing, clearly stated, partly implemented* • *Existing, clearly stated and substantially implemented*
			4.2.	Number of centres of expertise adhering to the policy defined in the country	Outcomes	*Number of reference centres*
			4.3.	Groups of rare diseases followed up in centres of expertise	Outcomes	Computation must be referred to the whole country *Covering all or most of rare diseases* *Covering only some rare diseases*
			4.4.	Centres of expertise adhering to the standards defined by the Council Recommendations - paragraph d) of preamble	Outcomes	*Percentage of centers of expertise adhered by the total of centers of expertise designed*
			4.5.	Participation of national or regional centres of expertise into European reference networks	Outcomes	*Index based on Number of centres of expertise cooperating with ERN by number of total of centres of expertise designed*

High ☐ Medium ☐ Low ☐ non-applicable ☐

List of Indicators		Intrinsic properties							Resource demand					Decision making			
		Understandability	Reliability	Validity	Consistency	Sensitivity	Specificity	Feasibility	Availability	Sustainability	Implementability	Workload demand	Timeliness	Applicability	Coherence	Comprehensiveness	Relevance
4.1.	Existence of a policy for establishing centers of expertise at the national/regional level																
4.2.	Number of centres of expertise adhering to the policy defined in the country																
4.3.	Groups of rare diseases followed up in centres of expertise																
4.4.	Centres of expertise adhering to the standards defined by the Council Recommendations - paragraph d) of preamble																
4.5.	Participation of national or regional centres of expertise into European reference networks																

Area 5.- Gathering the expertise on Rare Diseases at European level

Background: Covering the ***lack of information on RD*** for professionals has been one of the challenges of EUROPLAN. The existence of information sites for professionals can significantly improve both the clinical assistance provided by professional, as well as the patients' satisfaction. Promoting the existence of ***training activities and awareness*** educational campaigns among professionals could also contribute to that. In the same way, ***early diagnosis*** and timely access to appropriate treatment are very important for many rare diseases that are progressive in nature. ***Diagnosis delay*** is one of the claims frequently manifested by patients and families. Conversely, technologies evolves, many tests can now be performed, including those by robots, at low cost for a wide range of rare diseases, especially metabolic disorders and genetic conditions in general. To facilitate the application of all these technologies to reduce diagnosis delay is one of the major points looking for RD plans. The ***accuracy of diagnosis*** is also considered in the aims of this important area of work. In addition to diagnosis delay, accurate diagnosis and ***access to orphan drugs*** are also of the utmost importance. There are specific bottlenecks in access to orphan designated drugs (ODD) through the decision making process for pricing and reimbursement linked to rarity. The way forward is to increase collaboration at the European level for the scientific assessment of the (added) therapeutic value of Orphan Medicinal Products.

Key Message: The existence of information sites for professionals can improve the clinical assistance provided by professional. RD diagnosis delay has to be reduced while the new technologies have to be incorporated into clinical practice keeping in mind their clinical validity and utility. The validation of diagnostic test and RD laboratories are important aspects for the accurate diagnosis of RD (9). Accessibility to ODD treatment is a measurement of efficacy of a RD plan.

Rationale: Education and training programs addressed to health professionals will increase the quality of the care provided to RD patients. This could be of special interest for family practice professionals. Family doctors specialize in the management of common problems, but they can improve their role in the care of patients with RD, and they could provide a broad range of services to a wide variety of patients with rare diseases (26). The production of reliable educational materials must be a consequence of the RD plans and strategies, and the access to formative and informative resources will increase the professional ability and self-awareness, reducing psychological stress and the risk of professional burn-out that affects professionals involved in chronically ill patients-care. It is recommended to encourage cooperation in the area to generate evidence on which decisions should be based at Member States level. An evaluation of existing population screening strategies (including neonatal screening) for rare diseases and of potential new ones at EU level will be conducted by the Commission to provide Member States with the evidence (including ethical aspects) on which to base their political decision. Regarding to the access to OD, the Commission will set up a working party to exchange knowledge between Member States and European authorities on the scientific assessment of the clinical added value of OD. These collaborations could lead to non-binding common clinical added value assessment reports with improved information that facilitate the national pricing and reimbursement decisions, without pre-empting respective roles of the authorities.

