



**Mapping out the similarities and differences
between rare cancers and rare diseases
2015-2016**

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FOREWORD

The rare diseases community and the rare cancers community are often regarded as two different worlds. However, this is far from reality as the patients (and their families) affected by both conditions all share the same burden: the rarity and the many resultant complex and often devastating challenges.

Rarity, in the medical field, means that patients are often isolated and alone with their conditions, which most of the time are severe, debilitating and life-threatening/life limiting.

In the case of patients affected by rare cancers, they often fall between the world of rare diseases and the world of cancers, without knowing whether they belong to both communities or only one of them.

Patients (and those who care for them) who are affected by rare diseases, rare cancers, and also by rare diseases which may give rise to cancers, have expressed their need to map out the similarities and differences that exist between rare diseases (RD) and rare cancers (RC). The main objective is to better identify what priority advocacy actions need to be carried out together and where to join forces in order to improve access to equal and timely diagnosis as well as appropriate care, information and support.

The table below is the result of a year's work, started in November 2014 and conducted by Jan Geissler, co-founder and Vice-President of the Chronic Myeloid Leukemia Advocates Network, and Kathy Oliver, co-founder and Chair of the International Brain Tumour Alliance. Both patient advocates serve as EURORDIS representatives on the European Commission Expert Group on Cancer Control. They received support from the EURORDIS Policy Action Group on Rare Cancers and from Ariane Weinman, EURORDIS European Public Affairs Manager.

Rare Cancers Europe was consulted about the table in February 2015. The 60 patient organisations - members of EURORDIS concerned with rare cancers and rare diseases which may give rise to cancers - were consulted about the table from April to June 2015. These patient organisations are from 21 European countries and represent both adult rare cancers and paediatric cancers. They work either at the national level or at the European level. They all voice the patients' needs.

The table - highlighting the similarities and differences between patients affected by rare diseases and by rare cancers or rare diseases leading to cancers - was approved by the EURORDIS Board on 21 November 2015.

Mapping out the similarities and differences between rare cancers (RC) and rare diseases (RD)

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SIMILARITIES BETWEEN RARE CANCERS AND RARE DISEASES	DIFFERENCES BETWEEN RARE CANCERS AND RARE DISEASES
<p>1. The concept of rarity</p>	<p>1. The concept of rarity</p>
<p>Patients affected by rare cancers (RC) and rare diseases (RD) share many of the same challenges: especially the UNCOMMON nature (rarity) of their disease and all of its consequences on the life of a patient and their family, namely:</p> <ul style="list-style-type: none"> - difficulty accessing an accurate and timely diagnosis with often (very) long delays; - difficulty accessing highly specialised care and adequate treatments (difficulties in finding the right specialists / medical experts, long travels to access specialist centres...); - lack of research in comparison to more common diseases; - lack of registries and databases: many registries for rare diseases and rare cancers are scattered and/or not up-to-date: sometimes the operation of registries is stopped due to lack of funding; - few clinical trials because of the difficulties of organising clinical trials in small patient populations. <p>In general, patients either affected by RD or by RC feel isolated and alone with his/her rare disease/rare tumour.</p> <p>In the European Union, a condition is defined as rare when it affects “not more than five in 10 thousand persons in the Community” as delineated in the EU Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on Orphan medicinal Products.</p>	<p>It is acknowledged today that there are over 6000 RDs versus 198 identified RCs (this number evolves over time as research progresses and finds new genes related to RC).</p> <p>There are differences in the definitions of rare cancers and rare diseases, <u>the former being based on incidence and the latter being based on prevalence.</u></p> <p>The EU Commission has co-funded a project called RARECARE* which has provided an incidence rate for RC of less than 6/100,000/year. Diagnoses of rare cancers represent about 22% of all cancer cases diagnosed annually in the EU.</p> <p>In the US, the estimated incidence rate for RC is less than 15/1000/year.</p> <p>It is also important to emphasise that all cancers – including rare and common ones - are now being broken down into further smaller subgroups based on genetic characteristics. So there will even be types of breast cancer, lung cancer, etc. that become rare even though as a whole entity breast cancer and lung cancer are common.</p> <p>*RARECARE (Surveillance of Rare Cancers in Europe): http://www.rarecare.eu/ RARECAREnet (Information Network on Rare Cancers): http://www.rarecarenet.eu/rarecarenet/</p>

2. The severity and course of the disease	2. The severity and course of the disease
<p>The majority of RDs and all RCs are life threatening.</p> <p>For instance, rare cancers make up 22% of all cancer cases. Mortality from RC is much higher than in common cancers (five-year survival 65% vs. 47%, <i>source</i> RARECAREnet). All cancers in children are rare and about “6,000 children still die of cancer every year in Europe” (<i>source</i> SIOPe - <i>European Society for Paediatric Oncology</i>).</p> <p>Due to the severity of both RDs and RCs, patients can suffer greatly reduced quality of life. The patients’ families are also significantly impacted by the severity of the disease and the distress it causes.</p> <p>Therefore, patients living with RDs and RCs deserve a much greater focus of attention in terms of support, information, access to therapies and specialist medical care.</p>	
3. Paediatric population represents an important area of focus in both rare diseases and rare cancers	3. Paediatric population represents an important area of focus in both rare diseases and rare cancers
<p>RDs: over 50% affect children RCs: all paediatric cancers are rare</p>	<p>RARE CANCER: Incidence of paediatric cancers is relatively low in cancer (approximately 2% of rare cancer cases), but impact on long-term survivorship and quality of life can be very high in terms of, for example, possible delayed/long term toxicities resulting from treatment.</p> <p>On 18 November 2015, the European Society for Paediatric Oncology (SIOPE) has launched its ‘European Cancer Plan for Children and Adolescents’: http://www.siope.eu/SIOPE_StrategicPlan2015/#48</p>

