



National Rare Disease Plan for Ireland

2014 – 2018

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DEPARTMENT OF HEALTH

2014

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Department of Health
Hawkins House
Hawkins Street
Dublin 2
Tel: +353 (0)1 635 4000
Fax: +353 (0)1 635 4001
E-mail: doh@health.gov.ie
Web: www.doh.ie

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Minister's Foreword



It is my pleasure to introduce this plan on the care of people with rare diseases. This is a generic policy framework for rare diseases. Its scope is broad and it applies to all rare diseases, which can number up to 8,000 diseases affecting millions of EU citizens. The challenges faced by people with rare diseases cannot be overstated. There may be a dearth of expertise and knowledge about their condition. Their diagnostic odyssey may be long-lived as they strive to define their disease; and once diagnosed, the patient journey to treatment may be protracted because of the rarity of their condition. The suffering, uncertainty and inconvenience because of their odyssey also comes with health and social consequences. For carers and families of people suffering from rare disease, the burden is also heavy.

This policy framework envisages a combined approach with our EU partners and Northern Ireland to diagnose and treat people with rare diseases. We must deepen links with facilities and institutions in other countries where specialist services are available that may be absent in Ireland. The plan elaborates on Ireland's participation in European Reference Networks, which is the networking of knowledge and expertise through reference centres and teams of experts. These links are emphasized in the report to address the care of patients with rare diseases at both national and European levels.

The plan has recommended the establishment of a national clinical programme for rare diseases; such a clinical programme will support work on treatment programmes, accessing clinical trials, the designation of centres of expertise and the provision of information for patients and their carers. This work will be further enhanced by the recommendation that a national office for rare diseases be established. Indeed, I am pleased to report that in the process of drafting this plan, a national clinical programme for rare diseases has been established.

In January 2011, a national conference was held in Farmleigh with the support of EUROPLAN, which brought together patients, patients' organisations and healthcare professionals. It enabled patient, scientific, medical and industry representatives who work closely on the rare disease agenda to engage with relevant agencies in a coordinated and productive way. An additional consultation day was held in June 2012 with the specific purpose of facilitating further feedback on the progress of the plan, and an online survey facility was also launched in conjunction with this event. This consultative process provided an opportunity for a wide range of stakeholders to share their views and was very influential in shaping the development of the national plan. The Consultation Report will be published alongside this plan.

The publication of this Rare Disease Plan for Ireland is against the backdrop of major reform of our health service, reform that will deliver better access to high-quality health services. The plan brings certainty to the development of services and care for patients and their carers. I would, therefore, like to thank the Steering Group for their hard work, drive and commitment to drafting this plan and I look forward now to its implementation – for the benefit of all who suffer from rare diseases.

Dr. James Reilly, TD
Minister for Health

Acknowledgements

It is estimated that there are over 6,000 identified rare diseases. We know that many of these conditions are complex, severe and debilitating. There are many challenges for patients living with a rare disease in Ireland. Our public consultation highlighted the challenges involved in arriving at a timely and correct diagnosis as well as accessing appropriate medications and technology. We have tried to keep these issues at the centre of the plan.

I am very grateful to the hardworking and enthusiastic National Steering Group who developed this policy. The patients' organisations made significant contributions to the Steering Group and also the public consultation. Our work also benefited greatly from international experience including from a number of institutions and other countries.

Finally, sincere thanks to the Institute of Public Health and the Health Promotion Unit within the Department of Health who brought this plan to completion. It is our hope that this first national plan will alleviate the burden of rare diseases for patients and their families in the years to come.

Dr. John Devlin

Deputy Chief Medical Officer

Chairman of the National Steering Group on Rare Diseases

Acronyms used

AGNC	Association of Genetic Nurses and Counsellors
AGNSS	Advisory Group for National Specialist Services
APMI	Association of Pharmaceutical Manufacturers of Ireland
BBMRI	Biobanking and Biomolecular Resources Research Infrastructure
Care-NMD	Improving Care for Duchene Muscular Dystrophy
CAVOMP	clinical added value of orphan medicinal products
CIBERER	Centro de Investigación Biomédica en Red de Enfermedades Raras
CoE	Centre of Expertise
COMP	Committee for Orphan Medicinal Products, European Medicines Agency
CPA UK	Clinical Pathology Accreditation (UK) Ltd.
DECIPHER	Database of Chromosomal Imbalance and Phenotype in Humans Using Ensembl Resources
DNA	deoxyribonucleic acid
DPS	Drugs Payments Scheme
DYSCERNE	European Network of Centres of Expertise for Dysmorphology
EAHC	Executive Agency for Health and Consumers
EBE	European Biopharmaceutical Enterprise
EC	European Council
ECRIN	European Clinical Research Infrastructure Network
EMA	European Medicines Agency
ENOPE	European Network on Patient Empowerment
EN-RDB	European Network of Rare Bleeding Disorders
EpiRare	European Platform for Rare Disease Registries
EPNET	European Porphyria Network
ERIC	European Research Infrastructure Consortium
ERN	European Reference Network
ERNDIM	European Research Network for evaluation and improvement of screening, Diagnosis and treatment of Inherited Disorders of Metabolism
ESDN	European Skeletal Dysplasia Network
EUCERD	European Union Committee of Experts on Rare Diseases
EUROCAT	European Surveillance of Congenital Anomalies
EURODIS	European Organisation for Rare Diseases
EuropaBio	European Association for Bio-Industries
EUROPLAN	European Project for Rare Diseases National Plans Development
FP7	Seventh EU Framework Programme for Research and Technological Development
GA1	Glutaric Aciduria type 1
GENETESTS	Medical Genetic Information Resource
GMS	General Medical Services
GRDO	Genetic and Rare Disorders Organisation
HIPE	Hospital In-Patient Enquiry
HIQA	Health Information and Quality Authority
HMD	hereditary metabolic disease
Horizon 2020	EU Research and Innovation Programme
HRB	Health Research Board
HSE	Health Service Executive

HTA	health technology assessment
ICD	International Classification of Diseases
ICORG	All-Ireland Cooperative Oncology Research Group
ICRIN	Irish Clinical Research Infrastructure Network
IEP	individual education plan
IHSAB	Irish Health Service Accreditation Board
IMB	Irish Medicines Board
IMD	Inherited metabolic disorder
INAB	Irish National Accreditation Board
IPHA	Irish Pharmaceutical Healthcare Association
IPPOSI	Irish Platform for Patients' Organisations, Science and Industry
IRDIRC	International Rare Disease Research Consortium
ISD	Integrated Services Directorate
IT	information technology
IVF	in vitro fertilisation
KPI	key performance indicator
LTI	Long-term Illness Scheme
MCAD	Medium Chain Acyl CoA Dehydrogenase deficiency
MRCG	Medical Research Charities Group
NBS	newborn screening
NCHCD	National Centre for Hereditary Coagulation Disorders
NCIMD	National Centre for Inherited Metabolic Disorders
NCMG	National Centre for Medical Genetics
NCPE	National Centre for Pharmacoeconomics
NGO	non-governmental organisation
NICE	National Institute for Health and Care Excellence
NIH	National Institute of Health
NIHR	National Institute for Health Research
NNBSP	National Newborn Bloodspot Screening Programme
NOWGEN	Centre of Excellence in Public Engagement, Education and Professional Training in Biomedicine
OMIM	Online Mendelian Inheritance in Man
OMP	orphan medicinal products
OP	orphan drugs
Orphanet	Portal for rare diseases and orphan drugs
PKU	Phenylketonuria
PPSN	Personal Public Service Number
PSA	Patient Safety Agency
RARECARE	Surveillance of Rare Cancers in Europe
RoI	Republic of Ireland
SCNIR	Severe Chronic Neutropenia International Registry
SFI	Science Foundation Ireland
SOP	standard operating procedure
UKNEQAS	United Kingdom National External Quality Assessment Service