Health context: Existence of a comprehensive national and/or regional RD information systems, as well as help lines for professionals and development of clinical guidelines are very important milestones in the care to RD patients and families. Covering the lack of information on RD has been one of the challenges of EUROPLAN. It is evident that knowledge and information can improve clinical assistance, help in managing the disease for both the patients and care providers, and protect health care professionals from burn-out and psychological stress. Therefore, the promotion of information access should be part of any strategic plan on rare diseases. New genetic and biochemical diagnosis tests are feasible for clinicians and they can improve the patient quality of life reducing the diagnosis delay and providing important skills for the patient management. However, these tests have to be checked in order to assess their internal properties and cost-effectiveness (9). Population based screening programmes are challenging for health care systems. While technology provides new tools for early detection of diseases, they are not always properly assessed before their introduction for regular use in the health system. Policy makers need for standardized criteria to assist in making the right decisions about the diagnostic tests and the inclusion of new diseases in the neonatal screening program. Finally, ODD are one of the most important advances in the RD treatment. Some RD historically having bad prognosis, are now becoming chronic diseases with a high levels of quality of life (17, 21). The high cost of the ODD is usually seen by policy makers as one of the inconveniences of developing a RD plan. However, these actions should be seen from the perspective that patients treated with these drugs improve their health and their ability to contribute to society (7, 10).

Area 5.- Gathering the expertise on Rare Diseases at European level

Area to be explored	Aims	Actions		Indicators	Type of indicator	Answers
Gathering the expertise on Rare Diseases at European level	Improving education and training	Existence of a information sites for professionals provided by the plan/strategy	5.1.	Existence of a comprehensive national and/or regional RD information system supported by the government	Process	• *Yes, covers most RD* • *Yes, covers only some RD* • *Not formal decisions have been taken*
			5.2.	Help lines for professionals	Process	• *Yes, covers most RD* • *Yes, covers only some RD* • *Not formal decisions have been taken*
			5.3.	Clinical guidelines	Outcomes	*Number ranging between 0 to 30*
		Promoting training activities and awareness educational campaigns among professionals	5.4.	Number of such as activities promoted by the plan/strategy	Process	*Number ranging between 0 to 30*
	Ensuring early and accurate diagnosis	Develop screening policies	5.5.	Number of diseases included in the neonatal screening programme	Outcomes	*Number of diseases*
			5.6.	Number of diseases included in the neonatal screening programme properly assessed	Outcomes	*Index based on the number of disease tests assessed and included in the neonatal screening programme divided by the total number of diseases included in the neonatal screening program.*
		Ensure quality of RD diagnosis laboratory	5.7.	Existence of a public directory/ies of both genetic tests on Rare Diseases	Process	• *Yes* • *No* • *Under discussion*
			5.8.	Proportion laboratories having at least one diagnostic test validated by an external quality control	Outcomes	*Number of validated RD laboratories divided by the total number of RD laboratories*

	To ensure and accelerate accessibility to Orphan Designated Drugs (ODD)	Ensure the mechanism that facilitates ODD access and the reimbursement of their cost to patients after they got the market authorization by EMEA.	5.9	Number of ODD market authorizations by EMEA and placed in the market in the country	Outcomes	Index based on Number of ODD placed in the market by total of ODD approved by the EMEA
			5.10	Time between the date of a ODD market authorization by EMEA and its actual date of placement in the market for the country	Outcomes	Average days since the date of market authorization by EMEA until the official date of placement in the market in the country
			5.11	Time from the placement in the market in the country to the positive decision for reimbursement by public funds	Outcomes	Average days since the date of placement in the market until the reimbursement decision date in the country
			5.12	Number of ODD reimbursed 100%	Outcomes	*Number ranging 0 to 1,000*
		To develop mechanisms to accelerate ODD availability	5.13	Existence of a governmental program for compassionate use for Rare Diseases	Outcomes	• *No* • *Yes* • *In process*

High ☐ Medium ■ Low ■ non-applicable ☐

List of Indicators		Intrinsic properties							Resource demand					Decision making			
		Understandability	Reliability	Validity	Consistency	Sensitivity	Specificity	Feasibility	Availability	Sustainability	Implementability	Workload demand	Timeliness	Applicability	Coherence	Comprehensiveness	Relevance
5.1	Existence of a comprehensive national and/or regional RD information system supported by the government																
5.2.	Help lines for professionals																
5.3	Clinical guidelines																
5.4	Number of such as activities promoted by the plan/strategy																
5.5	Number of diseases included in the neonatal screening programme																
5.6	Number of diseases included in the neonatal screening programme properly assessed																
5.7	Existence of a public directory/ies of both genetic tests on Rare Diseases																