4. A public health challenge and priority	4. A public health challenge and priority
<p>Over the last two decades, campaigns to raise awareness of rare diseases and of rare cancers have developed all over Europe and beyond.</p> <p>For instance, Rare Disease Day, has dramatically increased awareness and alerted the general public about the burden of living with rare diseases.</p> <p>However, patient groups as well as professionals in both RD and RC fields continue to stress that the unmet needs of those living with an RD or an RC are not high enough on the political agenda and list of priorities.</p>	
5. Patient Empowerment	5. Patient Empowerment
<p>Patients and their families affected by rare diseases, including rare cancers, must be part of the decision-making process regarding the care which patients receive.</p> <p>To that end, patients and their families must:</p> <ul style="list-style-type: none"> - be well informed by healthcare providers and patient organisations; - have shared platforms to exchange their experiences; - be trained either by healthcare providers and/or patient organisations on issues such as genetic testing, patient registries, life cycle of medicinal products, access to social aid etc... <p>Patients' organisations must voice the needs and expectations of patients and their families. To achieve this, these organisations can participate in decision-making initiatives as equal stakeholders and fully accepted members of committees. Patients' organisations should also be involved in research projects relevant to their diseases.</p>	

<p>There are strong networks of patient organisations in both rare cancers and rare diseases, but by no means do all of the specific, different types of rare cancers and rare diseases have such groups.</p>	
<p>6. Research</p>	<p>6. Research</p>
<p>For both RC and RD, the research effort needs to be significantly boosted and amplified. Funding urgently needs to be increased to meet these ends.</p> <p>On one hand, more research projects for RC and RD have been undertaken over the last five years, notably with European funding from FP6, FP7 and now Horizon 2020.</p> <p>However, on the other hand, many rare diseases and rare cancers still do not attract sufficient interest from academic researchers, pharmaceutical companies and potential funders because of their small patient populations and the perceived small return on the major investment in time and money which it takes to bring a therapy to market.</p> <p>Research varies enormously across Europe; for instance, in the field of paediatric cancers, “there has been little progress in difficult-to-treat diseases over the last 5 years” (<i>source SIOPE</i>).</p> <p>To address the shortcomings of global coordination of research, consortia or research networks on a global scale are needed which may also include industry and government partnerships, e.g. IRDiRC (which includes rare cancers) and IRCI (International Rare Cancers Initiative).</p> <p>IRDiRC: International Rare Diseases Research Consortium This transatlantic initiative, launched in 2010 by the EC and the NIH, aims to deliver 200 new therapies for rare diseases (including rare cancers) and means to diagnose most rare diseases by 2020. The governance structure and members of IRDiRC can be found</p>	<p>RARE CANCER: RC might take synergistic benefit from research in common cancers (e.g. common pathways, organisation of oncology research, etc).</p> <p>There are also some specific research activities such as, for instance: The International Rare Cancers Initiative (IRCI) “is a joint initiative between Cancer Research UK (CRUK), the National Institute of Health Research Clinical Research Network: Cancer (NIHR CRN: Cancer), the National Cancer Institute (NCI), the European Organisation for Research and Treatment of Cancer (EORTC), the Institut National Du Cancer (INCa) and the National Cancer Institute of Canada Clinical Trials Group (NCIC CTG).” “The aim of this initiative is to facilitate the development of international clinical trials for patients with rare cancers in order to boost the progress of new treatments for these patients.” (http://www.irci.info/).</p> <p>RARE DISEASE: For RD, it is much more difficult to take advantage of research in other fields. Over 30 million people affected by heterogeneous rare diseases represent a real challenge for research. In July 2012, EURORDIS published a position paper on rare disease research, emphasising why this research is important: RD research models help stakeholders to understand health mechanisms and can serve to treat more common diseases. http://www.eurordis.org/sites/default/files/EURORDIS_Rapport_Research_2012.pdf</p>

<p>following this link: http://www.irdirc.org/governance-structure-members/</p> <p>The IRDiRC members include four patient groups: - the French Muscular Dystrophy Association, AFM, - EURORDIS - the US National Organization for Rare Disorders, NORD - the US Genetic Alliance</p> <p>The European Organisation for Treatment & Research on Cancer – EORTC - is a member as well.</p> <p>From the patient organisations' point of view, it is clear that patient groups for RCs and RDs must be involved in all aspects of research. This includes, for example, early input into the design of clinical trials, being involved in the work of ethics committees, and playing an active and meaningful role in regulatory approvals and health technology assessment (HTA) mechanisms.</p>	<p><u>RD research has benefitted from European funding:</u> The fragmentation of RD research needs a European response:</p> <ul style="list-style-type: none"> -FP6 (2002-2006): 59 RD-relevant projects, global budget € 230 million - FP7 (2007-2013): Over € 620 million invested in close to 120 projects launched in FP7 - H2020: continues strong investment through various funding mechanisms. <p><u>E-Rare: ERA-Net for Research Programmes on Rare Diseases</u> “E-Rare has been linking research funding organisations since 2006 to develop a coordinated European approach of rare diseases research.” E-Rare funds transnational collaborative research through yearly joint transnational calls to help foster various rare diseases research projects: “build patient registries, unravel underlying molecular defects and pathophysiological mechanisms, identify biomarkers, develop new diagnostics and perform clinical studies for the development of treatments”. The consortium E-Rare-3 (2015-2019) “comprises 25 institutions from 17 European, Associated and non-European countries. Its international dimension will be directly translated into close collaboration with IRDiRC and other relevant European and international initiatives.”</p>
<p>7. Delay in accessing a diagnosis</p>	<p>7. Delay in accessing a diagnosis</p>
<p>RD patients and RC patients face the same challenges in accessing a correct and timely diagnosis due to the rarity of their disease. Both RD and RC patients often face significant delay in accessing the correct diagnosis. Second opinions on pathology results for RD and RC are also often hard to obtain in some Member States (MS).</p> <p>There are also huge discrepancies amongst EU MS between the services offered in different centres. Mapping of expertise to guide patients to specialised hospital services is needed.</p>	<p>RARE CANCER: In some RCs, a correct diagnosis might be delayed as symptoms can mimic other diseases. Once a tumour has been detected, a pathologic diagnosis of the tumour is usually obtained quickly. However, the pathological diagnosis of RCs can be wrong because of a paucity of expert pathologists with experience of specific rare cancers and also because of the possibility of differing opinions (“inter-observer variability”).</p>