Executive Summary and Recommendations

Chapter 1: Rare disease in Ireland – Why we need a plan

This chapter defines rare diseases and estimates the level of these in the Irish population. It sets out the background in Ireland and in the European Union context, and includes the vision and underlying principles of this first National Rare Disease Plan for Ireland, covering the years 2014-2018.

Chapter 2: How the National Rare Disease Plan was developed

This chapter describes the national Steering Group that formulated the Rare Disease Plan and how it was developed with key stakeholders. In particular, it references the EUROPLAN Conference 2011 that led to the establishment of the Steering Group, the national consultation conference and the online public consultation, all of which played a key role in the development of the plan. A report on the public consultation process will be published alongside the National Rare Disease Plan for Ireland.

Chapter 3: Recognition of rare disease – Information and research

This chapter deals with the recognition of rare diseases and the availability of information and research on them. It begins with defining ‘a rare disease’ and then proceeds to cover pertinent areas on these topics, such as epidemiology, registers and computer information systems, exploring the strengths and weaknesses of each. It goes on to examine the research dimension of rare diseases, covering such areas as funding of research in Ireland, networks of researchers, participation in international initiatives and infrastructure. The final section explores the opportunities and challenges in the area.

The Steering Group recommends:

1. **Guidelines be developed on coding and recording of rare diseases** within relevant Irish health data systems that are consistent at European and global level. The Health Information and Quality Authority (HIQA) will have a role in this, given its functions regarding information standards, including coding standards.
2. The **publication of the Health Identifier Bill and the forthcoming Health Information Bill.**
3. The Department of Health and the Health Service Executive (HSE) put in place over 5 years a coherent system to conduct **broad epidemiological surveillance of rare disease in Ireland.** This epidemiological surveillance should include profiling of rare diseases among high-risk cultural and ethnic minority groups for the purposes of appropriate neonatal screening and improving diagnosis and outcomes.
4. A periodic **national report on the epidemiology of rare diseases** in Ireland be published by the Department of Health, similar to that prepared for the European EUROPLAN report, and that reporting on rare diseases be integrated into the existing HSE reporting on health and disability services.
5. **All existing databases to be mobilised.** Systems be put in place to enhance the utility of data held in relevant health service-based information systems, including hospital record, laboratory cytogenetic and molecular genetics data.
6. **Irish data on Orphanet be reviewed** and a plan for its development agreed, including an assessment of its relocation to an Irish centre if appropriate. This function should be supported by a National Office for Rare Diseases (*further information on the role of this proposed new office is provided in Chapter 4*).

7. Appropriate support be given for the ongoing **involvement of Irish registries in relevant European collaborations**, including the RARECARE and EUROCAT registries.
8. An **All-Ireland Network of Rare Disease Registries**, covering the island of Ireland, be developed and that this network work towards enhancing and standardising rare disease registries in line with HIQA draft guidelines, data protection legislation and international best practice. This function should be supported by the new National Office for Rare Diseases.
9. The development of any **future information systems provide for a rare disease code in a patient record** in order that all people with rare diseases may be easily identified. The development of a Rare Disease ID Card that could be linked to a person's PPSN should also be explored once the provisions of the proposed Information Bill have been enacted and promulgated.
10. **A rare disease research network be developed to:**
 - enhance the quality and relevance of rare disease research on the island of Ireland in a strategic manner in line with the priorities of this National Rare Disease Plan;
 - support the integration of rare disease research within relevant forthcoming Government research policy and legislation;
 - develop a clearly identifiable online presence, which would act to attract international interest and research partnerships;
 - Actively pursue potential international research partners; signpost new and established researchers to relevant resources and contacts;
 - facilitate greater international collaboration with relevant registries, organisations and consortia, including the International Rare Disease Research Consortium;
 - make proposals to the Department of Health with regard to Irish involvement in international networks such as E-Rare and engage in the rare diseases aspects of BBMRI-ERIC, ECRIN-ERIC and other EU infrastructures.
11. Research on rare disease in Ireland **adhere to the EURORDIS guiding principles** for conducting rare disease research.
12. The role of the **designated Centres of Expertise** in Ireland should include research relevant to rare disease, in particular with regard to registries, health service and translational research.
13. Ireland **becomes a member of ECRIN-ERIC** in due course and that the capacity of Ireland's five clinical research facilities to engage in rare disease research nationally or in collaboration with international collaborative research be enhanced.
14. The potential for **industry collaboration in research** relevant to rare diseases is explored, particularly with regard to research relevant to the diagnosis, treatment and management of rare disease.
15. The forthcoming **national biobanking plan** provides national coordination and quality standards for biobanking and embraces all opportunities for rare disease research and Ireland becomes a full member of BBMRI-ERIC when the national coordination of biobanking has been established.

Chapter 4: Prevention, diagnosis and care

This chapter provides a detailed focus on the issues around the prevention, diagnosis and treatment of rare diseases from an Irish context. Screening services, in the guise of the National Newborn Screening Programme, along with primary prevention measures, receive attention at the start of the chapter, with the former being assessed for its strengths and weaknesses. Genetic testing services in Ireland are examined as part of the diagnostic element of dealing with rare diseases, followed by treatment and care services available. The context for services for EU patients and the question of improving care and care services, such as respite and palliative care, are also discussed.