High ☐ Medium ■ Low ■ non-applicable ☐

5.8	Proportion laboratories having at least one diagnostic test validated by an external quality control															
5.9	Number of ODD market authorizations by EMEA and placed in the market in the country															
5.10	Time between the date of a ODD market authorization by EMEA and its actual date of placement in the market for the country															
5.11	Time from the placement in the market in the country to the positive decision for reimbursement by public funds															
5.12	Number of ODD reimbursed 100%															
5.13	Existence of a governmental program for compassionate use for Rare Diseases															

Area 6.- Empowerment of patient organisations

Background: Many difficulties and needs suffered by the RD patients are related to lack of information on RD. Promoting the access to information on RD of patients and their families can help them gain better knowledge of their process, as well as facilitate their access to diverse resources (1). This could reduce their level of uncertainty, and improve their perception about the resources that the community makes available for them. The production of reliable educational materials is an important result of RD patient organizations aimed at empowered RD affected patients and families, but it must be also a consequence of the RD plans and strategies. RD advocacy groups have existed for a long time but only when considering disease by disease. However, RD are defined as low prevalence diseases and most of them do not get the enough number of cases for creating their own association. Recently, large organizations and federations of different RD are joining to represent common interests although assuming their lack of specificity. It is also to be considered that social services have been the only possibility for supporting patients affected by RD for years, and they significantly support patients and families. Also, covering the lack of information on RD for patients has been one of the challenges of EUROPLAN. The existence of information sites can significantly improve the patients' satisfaction.

Key Message: To ensure that patients and patients' representatives are duly consulted at all steps of the policy and decision-making processes in the field of rare diseases, and that while new scientific knowledge is developing, social services continue to be the only support for many patients and families, and the existence of information sites for patients and families can improve their patients' satisfaction.

Rationale: Before large RD organizations started, RD were neglected due to the low number of cases by disease. Once these organizations started to work, many and important advantages have been achieved for RD patients and their families (1). The main idea of this area to be included in a RD plan is to facilitate the representation of families and patients when important decisions relevant to them are taken (12, 14). It is also to be considered that RD have many types of difficulties and most of them are health related. Chronicity and disability are consequences from the health status but the solution is not yet available and some type of social support has to be provided to patients. Respite Care and Therapeutic Recreational Programmes* can significantly improve the quality of life of both patients and their families (12, 14).

Health context: Patients care is not only a question of the health care system. Advocacy groups provide help to their patients and they also incentive professionals to achieve high levels of quality in the health care services that they provide. Social services are very important and they can improve the health status. Social services are always considered by the policy makers as important issues. Providing good services applicable to the RD difficulties are one of the best options adopted. Existence of a comprehensive national and/or regional RD information systems, as well as help lines for patients are very important for patients and families. Knowledge and information can help in managing the disease for both the patients and care providers, and empower patients. The promotion of information access for patients should be part of any strategic plan on rare diseases. Health care systems are final beneficiaries of this interaction between patients and professionals.

***Definition of Respite Care (13)**.

Respite care is provided on a temporary basis for people who normally live at home, so that their carers can have a break from care giving. One of the important purposes of respite is to give family members time and temporary relief from the stress they may experience while providing extra care for a family member living with a rare disease. Respite care is provided to give the person living with the RD time and place to perform recreational and meaningful activities away from their parents/other caregivers.

There are several different approaches/ services to offering respite care:

a) Centre based respite care: requires that the individual come to a day centre, respite group home with assisted living facilities or a nursing home institution.
b) Residential based respite: the person living with a rare disease goes away to be looked after by someone else/a "respite care family".
c) Domiciliary care: Some services allow a caregiver to come to the family's home and take over for a certain period so the care giver(s) can have some time off.

Definition of Therapeutic Recreational Programmes (13).

Any formally or informally organised recreation activity (e.g. summer camps, ad hoc trips) which has been setup with the needs of children or young adults with rare diseases in mind. Activities are centered on fun, leisure and entertainment. They may include regular or ad hoc activities, at offsite summer camp or at the association's site.

Examples of social services to integrate patients in their daily life (13).

- Educational support for patients, relatives and caretakers;
- Individual support at school at different schooling levels, for both pupils with rare diseases and teachers, including disease-specific good practices;
- Promotional activities aimed to foster higher education for people with rare diseases;
- Supporting mechanisms to enter and stay in work life for people with disabilities.