<p>The long delay in accessing a correct diagnosis may contribute to a worsening of the patient's condition and increasing the psychological burden of the disease on both the patient and his/her family.</p> <p>In 2015, access to a timely and correct diagnosis still remains one of the major challenges for patients affected by a rare disease or a rare cancer. Better coordination of medical expertise across Europe is urgently needed to reduce diagnosis delays as well as inequalities.</p>	<p>RARE DISEASE: RDs are often subject to significant delay regarding a proper clinical diagnosis. The results of the study carried out by EURORDIS on the long delays to diagnosis and access to adequate healthcare services in Europe are published in "The Voice of 12 000 Patients": www.eurordis.org/publication/voice-12000-patients</p>
<p>8. Screening</p>	<p>8. Screening</p>
	<p>RARE CANCER: The definition of screening in the field of RC is different than the one applied in the field of RD.</p> <p>In the field of RC, screening a person's genome is not used for early or advance detection as it is in RD, but instead applied for the purpose of matching a specific genetic aberration to a particular targeted therapy if an appropriate targeted therapy exists.</p> <p>Screening in rare cancers is also used to stratify patients with these rare cancers into certain arms of clinical trials. For example, the EORTC SPECTA programme is an example of a cancer screening programme for this purpose: http://www.eortc.org/taxonomy/news-categories/specta SPECTA = "Screening Patients for Efficient Clinical Trial Access"</p> <p>However, it is important to emphasise that screening in the rare cancer sense, i.e. screening for targets for specific drugs, is still not available routinely on many national health systems for patients with rare cancers. Screening of this type can be done but in some instances, the patient must pay privately to access screening facilities.</p>

	<p>Furthermore, it is important to note that only a few RCs currently have a well-identified genetic origin.</p> <p>RARE DISEASE: It is widely accepted that 80% of RDs are of genetic origin. Screening programmes are intended to identify the inherited probability of an RD. In the field of rare diseases, mapping of the human genome as well as the development of scientific technologies, such as “Next-Generation Sequencing (NGS)” bring hope to RD patients and families to speed up access to a proper diagnosis, and maybe prevent families from having several children affected by the same rare disease if the diagnosis is made in a timely fashion.</p> <p>One of the challenges faced by RD patients and their families is the limited access to available prenatal and newborn screening programmes. EU Member States do not all have the same genetic testing policy which leads to inequalities for patients depending on where they live in Europe.</p> <p>RD patient advocates are involved in promoting a more harmonised European policy on prenatal and newborn screening programmes.</p> <p>RD patient advocates are also involved in promoting fair access to existing genetic tests in Europe.</p>
<p>9. Prevention</p>	<p>9. Prevention</p>
<p>Prevention is not often applicable to the numerous rare diseases and rare cancers, and there are some examples where RD and RC overlap meaningfully in this respect. For example, people who suffer from some rare inherited syndromes have an increased risk of getting a brain tumour. These syndromes can also cause a number of different medical problems.</p> <p>Examples of these rare syndromes are: <u>Neurofibromatosis</u> type 1 and 2 <u>Tuberous sclerosis</u></p>	<p>RARE CANCER: RCs are mainly acquired diseases although primary prevention may be applicable in certain rare cancers. Prevention might take the form of avoidance of known carcinogens and toxic agents, and choosing a healthy lifestyle), while secondary prevention (population screening, early detection within programmes) is often not applicable.</p>

<p><u>Li-Fraumeni syndrome</u> <u>Von Hippel-Lindau syndrome</u> <u>Turner syndrome</u> <u>Turcot syndrome</u> <u>Gorlin syndrome</u></p> <p>Sources: http://ghr.nlm.nih.gov/condition/von-hippel-lindau-syndrome</p> <p>CRUK :http://www.cancerresearchuk.org/about-cancer/type/brain-tumour/about/brain-tumour-risks-and-causes</p>	<p>RARE DISEASE: Some (though not yet very many) RDs can be detected through screening / genetic testing to confirm or not the presence of an inherited disease.</p> <p>For a few rare diseases, when a newborn is diagnosed right after birth, the newborn can be immediately enrolled in a care protocol that will enable him/her to live a quite normal life, limiting the progression of the inherited disease. For instance, this is the case for PKU (phenylketonuria).</p> <p>Nevertheless, given the huge number of rare diseases, there is not one single test for confirming every rare disease.</p>
<p>10. Centres of Expertise</p>	<p>10. Centres of Expertise</p>
<p>Patients affected by rare diseases and rare cancers need to be treated in a specialised care unit as their condition requires a high level of expertise as well as multidisciplinary care.</p> <p>The EU Member States were encouraged by the Council Recommendation on an action in the field of rare diseases of 8 June 2009 to “identify appropriate centres of expertise throughout their national territory by the end of 2013, and consider supporting their creation.”</p> <p>Even though an important effort has been made in several EU MS to map out national medical expertise for rare conditions, these efforts need to be increased, sustained and promoted.</p> <p>For many rare cancer and rare disease patients, there is still a long journey to access the appropriate, expert care. Information on centres of expertise for rare diseases and specialised oncology centres should be further promoted.</p> <p>It is also important to emphasise that some rare diseases lead to (rare) cancers/tumours, e.g. neurofibromatosis, von Hippel–Lindau syndrome, tuberous sclerosis (to name only a very few) and these</p>	<p>RARE CANCER: RCs are usually treated in oncology centres. Therefore the existing infrastructure is already in place to focus on people with cancer. But of course, expertise in dealing with rare cancers needs to be comprehensively developed in existing cancer centres. Specialist multidisciplinary teams should be embedded in treatment and care approaches for rare cancers. Put simply, established cancer centres need to build specific capacity and resources for rare cancers as this does not always exist in general cancer centres.</p> <p>Sometimes a patient with a rare cancer may not be treated optimally because the centre where he or she is receiving medical attention may not have expertise in that patient’s type of rare cancer. So patients should be directed to oncology centres which do have expertise and capacity for their particular type of rare cancer.</p> <p>There are several reasons for this, one of them being that detecting a rare cancer is difficult, and sometimes the first symptoms are not associated with a cancer but mistaken for some other medical condition.</p>

diseases also need to be treated at centres of expertise.