The Steering Group recommends:

16. With respect to **pregnancy**:
 - a. where family members are known to be at risk of being carriers of genes for rare diseases, they have appropriate access to pre-conception genetic testing and counselling, which can inform them about the risks involved in becoming pregnant;
 - b. making evidence-based, high-quality pre-conceptual care available to women at higher risk of having babies with rare congenital anomalies (e.g. women with diabetes or epilepsy);
 - c. women are supported regarding preparation for a healthy pregnancy, including healthy diets and lifestyles, folic acid supplementation and good maternal ante-natal care, which can have a role in the prevention of a small number of rare conditions.
17. The HSE Governance Committee/Group on Newborn Screening within the Integrated Services Directorate be expanded to **include a patients' advocate**. The Committee should consider the population benefits of newborn screening, including whether programmes need to be expanded or modified, and the need for carrier screening. The Department of Health should also provide a policy framework for population-based screening programmes.
18. The Department of Health consider addressing the need for a **review of legislation** that indirectly impinges on the Newborn Bloodspot Screening Programme.
19. Governance arrangements for **'send out' genetic tests be strengthened**. This should include clinical guidelines for 'send out' tests and yearly audits of the quality and diagnostic yield of tests sent out from non-hospital sources in order to minimise wastage. A national funding perspective is required to maximise quality and cost-efficiency. Centres involved in testing should develop and use guidelines regarding the most commonly tested conditions.
20. The National Clinical Programme for Rare Disease through a National Office for Rare Diseases **develop the clinical and organisational governance framework** that will underpin care pathways and access to treatment for rare disease patients, particularly in the context of the transition from paediatric care to adult care.
21. National **Centres of Expertise (CoEs)** in Ireland be identified for groupings of rare conditions, based on clinical need and built on foundations already established. There is an urgent requirement for the HSE to map out CoEs and healthcare pathways, and to acknowledge the different role and competencies of CoEs and centres providing care at local level, such mapping to be aligned with the re-organisation of Irish hospitals into hospital groupings. It is also important that broader clinical guidelines take account of the requirements of rare diseases. The potential for cooperation on an all-Ireland basis should be realised. The designation of CoEs should be in accordance with the EUCERD quality criteria for CoEs.

22. The HSE **integrate CoEs into national funding planning**, with provision for adequate staffing for multidisciplinary care, as well as sustainable research infrastructure for clinical investigation in addition to competitive research.
23. The Department of Health and the Health Service Executive (HSE) encourage and support the national Centres of Expertise (when so designated) to **seek recognition as EU designated Centres of Expertise** or associated national centres in European Reference Networks for Rare Diseases (RD ERNs) according to the timeframe, framework and standards currently being developed at European level through the complementary work of EUCERD and the EU Cross-Border Healthcare Directive 2011/24/EU.
24. **Residential respite care be available for children** with rare diseases.
25. With respect to **palliative care**:
 - a. access is provided to appropriate palliative care for people with rare life-limiting conditions;
 - b. guidelines are developed in palliative care provision to address the complex and multisystemic nature of many rare life-limiting conditions;
 - c. the National Development Committee for Children's Palliative Care, chaired by the HSE, take account of the particular needs of children with rare disease in its ongoing programme of work;
 - d. the next National Cancer Strategy could elaborate further on how best to manage rare cancers, especially in the context of this National Rare Disease Plan, where there is a shared objective to detect and treat early patients with rare cancers.
26. Appropriate **modules relating to rare disease feature within all undergraduate and postgraduate programmes** of both medical professional and carer disciplines. In addition to developing competency requirements and training programmes for medical professionals and carers engaged with rare conditions, practical experience and exposure to patients with rare conditions is advantageous.
27. A system of **training in rare diseases for healthcare professionals** be addressed through their professional bodies with the support of all stakeholder groups, including patients and their families. Action in this area should build on initiatives already underway or in progress (as outlined in Recommendation 26 above).
28. The **establishment of a National Clinical Programme for Rare Diseases**. A key role for this clinical programme will be the mapping, development and implementation of care pathways for rare diseases.
29. The **establishment of a National Office for Rare Diseases** to facilitate the coordination and timely access to Centres of Expertise nationally and internationally, and to provide up-to-date information regarding new treatments and management options, including clinical trials.

Chapter 5: Enhancing access to appropriate drugs and technologies

The challenges associated with drugs and technologies is examined in this chapter. It explores the various paths existing for the designation of orphan drugs and technologies, both at European and Irish level; the associated avenues for making these available to patients through community and hospital drug schemes; and accompanying budgets for funding such access.

The Steering Group recommends:

30. The HSE develop a Working Group to bring forward appropriate decision criteria for the **reimbursement of orphan medicines and technologies**. The approach should include an assessment system similar to that for cancer therapies established under the National Cancer Control Programme and link with the CAVOMP at European level.
31. The HSE undertake a **preliminary economic evaluation** of current activity and costs for orphan medicine and technologies for rare disease patients across all hospitals settings.
32. Applications for the use of orphan medicines and technologies in hospitals be dealt with in the **context of a national budget**, rather than through individual hospital budgets, and that the HSE take account of this.
33. The HSE develop a publicly available **annual report documenting the use of both existing and new-to-market orphan medicines and technologies** in Ireland and a summary of applications received and decisions relating to those applications.
34. The existing **horizon scanning between pharmaceutical companies and the HSE**, including clinical value assessment authorities, continue and be enhanced so as to improve information available regarding orphan medicines in the pipeline and the future needs for these medicines.
35. The capacity to prescribe all orphan medicines and technologies for **ultra-rare conditions be limited to specialist teams** designated through the Centres of Expertise.
36. The HSE apply a set of **guidelines on the prescribing** of orphan medicines and technologies in Ireland. The HSE should evaluate clinical outcomes regarding use of orphan medicines.
37. Clinicians should provide data necessary to the **monitoring of prescription patterns** and pharmacovigilance, so as to ensure patient safety and high-quality healthcare.
38. Early dialogue between the HSE and companies who are running **clinical trials in Ireland** with Irish patients where license approval is imminent.
39. Sponsors could be offered an incentive to run trials in Ireland **increasing access to innovation** for Irish patients.

Chapter 6: Empowering, protecting and supporting rare disease patients and carers

This chapter provides the opportunity to draw on the issues of rare disease from the perspectives of the patient and the carer. It is about empowering both through various means such as protecting their rights, preserving equity and facilitating access to accurate and timely information. The benefits of providing holistic care packages are examined, together with the impetus for developing the effectiveness of patients' organisations.

The Steering Group recommends:

40. The **principles of patients' empowerment** be integral to all aspects of this National Rare Disease Plan for Ireland, both now and in the future, in recognition of the fact that patients and their carers require significant clinical and non-clinical support.
41. Arrangements be put in place to support the integration of the experience and expertise of rare disease **patients' organisations in the implementation and review** of this first national National Rare Disease Plan for Ireland.

- 42. **Patients' rights to appropriate assessment and treatment be realised** through a recognised national Centre of Expertise or by linkage through the patient's healthcare provider to recognised European Reference Networks (ERNs) and in the context of the EU Cross-Border Healthcare Directive 2011/24/EU.
- 43. The proposed National Office for Rare Diseases provide **support and information** to patients.
- 44. The National Rare Disease Plan for Ireland encompass a **holistic and person-centred** view of the lives of rare disease patients and their families, one that goes beyond healthcare issues.
- 45. The HSE and non-governmental organisations (NGOs) provide **ongoing support** for people living with rare diseases and that they cooperate and promote awareness of rare diseases.
- 46. The HSE and NGOs avail of the opportunity to promote awareness of and information on rare diseases on **Rare Disease Day**.

Chapter 7: Implementation, monitoring and review of the National Rare Disease Plan

This chapter acknowledges that this National Rare Disease Plan is being published at a time of significant health reform, including Universal Health Insurance as well as significant primary care and acute hospital reforms. It sets out implementation and monitoring arrangements through the service planning process, in addition to planning for the next National Rare Disease Plan in 2019.