Area 6.- Empowerment of patient organisations

Area to be explored	Aims	Actions		Indicators	Type of indicator	Answers
Empowerment of Patients	Establishment of a mechanism that ensures that patients are empowered to directly contribute to shaping healthcare policies that affect their lives	Promoting the existence of a RD patients' organizations that represent all RD patient associations	6.1.	Number of umbrella organisations specific on RD	Process	• *No* • *Existing only one organization* • *Existing more than one organizations*
			6.2.	Having a directory of RD patients organizations	Process	• *No* • *Yes* • *In process*
			6.3.	Number of Patients' associations	Outcomes	*Number of patients associations*
			6.4.	Number of diseases covered by patients' associations	Outcomes	*Number of diseases covered by patients' associations*
		Patients' organizations involvement in decisions affecting RD	6.5.	Permanent and official patients' representatives in plan development, monitoring and assessment	Process	• Yes, clearly established, substantially implemented and participation reimburse considered • Considered in the plan, not effectively implemented • Not considered
			6.6.	Participation of patients organizations in the development of RD research strategies	Process	• *Yes* • *Only as observers* • Are consulted before the final document i approved • *No*
			6.7.	Participation of patients organizations in the RD centres of expertise designation and evaluation	Process	• *Yes* • *Only as observers* • Are consulted before the final document i approved • *No*
		Support the activities performed by including patient organizations, such as awareness raising, capacity-building and training, exchange of information and best practices, networking, outreach to very isolated patients	6.8.	Resource (funding) provided for supporting the activities performed by patient organisations	Outcomes	*Number of Euros allocated for activities supporting patients' organizations*
			6.9.	Support to sustainable activities to empower patients, such as awareness raising, capacity-building and training, exchange of information and best practices, networking, outreach to very isolated patients	Outcomes	*Number of activities per year sponsored withi plan*

		Building - supporting the existence of comprehensive help line and information sites for patients provided by the plan/strategy	6.10.	Availability of Help line for RD	Process	• *Own help line* • *Referred RD help lines* • *Not formal decisions have been taken*
	Improving patients quality of life by supporting disability programmes and social services aimed at RD	Compensating disabilities caused by rare diseases	6.11.	Existence of official programs supporting patients and families with disabilities	Process	• *Not existing, not clearly stated* • *Existing, clearly stated, partly implement and enforced* • *Existing, clearly stated and substantially implemented and enforced*
			6.12.	Existence of an official directory of social resources for patients with disabilities	Process	• *Yes* • *No* • *In preparation*
		Supporting social services aimed at rare disease patients and their families	6.13.	Existence of national schemes promoting access of RD patients and their families to Respite Care services	Process	• *Yes* • *Yes, and it includes financial support to patients/families* • *No* • *In preparation*
			6.14.	Existence of public schemes supporting Therapeutic Recreational Programmes	Process	• *Yes* • *Yes, and it includes financial support to patients/families* • *No* • *In preparation*
			6.15.	Existence of programmes to support integration of RD patients in their daily life	Process	• *Yes* • *Yes, and it includes financial support* • *No* • *In preparation*
		Supporting rehabilitation programmes	6.16.	Existence of programmes to support rehabilitation of RD patients	Process	• *Yes* • *Yes, and it includes financial support* • *No* • *In preparation*

High ☐ Medium ■ Low ■ non-applicable ☐

List of Indicators		Intrinsic properties							Resource demand					Decision making			
		Understandability	Reliability	Validity	Consistency	Sensitivity	Specificity	Feasibility	Availability	Sustainability	Implementability	Workload demand	Timeliness	Applicability	Coherence	Comprehensiveness	Relevance
6.1	Number of umbrella organisations specific on rare diseases		■	■	■	■	■	■	■	■	■	■	■				
6.2	Having a directory of RD patients organizations		■	■	■	■	■	■	■	■	■	■	■				
6.3	Number of Patients' associations		■	■	■	■	■	■	■	■	■	■	■				
6.4	Number of diseases covered by patients' associations		■	■	■	■	■	■	■	■	■	■	■	■			
6.5	Permanent and official patients' representatives in plan development, monitoring and assessment													■			
6.6	Participation of patients organizations in the development of RD research strategies		■	■	■	■	■	■						■			
6.7	Participation of patients organizations in the RD centres of expertise designation and evaluation		■	■	■	■	■	■	■	■	■	■	■	■			
6.8	Resource (funding) provided for supporting the activities performed by patient organisations		■	■	■	■	■	■	■	■	■	■	■	■			