The rare disease and rare cancer patient communities must also be involved in the designation and evaluation of centres of expertise and specialised oncology centres as they bring a unique perspective to the table and are experts in what it is like to actually live with a rare disease or rare cancer.

On 24 October 2011, the EUCERD (EU Committee of Experts on Rare Diseases) adopted the “**Recommendations on Quality criteria for Centres of Expertise for Rare Diseases in Member States**”. The following Recommendations (advocated by the patient community) emphasise the need to work with patient organisations: “7. CEs collaborate with patient organisations to bring in the patients’ perspectives.

10. CEs contribute to and provide accessible information adapted to the specific needs of patients and their families, of health and social professionals, in collaboration with patient organisations and Orphanet.

19. Capacity to propose quality of care indicators in their area and implement outcome measures including patient satisfaction.

29. Links and collaboration with patient organisations where they exist.”

In addition, within the framework of National Plans for Cancer and National Plans for Rare Diseases adopted in many EU MS, the patient community has noticed that there is minimal linkage between these two types of plans.

The patient community urges EU MS to develop an appropriate bridge between RDs and RCs in order to provide better information to all stakeholders:

- national cancer plans should systematically include a section on rare cancers;
- national rare disease plans should systematically link to the section on rare cancers to be provided in national cancer plans.

RC patient organisations recognise the need to promote early referral to secondary care as central to their efforts in improving diagnosis.

RARE DISEASE:

One of the main issues for patients affected by a rare disease, which by definition is complex and heterogeneous, is to find the right healthcare specialist, with the relevant expertise to confirm the diagnosis, and provide appropriate treatment to manage the rare disease.

The Council Recommendation has encouraged EU MS to adopt a plan or strategy for rare diseases in order to establish a better healthcare framework for patients living with a rare disease. For instance, the Recommendation invites Member States to reference the specialists, healthcare units in clinics / hospitals with the relevant expertise in treating groups of rare diseases (metabolic rare disorders, lysosomal disorders, rare bleeding disorders, neuro-muscular disorders etc...). This initiative is very important to reduce delays in diagnosis and enables referral to **multidisciplinary care centres**.

As of November 2015, 21 EU MS out of 28 have adopted a national plan/strategy for rare diseases. This represents a major step forward at national level and also at the EU level.

However, a lot of work remains to be done in implementing the national plans/strategies in order to offer better health services to patients living with rare diseases.

Some EU MS have already designated national centres of expertise for rare diseases, while others are in the process of designating their national centres. This effort by EU MS to map out the expertise of RDs in their own countries and to designate centres of expertise for RDs should be strongly encouraged.

<p>With the aim of reducing diagnosis delays, the medical community needs to be well informed about centres of expertise for rare diseases and specialist oncology centres that exist in their country and also abroad (for instance, in neighbouring countries). In terms of referrals, this initiative would be very much welcomed. Moreover, it would also help address the need for reimbursement of a second opinion when necessary and available (see item 14 “healthcare and social costs”).</p>	
<p>11. European Reference Networks (ERNs)</p>	<p>11. European Reference Networks (ERNs)</p>
<p>The concept and criteria for ERNs are delineated in EU legal texts:</p> <ul style="list-style-type: none"> • EU Directive 2011/24/EU (9 March 2011) - application of patients' rights in cross-border healthcare Article 12 is on ERNs and Article 13 is on rare diseases. • Commission Delegated Act (10 March 2014) on “setting out criteria and conditions that European Reference Networks and healthcare providers wishing to join an ERN must fulfil” • Commission Implemented Act (10 March 2014) setting out criteria for establishing and evaluating European Reference Networks <p>On 31 January 2013, the EUCERD adopted the “Recommendations on European Reference Networks for Rare Diseases”. On 10 June 2015, the European Commission Expert Group on Rare Diseases (replacing the EUCERD) adopted an Addendum to these recommendations. The purpose is to revisit the EUCERD Recommendations in light of the Delegated and Implementing Acts of March 2014, and in view of the first call for ERNs to be launched in early 2016.</p> <p>The Addendum:</p> <p>1) suggests an illustrative grouping of RDs as a feasible approach to RD ERN planning and to ensure coverage of all RD eventually – 21 Thematic networks are proposed resulting from a consensus with expert stakeholders;</p>	<p>RARE CANCER:</p> <p><u>Paediatric Oncology:</u> In the field of paediatric oncology, DG SANTE is co-financing a pilot ERN called ExPO-r-Net: “European Expert Paediatric Oncology Reference Network for Diagnostics and Treatment”.</p> <p>ExPO-r-Net is a three-year project (March 2014-February 2017) that “will build a European Reference Network (ERN) for Paediatric Oncology. ExPO-r-Net aims to reduce the current inequalities in childhood cancer survival and healthcare capabilities in different EU Member States. ExPO-r-Net builds on and has been designed to be compatible with previously initiated EU projects in this field: ENCCA – EPAAC – PanCareSurFup – EUROSARC – INTREALL – ASSET”.</p> <p>ExPO-r-Net brings together more than 60 project partners from 17 countries. More information at www.expornet.eu</p> <p><u>Rare Cancers Europe and RARECARE: List of families of rare cancers</u> Rare Cancers Europe (RCE) is a multi-stakeholder platform (patient organisations, academia, nursing and industry) established in 2008. RCE aims at promoting the issue of rare cancers on the European policy agenda, identifying appropriate solutions and exchanging</p>

2) reinforces the principles of patient empowerment and patient involvement in the decision and opinion-making processes of RD ERNs given that patients and patient representatives are experts and co-producers of knowledge for their disease.