The Steering Group recommends:

- 47. An **Oversight Implementation Group** of relevant stakeholders, including patients' groups, led by the HSE be established to oversee and monitor implementation of the National Rare Disease Plan's recommendations and associated key outputs. The HSE will report to the Department of Health using key performance indicators (KPIs) on a periodic basis in accordance with reporting requirements under the National Service Plan. It should be noted that the European Union has mandated EUCERD's KPIs and that Ireland will have to report on these (*see Appendix 5*).
- 48. There should be **an overall review of the National Rare Disease Plan** prior to development of the next plan in 2019.

1. Rare disease in Ireland – Why we need a plan

1.1 Rare diseases in Ireland

A rare disease is defined in the EU as a disease or disorder affecting fewer than 5 in 10,000 of the European population. Although each disease is individually rare, there are a great many rare diseases. Collectively, rare diseases affect a large number of people. It has been estimated that European populations have a 6%-8% lifetime prevalence of having a rare disease (EURORDIS, 2005).

Rare diseases are significant contributors to a number of population health outcomes in terms of their high associated mortality, morbidity and disability. In particular, rare diseases are a significant contributor to early foetal loss and perinatal mortality, as well as infant and child mortality. For example, international estimates suggest that 20%-30% of infant deaths in developed countries are associated with a rare disorder (Posada de la Paz and Groft, 2010). Other estimates suggest that around 50%-75% of all rare diseases affect children and that about 30% of children with a rare disease die before their 5th birthday (Orphanet, 2013).

Rare diseases are also significant as a cause in sensory, physical and intellectual disabilities, as well as in the population health burden of chronic disease (Cystic Fibrosis Registry of Ireland, 2012).

European estimates for the prevalence of rare disorders have been recently produced by Orphanet. Around 80% of rare diseases are genetic in origin, although 80% of all rare disease patients are affected by just 350 rare diseases (Khoshnood *et al*, 2010).

However, while international and European estimates of rare disease are useful, it cannot be assumed that all estimates apply well to the Irish population. In particular, the National Newborn Screening Programme indicates a higher recorded prevalence of certain rare autosomal recessive disorders in Ireland (*see Appendix 3*). In addition, findings from national and international rare disease registries indicate a different prevalence in Ireland for a number of rare disorders, including cystic fibrosis and congenital anomaly (Odom and Segars, 2010; CSO, 2012; Rare Disease UK, 2009).

Population-level factors suggest that the epidemiology of rare genetic disease in Ireland may be changing. For example, factors such as increasing paternal and maternal ages and increased use of fertility therapies may also impact on the national profile of rare genetic disease. Ireland's increased ethnic diversity in the last few decades is also likely to have altered the spectrum of rare disorders presenting in Ireland in terms of both rare genetic disease and rare communicable disease (EURORDIS, 2013).

Rare diseases and the people whom they affect are diverse and this can create a challenge in developing meaningful policy to address needs. Similarly, the needs of rare disease patients span a broad range of medical specialties. However, while rare diseases certainly differ, rare disease patients share a distinct set of common challenges. Principal among these are challenges relating to access to specialist diagnosis and care, eligibility for relevant supports in their rare disease journey and a paucity of research and evidence-informed care pathways (European Council, 2009; EURORDIS and EUROPLAN, 2011). These challenges may be amplified in countries with small populations where services and policies have not been developed by virtue of small numbers of patients (Garcia and Nourisser, 2012).

In recognition of the challenges relating to the diagnosis and management of people with rare diseases, the European Council (2009) made a Recommendation on 'Action in the field of rare diseases' (2009/C 15/02). It proposed that Member States develop a national rare disease plan by 2013 and, in particular, the Council called for concerted action at EU and national level in order to:

- ensure that rare diseases are adequately coded and classified;
- enhance research in the field of rare diseases;
- identify centres of expertise by the end of 2013 and foster their participation in European Reference Networks;
- support the pooling of expertise at European level;
- share assessments on the clinical added value of orphan drugs;
- foster patients' empowerment by involving patients and their representatives at all stages of the decision-making process;
- ensure the sustainability of infrastructures developed for rare diseases.

The present report represents Ireland's response to the European Council Recommendation by providing a framework for action at national level.

1.2 Vision and principles of Ireland's National Rare Disease Plan

The vision set out in the rare disease strategies of some EU Member States features principles of equity and inclusion. Strategies in other European countries and EUROPLAN recommendations also feature commitments about embedding collaboration, accountability and innovation.

A vision and a set of principles are proposed for this first National Rare Disease Plan for Ireland. They are informed by European recommendations and the direction taken in rare disease strategies in other countries. They are also informed by the unique issues faced by rare disease patients in Ireland in view of its small population, along with the experiences of rare disease patients, their carers and health service providers as revealed in the consultation undertaken for the development of the National Rare Disease Plan.

Vision

An Ireland where –

- People with rare disease receive timely access to the best possible evidence-based, patient-centred and family-centred screening (as appropriate), diagnosis, treatment and care through all stages of their lives.
- The needs and experiences of people with rare disease are recognised, understood and addressed within all aspects of the Irish health system, including policy, services and research/information systems.

Principles

Five guiding principles are proposed for Ireland's National Rare Disease Plan. These are intended to guide the implementation and monitoring of the plan in the longer term. It is intended that the principles assist in ensuring that the execution of policy actions remains rooted in what is known to matter to rare disease patients and carers, and also in what is known to be effective in delivering effective change. These principles are:

- **Equity:** Patients resident in Ireland should receive the best possible evidence-based diagnosis and care irrespective of the rarity of their condition and the location of optimal care services. Equality in accordance with prevailing health and other legislation should underpin the provision of care.

- **Collaboration:** Cross-sectoral, cross-border and international cooperation are integral for Ireland to deliver on the vision for rare disease patients and a core activity of all policy actions.
- **Family-centredness:** Implementation of policy actions should be built around the development of coordinated packages of care for patients and their carers.
- **Sustainability:** A strategic approach to improving the situation of rare disease patients and carers should be sustainable. Policy actions should be implemented in a way that planning, delivering and monitoring rare disease issues become core work of the health system.
- **Transparency:** Progress with the implementation of the policy actions should be transparent to all stakeholders.

2. How the National Rare Disease Plan was developed

2.1 Steering Group and Subgroups

In January 2011, at a EUROPLAN Conference organised by patients' representative organisations in Ireland, the Department of Health announced its intention to commence work on a rare disease plan for Ireland. The Department convened a Steering Group to oversee the development of Ireland's first National Rare Disease Plan. Five subgroups were established to support the Steering Group, each subgroup being chaired by a member of the Steering Group. Subjects covered were research and information, Centres of Expertise, patients' empowerment on orphan drugs and technologies, and communications. Membership of the Steering Group and subgroups is listed in Appendix 1.

Each of the subgroups met and discussed the European recommendations and held extended discussions with other key stakeholders. Reports emanating from the subgroups informed the development of both the consultation process and this final report.

Challenges faced by the subgroups in the development of reports included:

- lack of data on the majority of rare diseases in Ireland, including specific information on health and disability services for people with rare diseases;
- capturing and reflecting the views of a diverse and dispersed set of stakeholders.