High ☐ Medium ■ Low ■ non-applicable ☐

6.9	Support to sustainable activities to empower patients, such as awareness raising, capacity-building and training, exchange of information and best practices, networking, outreach to very isolated patients															
6.10	Availability of Help line for RD															
6.11	Existence of official programs supporting patients and families with disabilities															
6.12	Existence of an official directory of social resources for patients with disabilities															
6.13	Existence of national schemes promoting access of RD patients and their families to Respite Care services															
6.14	Existence of public schemes supporting Therapeutic Recreational Programmes															
6.15	Existence of programmes to support integration of RD patients in their daily life															
6.16	Existence of programmes to support rehabilitation of RD patients															

Area 7.- Sustainability

Background: Efficient and effective actions for rare diseases depend on mobilising scarce and scattered resources in an integrated way, and also integrated into a common European effort.

Key Message: Ensuring that RD actions include appropriate provisions to ensure their sustainability over time.

Rationale: A Rare Diseases plan needs to provide an appropriate strategy that allows policy makers to monitor if activities developed in the plan are having a positive impact on patients quality of life to modify the resources provision in order to adapt the health care system to the particular needs of these diseases. However, these changes have to be cost-effective or at least provide some benefit to the patients (cost-utility). None of these changes can be achieved if actions are not well sustained and funded (5).

Health context: Most changes that a RD plan has to provide affect the health care system. The main idea of these changes is to improve the health services that patients need to receive.

Area 7.- Sustainability

Area to be explored	Aims	Actions	Indicators		Type of indicator	Answers
Sustainability	Include in the National/Regional Plan/strategy for rare diseases provisions on the need for addressing the issue of financial sustainability	Ensure through appropriate funding mechanisms the long-term sustainability of infrastructures developed in the field of information, research and healthcare for rare diseases	7.1.	Existing policy/decision to ensure long-term sustainability of the RD plan /strategy	Process	• *Yes* • *Not*
			7.2.	Amount of funds allocated for ensuring RD plan /strategy sustainability	Outcomes	*Millions of Euros invested per year*
		Cooperate with other Member States to address the need for sustainability of European-wide research infrastructures, common to all Member States and common to the highest possible number of rare diseases	7.3.	Existing policy/decision to ensure the contribution to support RD European infrastructures	Process	• *Not existing, not clearly stated* • *Existing, clearly stated, partly implemented and enforced* • *Existing, clearly stated and substantially implemented and enforced*

High ☐ Medium ☐ Low ☐ non-applicable ☐

List of Indicators		Intrinsic properties							Resource demand					Decision making			
		Understandability	Reliability	Validity	Consistency	Sensitivity	Specificity	Feasibility	Availability	Sustainability	Implementability	Workload demand	Timeliness	Applicability	Coherence	Comprehensiveness	Relevance
7.1.	Existing policy/decision to ensure long-term sustainability of the RD plan /strategy																
7.2.	Amount of funds allocated for ensuring RD plan /strategy sustainability																
7.3.	Existing policy/decision to ensure the contribution to support RD European infrastructures																