Source:

http://ec.europa.eu/health/rare_diseases/docs/20150610_erns_eucerdaddendum_en.pdf

The role of ERNs:

ERNs are intended to structure at EU level the provision of care **for all patients with a medical condition requiring a particular concentration of expertise in medical domains where expertise is rare** (Art.12 (2c) of EU Directive 2011/24/EU).

→ **This applies to rare diseases, including rare cancers**

The EC will launch a first call for ERNs in early 2016.

There has been a strong argument for grouping RDs into thematic ERNs and this is captured in the Addendum to the EUCERD Recommendations as mentioned above.

In order to make sure that no patients will be left out, EURORDIS (in extended consultation with its membership over the past few years) favours families of diseases or larger thematic groups to ensure that all rare diseases are included. Due to the multidisciplinary needs of rare diseases, and also rare cancers, it is expected that care for patients will be covered by multiple networks collaborating together.

Future ERNs should be established based on the two founding principles which:

- **ensure that every patient with a rare disease/ rare cancer will have a network to be referred to and will not be left out of the system;**
- **ensure the establishment of networks which group diseases in the most coherent way to facilitate high quality patient care.**

best practice.

RCE brings together 32 partners including EURORDIS.

The EU co-funded RARECARE project (2007-2010) - Surveillance of Rare Cancers in Europe - identified 186 rare cancers.

Based on the work of RARECARE, 12 “families” of rare cancers have emerged:

1. Head and neck cancers (cancers of nasal cavity and sinuses, nasopharynx, hypopharynx, larynx, salivary glands, oropharynx, oral cavity and lip, eye, middle ear)
2. Thoracic rare cancers (tumours of trachea, thymus, malignant mesothelioma)
3. Male genital and urogenital rare cancers (tumours of testis, penis, renal pelvis, ureter, urethra, and extragonadal germ cell tumours)
4. Female genital rare cancers (tumours of vulva and vagina, non epithelial tumours of ovary, trophoblastic tumours of the placenta)
5. Neuroendocrine tumours
6. Tumours of the endocrine organs (cancers of thyroid, parathyroid, adrenal cortex, pituitary gland)
7. Central Nervous System tumours (glial tumours, medulloblastoma, malignant meningioma)
8. Sarcomas (soft tissue sarcomas, bone sarcomas, gastrointestinal stromal tumours)
9. Digestive rare cancers (tumours of small intestine, anal canal, gallbladder and extrahepatic biliary duct)
10. Rare skin cancers and non-cutaneous melanoma (melanoma of mucosae and of the uvea, adnexal skin carcinomas, Kaposi sarcoma)
11. Haematological rare malignancies (acute myeloid leukaemia, myeloproliferative neoplasms, myelodysplastic and myeloproliferative neoplasms, histiocytic and dendritic cell neoplasms)
12. Paediatric cancers (all)

	<p>It is also interesting to note that in the future, we might no longer call a cancer by its body part but instead, by its molecular typing. This means that across different rare tumour types, the same treatment might be shared based on similar molecular profiles. It will therefore be even more important to work within and between reference networks for rare cancers so that learnings and practical applications could be achieved seamlessly.</p>
<p>12. Training of medical doctors, healthcare professionals</p>	<p>12. Training of medical doctors, healthcare professionals</p>
<p>Patients living with rare diseases and rare cancers often report that awareness of their conditions should be increased amongst healthcare professionals as should training about their conditions.</p> <p>The below proposals have been highlighted by the patient community:</p> <ul style="list-style-type: none"> • Medical students should be systematically provided with courses on rare diseases and rare cancers in their curriculum. Some EU countries have already introduced such type of courses, but this effort should be further promoted in all EU countries. • Nurses as well as other healthcare professionals should be given specialist training in rare cancers and rare diseases so they are better informed about these conditions. • The patient community also encourages training of doctors using virtual learning tools and other educational resources to help disseminate knowledge and new technologies. • In addition, the rare disease and rare cancer patient communities emphasise that patients and/or their carers are often experts about their rare condition. Therefore, patient organisations should be systematically involved in the design of rare disease/rare cancer courses for healthcare professionals. <p>As regards career pathways, opportunities and incentives should be provided to young healthcare professionals and to those still in</p>	

<p>training who wish to specialise in the field of rare diseases (which is very wide) or in rare cancers.</p>	
<p>13. Access to treatments: Sharing of best practices/clinical guidelines, protocols</p>	<p>13. Access to treatments: Sharing of best practices/clinical guidelines, protocols</p>
<p>The sharing of best practices, clinical guidelines and protocols for the care and management of patients is crucial both for RD and RC given the rarity of these conditions and the scattered expertise to treat them.</p> <p>Within the future ERNs, the sharing of best practices and clinical guidelines should be enhanced as these aspects will constitute two of the key components of these future ERNs.</p> <p>The rare diseases field might have to learn from the rare cancers field about sharing protocols within and across European countries.</p> <p>We need to make the most of rare cancer and rare disease infrastructures to raise the profile and understanding of these diseases.</p>	<p>RARE CANCER: Some rare cancers have guidelines established already.</p> <p>Some of these are national guidelines (for example, in the UK with NICE’s “Improving Outcomes in Brain and CNS Tumours”) and there are also pan-European guidelines produced for some rare cancers.</p> <p>The European Society of Medical Oncology (ESMO) has done a great deal of work on clinical practice guidelines. The list can be found at www.esmo.org/Guidelines. Many of them are for rare cancers such as sarcomas and gist, high-grade malignant glioma, head and neck cancers (to name a few).</p> <p>RARE DISEASE: Within national plans for rare diseases, some countries are establishing medical guidelines for some rare pathologies at national level.</p> <p>Some medical doctors have also established informal links with other doctors within their specialty either in the same country or across borders, in order to share clinical guidelines at national, European and/or international levels.</p> <p>The four year project RARE-Best Practices (January 2013-December 2016) is funded by the European Commission under the FP7 Cooperation Work Programme: Health-2012. The main goal of the project is to create an online database and networking platform to facilitate the sharing, the evaluation and the development of RD best practice guidelines, in order to improve patient health outcomes across Europe: www.rarebestpractices.eu</p>