2.2 Consultation process

The Department of Health, with the support of the Steering Group and allied subgroups, undertook a strategic consultation process between June and August 2012. Two methods were employed: the holding of a consultation event and the gathering of information through an online survey.

The consultation day was launched by Minister James Reilly in Farmleigh on 11th June 2012. A wide range of participants were invited. To complement the findings from this event and ensure a comprehensive and widespread consultation, an online survey was also available to the public for five weeks during June and July.

The findings of the consultation process are being published in a separate report, but in the meanwhile, its key findings are highlighted in the relevant chapters throughout this report and they are also reflected in the plan's recommendations.

Figure 1 sums up the key elements, both national and international, that informed the development of this National Rare Disease Plan for Ireland.

Figure 1: Key determinants that informed the development of Ireland's first National Rare Disease Plan



2.3 Other determinants of the National Rare Disease Plan

In developing Ireland's first National Rare Disease Plan, the Steering Group was keenly aware of the need to maximise benefits and synergies with other rare disease developments internationally. In particular, as the UK was developing a rare disease plan along within a similar timescale, it was recognised that efforts should be made to realise shared benefits for rare disease patients on the island of Ireland. Thus, members of Ireland's Department of Health met with their counterparts in Northern Ireland to consider these issues. Further ongoing communication will be maintained for the purposes of ensuring an appropriate joint approach on potential areas for collaboration.

It was also recognised that other European countries were further along in the development of rare disease plans. For example, France has published its second rare disease plan, with clear learning from the previous edition. Such experience should inform the Irish planning process (EURORDIS, 2013). The Steering Group, therefore, attempted to ensure that the direction of the Irish plan would have a reasonable fit with the broad direction of plans in other European countries. In addition, efforts were made to integrate elements of European and global best practice as set out by key lead agencies at European level, including EURORDIS and EUROCDERD.

3. Recognition of rare diseases – Information and research

3.1 Information on rare disease in Ireland

3.1.1 Definition of rare disease

This chapter is based on the 2010 recommendations proposed by EUROPLAN in its guidance document on the development of national plans for rare diseases (EUROPLAN, 2010).

The European definition considers a disease to be rare if it occurs with a prevalence of <5 (5 or less) per 10,000 of the European population (European Parliament and European Council (2000) – EU Legislation Regulation (EC) No. 141/2000 on orphan medicinal products) and this definition is recognised in Ireland. Since Ireland has a relatively small population, rates for rare occurrences are subject to significant fluctuation. This may mean that some diseases that have a slightly higher underlying prevalence within the Irish population are considered rare diseases for the purposes of the Irish plan.

The definition encompasses:

- rare diseases affecting both adults and children;
- rare diseases irrespective of the severity of that disease;
- rare genetic diseases;
- rare congenital anomalies;
- rare communicable (infectious) diseases;
- rare subtypes of common conditions (e.g. cancer or heart disease);
- rare adverse drug reactions;
- ultra-rare diseases.

There are approximately 6,000 rare diseases recorded on the Orphanet database (*see* www.orpha.net).¹

The general definition of prevalence of <5 per 10,000 is useful, but is not applicable in all circumstances. For example, in the case of rare congenital anomaly, prevalence at birth is used. The definition of a rare cancer in Ireland differs from the overall definition used for rare disease. Cancers with an annual *incidence* of less than 6 per 100,000 European population are considered rare. These definitions have been derived in response to issues such as short life expectancy and are considered complementary to the overall wider definition.

There is currently no European definition of ultra-rare disease. In England and Wales, ultra-rare diseases are considered as those with a prevalence of less than 1 per 50,000 population, equivalent to diseases with less than 1,000 known cases in the region. Adopting a similar definition for Ireland would mean that diseases considered ‘ultra-rare’ are those for which there are less than 100 confirmed cases in Ireland.

3.1.2 Epidemiology

The precise number of people in Ireland with a rare disease is unknown. This lack of basic epidemiology on most rare diseases can contribute to a lack of recognition and hinder the development of appropriate services and policy. For example, basic estimates of the numbers of patients affected by a particular rare disease are required to inform appropriate health and social service commissioning and workforce planning. Data from health service information systems is required in order that the health service can develop and agree clear guidelines for services to meet the needs of rare disease patients and to assess how Irish health services are performing relative to international standards.

1. Orphanet is the reference portal for information on rare diseases and orphan drugs, for all audiences. Its aim is to help improve the diagnosis, care and treatment of patients with rare diseases. It is led by a consortium of around 40 countries, coordinated by France's Inserm team (the French National Institute of Health and Medical Research). National teams are responsible for the collection of information on expert centres, medical laboratories, ongoing research and patient organisations in their country.

Reliable population-based estimates for some rare diseases are available in Ireland. Estimates are available for:

- rare cancers;
- conditions included in the national newborn screening programme;
- a small subset of specific rare diseases allied to established rare disease registries.

Incidence of rare cancers in Ireland is monitored by the National Cancer Registry of Ireland as part of their involvement in the pan-European RARECARE project.

Where data is collected well in Ireland, this is done by particular organisations on a particular rare disease or group of rare diseases. There is currently no mechanism in place to collate relevant data from rare disease registries and other sources. No national reporting mechanism has been established in respect of the overall spectrum of rare disease in Ireland. In addition to the numbers of people affected by rare disease, there is little known about the spectrum of rare disease in Ireland in terms of types of condition, age profile, mortality or morbidity.

The Orphanet database (www.orpha.net) is the mechanism for collecting data on rare diseases in Ireland and across Europe. It is used to derive European prevalence estimates and also as an information portal for patients, health professionals and researchers. Nowgen (part of the NIHR Biomedical Research Centre in Manchester) currently coordinates Orphanet for Ireland and the UK. The quality and quantity of Irish data on Orphanet is in need of review.

3.1.3 Registries of rare diseases

Patients' registries provide an important source of information on rare disease in Ireland. Well-operated and resourced patients' registries can:

- monitor prevalence and incidence, and signal early warning of increases;
- instruct the appropriate development of services nationally or, where numbers are low, instruct the appropriate development of care pathways using specialist services abroad;
- establish the natural history of the disease – the disease characteristics, management and outcomes with or without treatment;
- monitor safety after the introduction of new or experimental treatments;
- assess clinical effectiveness of new interventions;
- monitor care outcomes and allow comparison with European or international standards;
- provide an inventory of patients who can be approached for clinical research and participation in multi-centre trials;
- provide data to inform health economic assessments, such as cost of illness and cost-effectiveness studies.

There is no single national rare disease registry in Ireland. There are a number of individual registries, specific rare disease registries and registries with a wider remit which also record cases of rare disease (see Appendix 2). An analysis of patients' registries in Ireland has recently been completed by the Irish Platform for Patients' Organisations, Science and Industry (IPPOSI) and its report, *Towards a National Strategy for Patient Registries in Ireland*, is to be published shortly; information is available at <http://www.ipposi.ie/index.php/news-a-events-mainmenu-28/158-patient-registries-meeting-10-may-2011>. This analysis found significant diversity in the governance, data quality, coverage and funding arrangements of patients' registries.