References

1. Aymé S, Kole A, (2008). Groft S. Empowerment of patients: Lessons from the rare disease community. Lancet 371: 2048–51.
2. Cambridge Advanced Learner's Dictionary. Cambridge University Press 2009.
3. Carmin JA (ed). (2009). Check your success. A Community Guide to Developing Indicators. http://www.uap.vt.edu/checkyoursuccess/indicators.html
4. Commission of the European Communities. (2008). 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. Brussels, 11.11.2008. COM(2008) 679 Final
5. Commission of the European Communities. (2008). Proposal for a Council Recommendation on a European action in the field of rare diseases. Brussels, 11.11.2008. COM(2008) 726 final
6. Dictionary of Accounting Terms. (2005). Barron's Educational Series, Inc., New York. http://www.allbusiness.com/glossaries/consistency/4948891-1.html
7. EMEA (CHMP). (2004). Guideline on Compassionate Use of Medicinal Products, Pursuant to Article 83 of Regulation (EC) No 726/2004 http://www.emea.europa.eu/pdfs/human/euleg/2717006enfin.pdf
8. E-Rare (ERA-Net for research programs on rare diseases) (2009). http://asso.orpha.net/ERANET/cgi-bin/articles.php?lng=en&pg=17
9. EuroGenTest. 6th Frame Programme Harmonizing genetic testing across Europe. (2009). Best Practice Guidelines for Molecular Genetic Testing http://www.eurogentest.org/web/info/public/unit1/eqa/molecular_genetics/guidelines.xhtml
10. European Commission. (2009). Improving access to orphan medicines for all affected EU citizens, adopted by the EU High level Pharmaceutical Forum. http://ec.europa.eu/pharmaforum/
11. European Pathway Association. Clinical / Care Pathways. (2005). Slovenia Board Meeting. http://www.e-p-a.org/000000979b08f9803/index.html
12. EURORDIS position papers.(2009). http://www.eurordis.org/article.php3?id_article=1295
13. EURORDIS. The Voice of 12,000 patients. Publication of EurordisCare2 & EurordisCare3. http://www.eurordis.org/IMG/pdf/voice_12000_patients/EURORDISCARE_FULLBO_OKr.pdf
14. EURORDIS. (2007). Rare Disease Patient Solidarity (Rapsody). New services aimed at improving the daily lives of people living with a rare disease. http://www.eurordis.org/IMG/pdf/draft-leaflet_rapsody08-1.pdf
15. EURORDIS. (2007). Report on the European Workshop on Centres of Expertise and Reference Networks for Rare Diseases http://www.eurordis.org/IMG/pdf/EU_workshop_report_3.pdf
16. Évaluation du Plan national maladies rares 2005-2008. (2009). Haut Conseil de la santé publique. Ministère de la Santé et des Sports, Haut Conseil de la santé publique, April. http://ec.europa.eu/health/ph_threats/non_com/rare_4_en.htm
17. Francis DR. (2002). Orphan Drugs Cure Rare Diseases. NBER Digest. http://www.nber.org/digest/may02/may02.pdf
18. French National Plan for Rare Diseases 2005 – 2008. (2004). Ensuring equity in the access to diagnosis, treatment and provision of care. Secrétariat d'Etat aux personnes handicapées, Ministère de la santé et de la protection sociale. http://www.sante-jeunesse-sports.gouv.fr/IMG/pdf/French_National_Plan_for_Rare_Diseases.pdf

19. Holmgren P. Forest (2003). Resources Development Service. Forestry Department Food and Agriculture Organization of the United Nations. http://www.fao.org/forestry/5847-1-0.pdf
20. Klazinga N, Stronks K, Delnoij D, Verhoeff A. (2001). Indicators without a cause. Reflections on the development and use of indicators in health care from a public health perspective. International Journal for Quality in Health Care 13:433-438. http://intqhc.oxfordjournals.org/cgi/reprint/13/6/433
21. Lichtenberg FR. (2009). The Effect of New Drugs on Mortality from Rare Diseases and HIV. National Bureau of Economic Research. NBER Working Papers. http://ideas.repec.org/p/nbr/nberwo/8677.html
22. McGlynn EA. (1997). Six challenges in measuring the quality of health care. Health Affairs 16(3): 7-21.
23. Miller GA (ed). (2009). WordNet, Princeton University. The Trustees of Princeton University.http://wordnet.princeton.edu/
24. Murray, Christopher J L (2007). Health Statistics 2. Towards good practice for health statistics: lessons from the Millennium Development Goal health indicators. Lancet 369: 862-873
25. Nikolai LA, Bazley JD, Jones JP. (2009), Intermediate accounting. Eleventh Edition, South-Western Cengage Learning, Mason OH.
26. Phillips WR. (2004). Zebras on the commons: rare conditions in family practice. J Am Board Fam Pract 17(4):283-6.
27. Porta M. (2008). A Dictionary of Epidemiology. 5th ed. Oxford University Press, New York.
28. Pritchard RD, Ashwood EL. (2008). Managing Motivation: A Manager's Guide to Diagnosing and Improving Motivation. Routledge Taylor & Francis Group, New York.
29. Rare Diseases Task Force. (2008). Health Indicators for Rare Diseases: State of the Art and Future Directions. June. http://ec.europa.eu/eahc/documents/news/technical_meetings/FinalReportRDTFHI_Sept08.pdf
30. Rare Diseases Task Force. DG SANCO. (2008). Assessing the Added value of European Reference Networks in the Field of Rare Diseases Draft background document for the Rare Disease Task Force Standard of Care Workshop 11 March
31. Rare Diseases Task Force. DG SANCO. (2008).Coding and Classification of Rare Diseases at Orphanet. State-of-the-Art January
32. Rare Disease Task Force. (2008). Patient Registries and Databases in the Field of Rare Diseases: Technical, legal and ethical issues Patient Registries and Databases Workshop 13 March.
33. Rochet C, Bout-Colonna L, Keramidas O. The Risks of Efficiency Indicators in the Monitoring of Public Policies. EGPA 2005- Reforming the Public Sector – University of Bern. http://pagesperso-orange.fr/claude.rochet/pdf/Paper_Rochet_BoutCol.pdf
34. Strategy on European Community Health Indicators (ECHI) (2004). Network of Competent Authorities on Health Information. European Commission Health & Consumer Protection Directorate-General. Luxembourg, 5-6 July. http://ec.europa.eu/health/ph_information/documents/ev20040705_rd09_en.pdf
35. WordNet (r) 2.1 (2005). http://onlinedictionary.datasegment.com/word/applicability