14. Healthcare and social costs	14. Healthcare and social costs
<p>For both RD and RC, overall healthcare and social costs can be much higher than for those with a “common” condition, because treatments are often very expensive and not always reimbursed (e.g., off label use, therapy rejected by HTA because it has been deemed to be not cost effective, etc).</p> <p>Referrals for a second opinion, if in fact a second opinion is available, are not always covered by health insurance. In addition, travel costs to access appropriate care are often not covered by insurance. This adds to the economic burden of the disease on the patient and family.</p> <p>Furthermore, caregivers - often a parent or a husband or wife - of people with RD or RC often have to themselves stop working and be subject to a major reduction in their family’s economic stability because they have to stay home and take care of their loved ones.</p> <p>Therefore both RC and RD families can be driven to the edge of destitution as a result of the diagnosis of an RC or RD. The social and economic burden on the patients and families, in addition to the suffering caused by the disease, should be emphasised and quantified in order to encourage social and healthcare authorities to take appropriate measures to improve the situation.</p> <p>Source: The following publication has been deemed useful to outline the societal impact of cancer and long-standing illness at the workplace, to carers and to the society: “Cancer and in general long-term illnesses at workplaces” (IP/A/EMPL/FWC/2006-05/SC3) published by the Policy Department Economic and Scientific Policy of the European Parliament.</p>	

<p>15. Orphan Drugs: Development</p>	<p>15. Orphan Drugs: Development</p>
<p>In the EU, the Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products was a cornerstone to provide economic incentives to develop drugs for rare diseases (including rare cancers).</p> <p>This Regulation has considerably boosted the development of drugs intended for small populations.</p> <p>As of October 2015 and since 2000:</p> <ul style="list-style-type: none"> - 1564 orphan designations have been granted by the European Commission based on the positive opinions of the EMA scientific Committee for Orphan Medicinal Products (COMP) - 112 Orphan Medicinal Products received an EU Marketing Authorisation by the European Commission based on the positive opinions of the COMP and the Committee for Human Medicinal Products (CHMP). Out of the 112 OMPs, 84 OMPs still have a market exclusivity of 10 to 12 years. <p>Source: 'The [EU] Community Register lists all medicinal products for human and veterinary use as well as orphan medicinal products that have received a marketing authorisation through the centralised procedure': Register of designated Orphan Medicinal Products (by number): http://ec.europa.eu/health/documents/community-register/html/orphreg.htm</p>	<p>RARE CANCER:</p> <p>Over one-third of Orphan Drugs are intended to treat rare cancers. All paediatric cancers are rare. The EMA published the following information in 2013: 8.8% of agreed Paediatric Investigation Plans (PIP) and 6.2% of waivers were in the field of oncology.</p>
<p>16. Orphan Drugs: HTA/Value Assessment and Access</p>	<p>16. Orphan Drugs: HTA/Value Assessment and Access</p>
<p>Orphan drugs and their accompanying legislation are of course very relevant to both RD and RC.</p> <p>Orphan drugs are innovative treatments, and therefore are costly. Sometimes, their price is so high that some EU countries are</p>	

<p>reluctant to purchase them. There are major discrepancies between European countries in terms of accessing orphan drugs.</p> <p>In order to reduce access inequalities, the EUCERD (European Union Committee of Experts on Rare Diseases) adopted in September 2012, a Recommendation on the Clinical Added Value of Orphan Medicinal Products Information Flow (CAVOMP): www.eucerd.eu/?page_id=13</p> <p>In parallel, the European Commission has launched an initiative on “Mechanism of Coordinated Access to orphan medicinal products (MoCA)” to seek collaborative ways to identify and assess the added value of orphan medicinal products between a company and competent authorities.</p> <p>In a nutshell, MOCA and CAVOMP are intended to bring together relevant stakeholders in order to establish an early dialogue and gather enough data to find a consensus on the potential clinical added value of a specific product intended for a small population of patients. The stakeholders involved are the sponsor, clinicians, patients, healthcare professionals and competent authorities, namely the EMA and HTA agencies.</p> <p>The common assessment of the clinical added value of a product is a key factor for setting its price.</p> <p>Agreeing on a common assessment of the clinical added value of an orphan product is aimed at accelerating its marketing authorisation’s approval by the EC and its access to patients in EU countries.</p>	
<p>17. Clinical Trials in small populations</p>	<p>17. Clinical Trials in small populations</p>
<p>Patients living with a rare disease or a rare cancer are concerned by the lack of enough clinical trials (CTs) in these small populations. The clinical trials in small and vulnerable populations face the same major difficulties that are often challenging to overcome for the sponsors and researchers for legal, regulatory and financial</p>	

reasons:

- few patients;
- often, CTs involve children (more legal requirements);
- multicentre trials (difficult to set up multicentre trials in different countries);
- conventional statistical methods to evaluate new therapeutic approaches for any given rare diseases/rare cancers are limited due to the small number of patients concerned, and therefore are not appropriate to demonstrate the efficacy and safety of therapies.

There is an urgent common need to adapt clinical trial designs so they are more appropriate to small populations of patients.