Currently the EUROCAT, Cystic Fibrosis and SCNIR registries are linked with European counterparts. Registers need to comply with Data Protection Acts. The Health Information Bill is intended to allow the Minister for Health to prescribe certain registers, which will help to ensure population-wide availability of relevant data for those registers. When developing or improving registries, the recently published Patient Identifier Bill (2013) and the *e-Health Strategy for Ireland* (HSE *et al*, 2013) will be important.

3.1.4 Recording of rare disease in health service information systems

There is currently a very limited capacity to trace rare diseases within mainstream health information systems in Ireland, such as Vital Statistics (deaths and births) and the Hospital Inpatient Reporting System (HIPE), since these systems rely on the ICD-10 coding system. Within hospital inpatient data, many cases of rare disease are 'masked' behind commonly diagnosed conditions (such as epilepsy or autism). A list of potential sources of information on rare diseases in Ireland is provided in Appendix 2. There are no national standards or guidelines regarding the appropriate recording of rare diseases within Government surveys or mainstream health information systems beyond the limited provisions available through ICD-10. ICD-10 (AM) is used in HIPE and ICD-10 in Vital Statistics. ICD-11 is currently being developed by the World Health Organization and is expected to be finalised in 2015. It should be noted that although this new classification may be an improvement on the current ICD-10 based classifications, it may not necessarily provide the level of data required. There is currently no facility to cross-reference cases of rare diseases across mainstream health information systems or between mainstream health information systems and most patients' registries. The role of unique patient identifier is critical here and the Health Identifiers Bill, published in December 2013, provides alphanumeric identifiers for individuals and health service providers. This Bill will be enacted in 2014.

Hospital record and laboratory data (cytogenetic and molecular genetics) are of particular relevance to a better understanding of rare disease, and particularly ultra-rare disease, in Ireland, but these data are currently underutilised. Analysis of such data would greatly enhance our understanding of national patterns of rare disease and inform needs assessment for services required by many rare disease patients.

KEY POINTS FROM THE CONSULTATION PROCESS

Information on rare disease

- Better basic health intelligence on the number of people with rare diseases was seen as critical to awareness and advocating for appropriate service and policy developments.
- Clear policy, data protection and ethical frameworks were seen as critical for rare disease research.
- Development of basic epidemiology of rare diseases in Ireland through rare disease registries was seen as a priority.
- Irish involvement in Orphanet was seen as positive, but underdeveloped.
- Rare disease registries were considered a critical tool to support many types of rare disease research. Respondents were supportive of either a single rare disease registry or a federation of rare disease registries.

3.2 Towards improved information on rare diseases in Ireland – Challenges and opportunities

3.2.1 Strengths and weaknesses of information on rare diseases in Ireland

The Research and Information Subgroup of the Steering Committee were tasked with identifying the strengths and weaknesses of the current system of information on rare diseases in Ireland. An overview of its findings, together with key findings from the consultation process, is provided below.

Strengths of the current system

- National Cancer Registry and linkages on RARECARE project.
- A small number of high functioning Irish rare disease registries.
- Department of Health commitment to the Health Information Bill and the need to adopt a universal patient identifier.
- Information collected through the national Newborn Screening Programme.
- Irish membership of EUROCAT (a European network of population-based registries for epidemiological surveillance of congenital anomalies) and other European registries.
- Membership of Orphanet.

Weaknesses of the current system

- Lack of clarity on implications for rare disease information in forthcoming policy and legislation (e.g. Health Information Bill, Tissue Act).
- No requirement for the Department of Health or any other body to report on national profile of rare disease.
- No system established to collate and analyse available data and report on national profile of rare diseases.
- ICD-10 coding system is a blunt instrument for recording rare disease.
- Lack of specific health information standards for coding and reporting of rare diseases, prohibiting meaningful identification of rare diseases within national health information systems.
- Hospital record data and diagnostic laboratory data underutilised, with lack of capacity in terms of data management systems.
- No transparent communication system in place to facilitate translation of rare disease data and evidence into health service policies relating to appropriate workforce planning and commissioning of services.
- Lack of overall strategic approach to rare disease registries, with diversity of standards, governance and fragmentation of resources across registries, and with no single rare disease registry in place.
- Challenge presented by substantial number of diseases/disorders with no name.

Members of the Research and Information Subgroup held a seminar in March 2012 to inform the work of developing recommendations on research and information on rare disease in Ireland. The seminar featured national and international presentations on the development of:

- European collaborative research and an Irish registry related by motor neurone disease/ALS;
- the CIBERER Rare Disease Research Network in Spain;
- clinical trials for rare disease treatments in Ireland;
- the Rare Disease Foundation in France in the context of the first French National Rare Disease Plan.

Seminar proceedings were developed to capture key findings from the presentations and the structured panel discussion. These proceedings have informed the Steering Group and its recommendations on rare disease research.

3.2.2 Steering Group recommendations on information on rare diseases in Ireland

The Steering Group recommends:

1. **Guidelines be developed on coding and recording of rare diseases** within relevant Irish health data systems that are consistent at European and global level. The Health Information and Quality Authority (HIQA) will have a role in this, given its functions regarding information standards, including coding standards.
2. **The publication of the Health Identifier Bill and the forthcoming Health Information Bill.**
3. The Department of Health and the Health Service Executive (HSE) put in place over 5 years a coherent system to conduct **broad epidemiological surveillance of rare disease in Ireland**. This epidemiological surveillance should include profiling of rare diseases among high-risk cultural and ethnic minority groups for the purposes of appropriate neonatal screening and improving diagnosis and outcomes.
4. A periodic **national report on the epidemiology of rare diseases** in Ireland be published by the Department of Health, similar to that prepared for the European EUROPLAN report, and that reporting on rare diseases be integrated into the existing HSE reporting on health and disability services.
5. **All existing databases to be mobilised.** Systems be put in place to enhance the utility of data held in relevant health service-based information systems, including hospital record, laboratory cytogenetic and molecular genetics data.
6. **Irish data on Orphanet be reviewed** and a plan for its development agreed, including an assessment of its relocation to an Irish centre if appropriate. This function should be supported by a National Office for Rare Diseases (*further information on the role of this proposed new office is provided in Chapter 4*).
7. Appropriate support be given for the ongoing **involvement of Irish registries in relevant European collaborations**, including the RARECARE and EUROCAT registries.
8. An **All-Ireland Network of Rare Disease Registries**, covering the island of Ireland, be developed and that this network work towards enhancing and standardising rare disease registries in line with HIQA draft guidelines, data protection legislation and international best practice. This function should be supported by the new National Office for Rare Diseases.
9. The development of any **future information systems provide for a rare disease code in a patient's record** in order that all people with rare diseases may be easily identified. The development of a Rare Disease ID Card that could be linked to a person's PPSN should also be explored once the provisions of the proposed Information Bill have been enacted and promulgated.