Annex 1. Standard Definitions use for indicators assesment

A) Intrinsic properties

● **Understandable:** A good indicator is one that everyone can understand. People should be able to relate it to some common knowledge or personal experience (3).

● **Reliability:** Reliability refers to the degree of stability exhibited when a measurement is repeated under identical conditions. It can also be defined as the degree to which the results obtained by a measurement procedure can be replicated. Lack of reliability may arise from divergences between observers or instruments of measurement or inestability of the attribute being measured (23, 24, 27), or variability in the information sources.

● **Validity**: Relative absence of bias or systematic error. In reference to indicators, it would mean that the information provided is accurate (3, 27).

● **Consistency:** Close conformity between the findings in different samples, strata, or populations, or at different times or in different circumstances, or in studies conducted by different methods or investigators. In reference to RD indicators, .it would mean that the information provided is comparable across time and places (6, 19, 27-28).

● **Sensitivity** Sensitivity is the probability of correctly diagnosing a situation or the probability of correctly classifying any given situation with an indicator. However, there could be another meaning applied for indicators: *"Sensitivity testing"* is in the analysis on some situation, the ability to detect changes in the situation analysed when one or several parameters change (27).

● **Specificity**: is the probability of correctly identifying a non-existing circumstance when it is true that this circumstance does not exist (27).

● **Feasibility** is defined as the viability, practicability, or workability of a task, program or intervention. In reference to information systems and specifically to RD indicators, feasibility would refer to the viability of collecting, measuring and recording the indicator. Effective indicators are based on data that is easy to access or that can be measured directly at the setting (3, 27).

B) Resource demand

● **Availability**: **is** the fact that something can be easily obtained or reached. In reference to RD indicators it can refer to the degree of difficulty or easiness to which it can be obtained (2).

● **Sustainability:** the possibility of maintaining a specific intervention, program or task through time. In reference to information systems, it would mean that it will be possible to maintain the measurement of the indicator through time (27).

● **Implementation:** Effecting or putting in practice, or providing a practical means for accomplishing something. In reference to RD indicators, it would refer to the potential for the indicator to be implemented in a country health information system (23).

Workload demand: amount of work or number of work units assigned to a particular resource over a given period http://www.businessdictionary.com/definition/workload.html. In reference to RD indicators, it would refer to the amount of work necessary to measure, record and maintain the indicator. This can be divided in the workload needed for the two following attributes.

● **Timeliness** means that information is made available to decision makers before it loses its ability to influence decisions (25). In reference to RD indicators it would mean that the information provided by the indicator is on time to assist with effective decision making.

C) Decision making

● **Applicability:** quality of being applicable or fit to be applied. In reference to RD indicators it would mean that the information provided by the indicator can be used for practical decision making (35).

● **Coherence**: Epidemiological coherence is the extent to which a biological, clinical, or social observation is coherent with epidemiological evidence (1). In this particular case, coherence will be applied to the evidence knowledge and not only epidemiological information (27).

● **Comprehensiveness:** Comprehensiveness means that the indicator set covers the range of services, types of conditions, population groups, settings of care, and competing perspectives (2) for with it has been designed (22).

● **Policy relevance:** Indicators should be related to the goals of the strategy plan and enable you to evaluate whether the objectives have been achieved (3).