Some elements of response:

- In 2007, the **EMA** issued the “Guideline on Clinical Trials in Small Populations“
www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003615.pdf
- **Rare Cancers Europe:** “Methodological recommendations for clinical studies in rare cancers: a European consensus position paper”, www.rarecancerseurope.org
- Three EU projects funded under FP7:
 - **ASTERIX project** led by Professor Kit Roes at UMC Utrecht, Netherlands
www.asterix-fp7.eu/
 - **IDEAL project** led by Professor Ralf-Dieter Hilgers at the RWTH Aachen University, Germany
www.ideal.rwth-aachen.de/
 - **InSPiRE project** led by Professor Nigel Stallard at the University of Warwick, United Kingdom
www2.warwick.ac.uk/fac/med/research/hscience/stats/currentprojects/inspire/

These three projects explore new methods for design and

<p>analysis of clinical studies in small population groups. All three projects bring together experts in clinical trial methodology and statistics in small populations and patient organisations from across Europe.</p>	
<p>18. Registries</p>	<p>18. Registries</p>
<p>For those affected with a rare disease or a rare cancer, it is highly important to collect relevant clinical data for diagnostic and epidemiology purposes as well as research in order to better treat today's patients and eventually find a cure for patients in the future.</p> <p>On 5 June 2013, the EUCERD adopted "Core Recommendations on Rare Disease Patient Registration and Data Collection": www.eucerd.eu/?page_id=13</p> <p><u>Common area of action in the field of data registration:</u> The EU wants to harmonise information systems both for cancers and rare diseases across Europe, notably through the EC Joint Research Centre (JRC) based in Ispra, Italy.</p> <p>Synergies between rare diseases registration (especially for those rare diseases with a predisposition for causing rare cancers) and rare cancers registrations must be sought to ensure that patient data are comprehensively captured and shared in a legal and ethical manner.</p>	<p>RARE CANCER: Registries in the field of cancers started a long time ago and are quite well structured. Registration of rare cancers should be done within the established population-based registries. Patient organisations emphasise that existing cancer registries should provide for the information needs of people who have rare cancers. There also exist various childhood cancer registries, even within the same country.</p> <p>In the specific field of rare cancer registries, the following projects have been/are instrumental in collecting information on rare cancers:</p> <ul style="list-style-type: none"> - RARECARE (Surveillance of Rare Cancers in Europe, 2007-2010) - RARECAREnet <p>RARE DISEASE: Many rare diseases do not have a registry and amongst existing registries, few of them are well structured. The management of registries varies greatly from one condition to another, for instance between very rare diseases and less rare diseases. Very often, the sustainability of RD registries is at stake due to lack of funding.</p>

19. BioBanks	19. BioBanks
	<p>RARE CANCER: Some “universal” biobanks in cancer already exist which can also be used for RC biobanking. Enough resources for RC should be foreseen within those biobanks. However, biobanks specific to some rare cancers also exist separately from universal banks and some biobanks take advantage of information technology to create dedicated rare-cancer-specific biobanking data.</p> <p>In the UK, for example, there is a networked biobank which brings together a range of institutions and the brain tumour tissue samples they have individually collected in order to pool knowledge and resources: “BRAIN UK, operating at the University of Southampton, will link existing archives of brain tumour tissue in a virtual network so that researchers can gain access to unprecedented levels of tissue to support their much needed research into better treatments and a cure for brain cancer.” See http://www.brainstrust.org.uk/news-detail.php?id=421 It is important to note that patient organisations play a crucial role in this initiative.</p> <p>RARE DISEASE: <u>EuroBioBank network: http://www.eurobiobank.org</u> Established in 2001, EuroBioBank is the only network dedicated specifically to rare disease research in Europe. The network provides human DNA, cell and tissue samples as a service to the scientific community conducting research on rare diseases. “About 130,000 samples are available across the network and can be requested via the online catalogue. Approximately 13,000 samples are collected each year and 7,000 samples distributed in Europe and beyond. The biological samples are obtained from patients affected by rare diseases, including rare neuromuscular disorders.”</p>

	<p>The EuroBioBank Network is composed of 25 members, of which 21 biobanks from nine European countries (France, Germany, Hungary, Italy, Malta, Slovenia, Spain, United Kingdom and Turkey) as well as Israel and Canada. It is coordinated by the Fondazione Telethon (Italy). Moreover, EuroBioBank is an active collaborator of BBMRI.</p> <p><u>BBMRI – ERIC: Biobanking and BioMolecular resources Research Infrastructure – European Research Infrastructure Consortium</u> BBMRI-ERIC is one of the largest health research infrastructures in Europe today. BBMRI-ERIC primarily aims at establishing, operating, and developing a pan-European distributed research infrastructure of <i>biobanks</i> and <i>biomolecular resources</i>. This will facilitate the access to biological resources as well as biomedical facilities and support high-quality biomolecular and medical research.</p> <p>There are 13 EU Member States who are full members (Austria, Belgium, Czech Republic, Estonia, Finland, France, Germany, Greece, Italy, Malta, The Netherlands, Sweden, UK). The observers include Norway, Poland, Switzerland, Turkey and the IARC/WHO.</p>
<p>20. Psychosocial aid</p>	<p>20. Psychosocial aid</p>
<p>Patients living with a rare disease or a rare cancer face the difficulty of finding social services and psychological support adapted to their needs. This is due to the rarity of each disease, the extensive variations of expressions of the diseases, the paucity of medical experts as well as professionals in the social area to help patients and families.</p> <p>Therefore, there is a great demand for social support as well as psychological support as patients and their families are often very isolated and deserve to be helped.</p> <p>Care should not be restricted to medical and paramedical aspects, it should also take into account social support, inclusion and psychological and educational development.</p>	<p>RARE CANCER: In the field of cancers, the discipline of “psycho-oncology” has been established, with the availability of psycho-oncology at a number of centres.</p> <p>The International Psycho-Oncology Society (IPOS) was created in 1984 to “foster international multidisciplinary communication about clinical, educational and research issues that relate to the subspecialty of psycho-oncology. Two primary psychosocial dimensions of cancer are 1) Response of patients, families and staff to cancer and its treatment at all stages; 2) Psychological, social and behavioural factors that influence tumour progression and survival.”</p> <p>http://www.ipos-society.org/</p>

To resolve the lack of sufficient information and aid from public services, in many cases, the patients and/or the parents of patients have established their own patients' organisations. They provide other patients and families with relevant information on:

- the description of the disease;
 - where to find medical experts (whenever possible);
 - where to find informed social workers;
 - rights of the patient;
 - access to social aid;
- etc.