3.3 Research

3.3.1 Rare disease research in context

For people with a rare disease or parents of children with rare disorders, there are often many unknowns. These unknowns can be related to the cause of their disease, the likely effects, the availability of effective treatment and, indeed, their life expectancy and expected quality of life. Many such unknowns are rooted in a lack of research on their condition. For this reason, patients' organisations and advocates often place a premium on the development of rare disease research. However, rare disease research is often challenging. The small number of potential study participants creates issues with the meaningfulness of findings, as well as data protection and ethical issues. Consequently, those interested in rare disease research often have no choice but to collaborate across borders or jurisdictions. This can often be a difficult and slow process, with additional challenges in raising research funds, which might act as a disincentive for some researchers. Access to the appropriate level of funding or specialist expertise is also challenging.

A strategic approach to research on rare disease requires action on many fronts and across different types of research. For example, where the cause of a rare disorder is poorly understood, basic and applied biomedical-type research is critical. For other disorders, an emphasis on clinical trials for potentially effective treatments, or an emphasis on health service audit, may be more urgent.

Qualitative research, documenting the lived experience of patients with rare disease and their families, is also an important component of rare disease research and complements the quantitative studies. As part of their rare disease journey, patients and their carers/parents may need to interface in quite unique ways with the education system, the built environment, employment and social services. Broader research can help inform decisions on the supports a patient may need, whether those supports may be related to State or privately provided services, or support of an emotional, financial or practical nature.

It is notable that the second Rare Disease Plan developed by France increased its emphasis on the amount and the breadth of research (Garcia and Nourissier, 2012) and concentrated on developing rare disease research in a more strategic manner.

KEY POINTS FROM THE CONSULTATION PROCESS

Research

- Clear policy, data protection and ethical frameworks were seen as critical for rare disease research.
- Many types of research were recognised as important, with clinical research and clinical trials particularly emphasized.
- Health service and primary care research were also prioritised.
- Development of basic epidemiology of rare diseases in Ireland through rare disease registries was seen as a priority.
- The development of designated Centres of Expertise and sustainable funding mechanisms were the priority actions for enhancing rare disease research.

3.3.2 Funding of research on rare disease in Ireland

There is currently no dedicated national research programme for rare diseases or specific funding streams operating in Ireland (in line with other disease areas). There is no dedicated central fund or grant-awarding body specific to rare disease research in Ireland. However, rare disease researchers have been successful in applying for and delivering on grants from the Health Research Board (HRB) and Science Foundation Ireland. There are also examples of rare disease research groups, which are focusing on conditions such as epidermolysis bullosa and retinitis pigmentosa, attracting funding from international medical research charities such as DEBRA International and the Wellcome Trust.

The Medical Research Charities Group (MRCG) supports patients' organisations and charities to engage in research. It represents the joint research interests of these charities at national level and also acts as a support and networking organisation. The MRCG/HRB Joint Funding Scheme was developed with a particular emphasis on supporting rare disease research and has funded a significant number of research projects since 2006. The scheme includes some features particularly supporting rare disease research. In this scheme, the HRB co-funds research projects with charities (typically in a 50/50 split of the cost, with up to 75% HRB support for very small, mostly rare diseases charities). Contrary to other HRB schemes, research can be carried out in Ireland or abroad, acknowledging the lack of expertise in some rare disease areas and the need for international cooperation particular to rare diseases. Applications relevant to rare disease research to date have performed very well within the competitive research grant application process. The scheme encourages charities to develop a research strategy and the charities submit applications aligned with their research strategy to the scheme.

Due to the quantity and quality of applications received, research funded under the MRCG/HRB Joint Funding Scheme principally relates to the more common rare disorders. This would be consistent with the European experience, where funding was strikingly focused on a small number of the more 'common' rare diseases. In keeping with the European experience, the main determinants for reaching a significant level of research activity for a given rare disease appear to be (1) the existence of an active patients' organisation; (2) patients' registry; and (3) linkages to European networks.

The Research and Information Subgroup of the Steering Group noted that research activity in the following areas was underdeveloped:

- diagnostic journey and management of rare disease in the primary care setting;
- cost of illness and cost-effectiveness studies;
- comparison of patients' outcomes with international standards and service audit;
- interface between aspects of rare disease and education, employment and disability services;
- palliative (end of life) care for people with rare diseases, especially children.

HRB and MRCG have been actively encouraging charities to consider submitting applications in health services research.

3.3.3 Leadership in rare disease research in Ireland

Patients' organisations are often the catalysts of rare disease research. In Ireland, as across Europe, they have shaped the research agenda, facilitated the involvement of patients in research and contributed financially to seed funding for research projects. Supporting the development of patients' organisations and fostering leaders in those organisations, with the capacity to work with health service providers and planners on rare disease research, is clearly a priority. 'Fighting Blindness', for example, was key to the establishment of a research group in Trinity College, Dublin, which undertakes research into the rare eye condition, retinitis pigmentosa. Similarly, by co-funding a lectureship position with Science

Foundation Ireland, DEBRA Ireland has been central to the establishment of an epidermolysis bullosa research group in the National University of Ireland, Galway.

Clinicians providing a service to patients with rare diseases are also in a unique position to lead on meaningful clinical research. However, there is currently a lack of supports available to clinicians in Ireland to become involved in rare disease research. These supports relate to:

- access to appropriate national higher training opportunities and integration of rare disease research into the career development pathway for specialists;
- dedicated research time;
- appropriate staffing and facilities.

Rare disease clinicians, like other clinicians, are eligible to apply to existing HRB schemes, from career development fellowships to project or programmatic funding. Only a few choose to do so. Barriers may include such structural issues as single-handed service delivery posts with large caseloads, but also the fact that research in rare diseases may be less appealing because it is more difficult, often slow, requires collaboration and needs multi-author partnerships to secure grant funding.

3.3.4 Networks of rare disease researchers

For a country the size of Ireland, national networks researching specific rare diseases do exist, but in an informal *ad hoc* way. Networking occurs through the umbrella groupings of patients' organisations such as MRCG, IPPOSI and the Genetic and Rare Disease Research Organisation, as well as the clinicians and research departments linked with these organisations. However, for new researchers wishing to initiate rare disease research or for established rare disease researchers wishing to link with new research expertise or avail of specific infrastructure (e.g. animal testing, genomics), there is no network specifically to signpost and support this type of activity. The lack of a central information source providing links to rare disease researchers and relevant facilities and expertise in Ireland has been identified as an obstacle to the growth and development of rare disease research here.

International networks of rare disease researchers are supported through the participation of clinicians, researchers and patients' organisations in international research groups, professional associations and societies.

During the lifetime of its current strategy, the Health Research Board (HRB) has invested strongly in research on Population Health and Health Services. Through various capacity building schemes and project funding, high-quality researchers are supported to study effectiveness, cost-effectiveness, mixed-methods research, evaluative research methods, quality of life, and population groups across the lifecourse and in different non-hospital settings. This is a growing resource of expertise and access to funding, which the rare disease research community can avail of.