Annex 2. Table Sumary of Indicators

. Process indicators ☐ Outcomes indicators ☐

AREAS						
1	**2**	**3**	**4**	**5**	**6**	**7**
Plans and strategies in the field of RD	**Adequate definition, codification and inventorying of RD**	**Research on RD**	**Centres of expertise and European reference networks for RD**	**Gathering the expertise on RD at European level**	**Empowerment of patient organisations**	**Sustainability**
Existence of regulations/laws that support the creation and development of a RD plan	Adoption of the EC RD definition	Existing a RD National/Regional research programmes	Existence of a policy for establishing centers of expertise at the national/regional level	Existence of a comprehensive national and/or regional RD information system supported by the government	Number of umbrella organisations specific on RD	Existing policy/decision to ensure term sustainability of the RD plan
National/regional (percentage of regions)	Type of classification used by the health care system	RD research programme monitoring	Number of centres of expertise adhering to the policy defined in the country	Help lines for professionals	Having a directory of RD patients organizations	Amount of funds allocated for ens plan /strategy sustainability
Existence of a coordination mechanism	Developing policies for recognising RD by the care information systems	Number of RD research projects approved by year (if possible yearly starting the year before plan commencement)	Groups of rare diseases followed up in centres of expertise	Clinical guidelines	Number of Patients' associations	Existing policy/decision to ensure contribution to support RD Europe infrastructures
Existence of an expert advisory committee	Registering activity	Clinical trials funded by public bodies	Centres of expertise adhering to the standards defined by the Council Recommendations - paragraph d) of preamble	Number of such as activities promoted by the plan/strategy	Number of diseases covered by patients' associations	
Existence of an external evaluation body / procedure	Number of diseases included	E-RARE joining	Participation of national or regional centres of expertise into European reference networks	Number of diseases included in the neonatal screening programme	Permanent and official patients' representatives in plan development, monitoring and assessment	
Number of priority areas included in the plan		Including public health and social research, in the field of RD		Number of diseases included in the neonatal screening programme properly assessed	Participation of patients organizations in the development of RD research strategies	
Budget of plan/strategy		Research platforms and other infrastructures are also funded by the research programme		Existence of a public directory (ies) of both genetic tests on RD	Participation of patients organizations in the RD centres of expertise designation and evaluation	
		Number of young scientists recruited every year to work specifically on RD		Proportion laboratories having at least one diagnostic test validated by an external quality control	Resource (funding) provided for supporting the activities performed by patient organisations	
		There are specific public funds allocated for RD research		Number of ODD market authorizations by EMEA and placed in the market in the country	Support to sustainable activities to empower patients, such as awareness raising, capacity-building and training, exchange of information and best practices, networking, outreach to very isolated patients	
		Funds specifically allocated for RD research actions/projects per year since the plan started		Time between the date of a ODD market authorization by EMEA and its actual date of placement in the market for the country	Availability of Help line for RD	
				Time from the placement in the market in the country to the positive decision for reimbursement by public funds	Existence of official programs supporting patients and families with disabilities	
				Number of ODD reimbursed 100%	Existence of an official directory of social resources for patients with disabilities	
				Existence of a governmental program for compassionate use for RD	Existence of national schemes promoting access of RD patients and their families to Respite Care services	
					Existence of public schemes supporting Therapeutic Recreational Programmes	
					Existence of programmes to support integration of RD patients in their daily life	
					Existence of programmes to support rehabilitation of RD patients	

Annex 3. List of EUROPLAN Working Group on Indicators

ASSOCIATED PARTNERS

VALENTINA BOTTARELLI
LAURA FREGONESE
JOLANDA HUIZER
EDMUND JESSOP
LILISBETH PERESTELO-PÉREZ
ARRIGO SCHIEPPATI
PEDRO SERRANO AGUILAR
RUMEN STEFANOV
DOMENICA TARUSCIO
VALLO TILLMANN
LUCIANO VITTOZZI

TEMPORARY ADVISORS

ROSETTA CARDONE
MARIA ELENA CONGIU
CLAUDIA LILIANA DELGADO GONZALEZ
EMMA DE FEO
GEMMA GATTA
M. CARMEN MARTOS-JIMENEZ
AMPARO MONTESINOS ALONSO
JANOS SANDOR
SARKA VEJVALKOVA
ANTONI MONTSERRAT
CHRISTEL NOURISSIER