Patients' organisations also help patients and families find solutions for integration at school, in workplaces, and in society at large.

Some patient organisations have set up their own helpline to provide assistance and psychological support to patients and families.

In addition, some patient organisations fund research for their diseases, and help develop and design clinical trials and registries.

Patient organisations have said that centres of expertise should provide not only medical care but also links with social services. This notion has been integrated into the Recommendations from the EUCERD on **Quality Criteria for Centres of Expertise for Rare Diseases in Member States** (24 October 2011): "Criteria for designation of CEs for RD in MS...[Reco] 25. Demonstration of a multi-disciplinary approach, when appropriate, integrating medical, paramedical, psychological and social needs (e.g. RD board)".

In 2015, patient organisations are becoming recognised as being major players in healthcare pathways as well as in research projects. The image of patient organisations has changed a lot compared to 15 years ago. Patient organisations now voice patients' needs in many fora, high-level working groups and regional, national, European and International decision-making committees.

Psycho-oncology has become more widely available, even if not yet adequately resourced. This discipline needs to be part of the multidisciplinary team and also promoted by patient organisations as being vital in helping people with rare malignancies.

Paediatric and Teenage/ Young Adult Cancer:

Whilst unemployment in general has increased in Europe, these increases have been disproportionately high amongst young people. But there is a group of people threatened by exclusion from the labour market and society at large which is often neglected: young people between 15 and 25 years who have survived childhood cancer and are trying to find their way back to life, work and education. Research shows that increased risks of unemployment were observed within all cancer diagnoses (Paediatric Blood Cancer 2008).

What is lacking are individual counselling programmes for young people who have survived cancer (childhood cancer survivors) to help them find a career perspective which is realistic, takes into account any health restrictions, but – most importantly - also builds on and enhances existing strengths and competences.

RARE DISEASE:

Given the wide variety of rare diseases, the solutions for social support and for psychological support vary greatly according to the different types of diseases and the national healthcare and social systems. Patients and their families are often confronted with very complex situations.

Some common solutions or trends in policy making are being developed as explained in the left column.

Nevertheless, patient organisations still sometimes struggle to be recognised as equal stakeholders amongst healthcare professionals, academia and industry.

Besides the work of patient organisations, some centres have been developed (even at national level in Sweden and Norway) to offer specific social support to people living with chronic and severe diseases.

EURORDIS has led a Work Package within the EUCERD Joint Action (2012-2015) on '**Specialised Social Services and Integration of Rare Diseases into Social Policies and Services**'. Within the framework of this project, EURORDIS is mapping the services available across Europe and promoting awareness-raising activities for the purpose of highlighting the need for these services.

The following services have been identified and are being mapped. Some services receive public funding, while others only receive private funding.

- **Therapeutic Recreation Programmes (TRP):** organised recreation activity (summer camp, ad hoc trip) that allow patients living with rare disease/cancer (mainly children) the possibility to take a break from focusing on their disease and treatment to concentrate on fun and leisure. TRP can also focus on different empowerment and disease/symptom management activities.
- **Respite Care Services (RCS):** welcome people living with rare diseases, so that their carers can have some short-term relief from caregiving. RCS can be offered in various ways: residential respite, domiciliary care, day care respite and emergency respite.
- **Adapted Housing:** group homes, supported by specialist staff, aiming to help people living with rare diseases to enjoy the highest possible level of autonomy, in their own home, where they often feel isolated.

<ul style="list-style-type: none"> • Resource Centres: a combination of information provision, social and medical services, often under partnership or cooperation with centres of reference/expertise. These centres are specialised in handling rare complex cases and provide services such as training courses, information and guiding, information about social services, documentation and research, daily support therapies, medical and psychological consultations. <p>A map of the above mentioned services currently identified across Europe can be found on the EURORDIS' website: http://www.eurordis.org/specialised-social-services</p> <p>EURORDIS together with the Commission Expert Group on Rare Diseases (replacing the EUCERD) is working on the development of Recommendations on Social Care in Rare Diseases, to address the issue of rarity and to recognise the specific needs of those diagnosed with a rare disease/rare cancer.</p>	
<p>21. (Long-term) Follow-up of rare disease survivors and childhood cancer survivors</p>	<p>21. (Long-Term) Follow-up of rare disease survivors and childhood cancer survivors</p>
	<p>RARE CANCER: It is important to address long-term toxicity, cancer treatment consequences and quality of life – all aspects of cancer survivorship. With an 80% cure rate, the number of childhood cancer survivors – presently estimated to be 300.000 to 500.000 in Europe – is likely to continue to increase. Therefore, improving quality of life for these survivors is a major goal. The PanCare network was established in 2008 to address this issue. PanCare is a pan-European multidisciplinary network of health professionals, survivors of a paediatric malignancy and their families, who collaborate to reduce the frequency, severity and impact of late side-effects of treatment, with the aim to ensure that every survivor of childhood cancer receives optimal long-term care: www.pancare.eu</p>

RARE DISEASE:

Given the wide number of rare diseases, the situation faced by the patient can be very different from one disease to another, which makes it very difficult to provide an overall assessment.

Some rare diseases can be seriously debilitating and disabling but the life expectancy of the patient may be 30 years or more. The daily care, both medical and paramedical, is very complex and has a serious impact on the patient and the family. The long-term follow up of the patient is a key issue for both the individual patient and the parents who are often the carers and who frequently worry about what will happen to their children when they are no longer there to look after them.

National plans/national social infrastructures must offer adequate help to these specific cases.

In the case of some other rare diseases, such as cystic fibrosis for instance, new and improved treatments have been made available over the past decades. These diseases, though not cured, are better understood and managed. Therefore, the life expectancy of patients has significantly increased. Nevertheless, these patients must take heavy treatments for the rest of their lives and they need to be monitored carefully.