3.3.5 Participation in international research initiatives and multinational clinical trials

There is limited capacity in rare disease research among Irish researchers, which has led to limitations to their collaboration with European counterparts, in the context of international research such as FP7 (7th EU Framework Programme for Research and Technological Development). There will be opportunities in the *Horizon 2020* programme for rare disease research. Ireland needs to grow national capacity in research in rare diseases in order to be in a position to join initiatives such as *E-Rare*.² Irish patients with rare disease will benefit if a structured approach is developed to reach a critical mass of patients for clinical trials and exploiting international expertise.

2. E-Rare (ERA-Net on rare diseases) is a network of partners – public bodies, ministries and research-funding organisations – from 12 countries, responsible for the development and funding of national/regional research programmes on rare diseases. E-Rare fosters research on rare diseases in Europe. E-Rare partners systematically exchange information on rare disease research and organise joint funding initiatives.

As part of the European Clinical Research Network Infrastructure (ECRIN), the Irish Clinical Research Network Infrastructure (ICRIN) has successfully applied for funding through the European Commission's FP7 Integrating Activity call. ICRIN is part of a work package, led by Orphanet, focusing on rare disease clinical research. The purpose of the work package is to facilitate the involvement of Irish patients in clinical trials for rare diseases. It aims to create a European hub and network for rare disease clinical research, to develop tools to facilitate clinical research and to map relevant expertise and resources across Europe. Once in place, this initiative should provide Irish researchers with support to conduct successful, international rare disease clinical trials. As part of this programme, there will be a call for clinical trials in rare diseases, which will afford Irish researchers an opportunity to apply for funding for specific clinical trials.

3.3.6 Infrastructure, technological platforms and biobanking

As a small country, Ireland could not fund technology platforms and infrastructures specifically for rare disease. However, a structured approach to facilitate rare disease researchers to avail of existing infrastructure is in need of development. The required infrastructure for clinical research has been developed mostly by the Health Research Board (HRB), through funding from the Department of Health, in the form of Clinical Research Facilities (CRFs), advanced plans for a national coordination mechanism to deliver multisite clinical trials, a recent call to establish Clinical Trials Networks and the Irish Clinical Research Infrastructure Network (ICRIN).

The need to support biobanking activity in Ireland has been recognised in a number of reports and Government strategies in recent years, including the *Action Plan for Health Research, 2009-2013* (Action 2.16 of which states: 'Identify priority biobank and other infrastructural requirements to underpin clinical research') and *Implementation of Research Prioritisation: Priority Area E – Medical Devices Action Plan, July 2013* (which states: 'Take steps to establish a national biobanking system and support infrastructure').

The HRB is working with other relevant funders (SFI, Enterprise Ireland and the Department of Agriculture, Food and the Marine) towards establishing a national biobanking system and support structure.

Biobanks³ are of particular relevance to rare disease because biobanked samples can be used to:

- undertake basic research, such as disease gene identification;
- elucidate biological pathways underlying disease;
- identify biomarkers or drug targets;
- test the effects of new drugs;
- identify patients who may benefit from new treatments;
- facilitate translational research.

It is hoped that Ireland will become a member of BBMRI-ECRIN, the European research infrastructure for biobanking, if and when a national biobanking structure has been established. This would potentially give access for Irish research to European biobanks in rare diseases.

3.4 Towards better research on rare diseases in Ireland – Challenges and opportunities

3.4.1 Strengths and weaknesses of rare disease research in Ireland

The Research and Information Subgroup of the Steering Group were tasked with identifying strengths and weaknesses of research on rare diseases in Ireland. An overview of its findings, together with key findings from the consultation process, is provided below.

3. Biobanks are defined as a collection of biological samples, such as blood, tissue or DNA, plus associated epidemiological, clinical and research data.

Strengths of the current system

- Rare disease research performing well within MRCG/HRB Joint Funding Scheme.
- Some successful models and projects bringing in international funding.
- MRCG is a platform for rare disease patients' organisations to become involved in research.
- Professional societies, groups and seminars are a forum for sharing of research interests and findings (e.g. Irish Society of Human Genetics).
- ECRIN/ICRIN involvement in rare disease research and facilitation of multinational clinical trials.
- Opportunities for rare disease research presented by ongoing national longitudinal studies and surveys.

Weaknesses of the current system

- Like many disease groups, there is no central source of information on rare disease research, such as an office for rare disease, rare disease research platform or designated Centre of Expertise with this role.
- Lack of structured, reliable, complete and accessible information systems/registers.
- Networking of rare disease researchers occurring on an *ad hoc* basis.
- Overall low level of international collaboration.
- No overall strategic approach to rare disease research.
- Limited supports for clinical specialities relevant to rare diseases conducting research in terms of dedicated staff time, resources and linkages with career development pathways (rare diseases share this issue with other disease areas).
- Majority of research focused on 'common' rare diseases rather than 'rare' rare diseases.
- Little activity in terms of rare disease research in primary care setting.
- Lack of research on broader aspects of rare disease, including education, disability, employment, social services and end-of-life care.

3.4.2 Steering Group Recommendations on research on rare disease in Ireland

The Steering Group recommends:

- 10. A rare disease research network** be developed to:
 - enhance the quality and relevance of rare disease research on the island of Ireland in a strategic manner in line with the priorities of this National Rare Disease Plan;
 - support the integration of rare disease research within relevant forthcoming Government research policy and legislation;
 - develop a clearly identifiable online presence, which would act to attract international interest and research partnerships;
 - actively pursue potential international research partners;
 - signpost new and established researchers to relevant resources and contacts;
 - facilitate greater international collaboration with relevant registries, organisations and consortia, including the International Rare Disease Research Consortium;
 - make proposals to the Department of Health with regard to Irish involvement in international networks such as E-Rare and engage in the rare diseases aspects of BBMRI-ERIC, ECRIN-ERIC and other EU infrastructures.

11. Research on rare disease in Ireland **adhere to the EURORDIS guiding principles** for conducting rare disease research.
12. The role of the **designated Centres of Expertise** in Ireland should include research relevant to rare disease, in particular with regard to registries, health service and translational research.
13. Ireland **becomes a member of ECRIN-ERIC** in due course and that the capacity of Ireland's five clinical research facilities to engage in rare disease research nationally or in collaboration with international collaborative research be enhanced.
14. The potential for **industry collaboration in research** relevant to rare diseases is explored, particularly with regard to research relevant to the diagnosis, treatment and management of rare disease.
15. The forthcoming **national biobanking plan** provides national coordination and quality standards for biobanking and embraces all opportunities for rare disease research and Ireland becomes a full member of BBMRI-ERIC when the national coordination of biobanking has been established.

4. Prevention, Diagnosis and Care

Because of the large number of different rare diseases, their low prevalence, their specificity and the expression of diseases without predominant symptoms, provision of services poses challenges for all societies. This is all the more so in countries such as Ireland with a relatively small population and, as outlined in Chapter 3, with a relatively high prevalence of some rare diseases.

In this situation, accessible, equitable and quality services can only be provided with the cooperation of many stakeholders and functions, including information provision, research, orphan drug and other therapy development, professional training, social services as well as medical service provision. For this reason, the discussion and recommendations in this chapter need to be read in conjunction with those in other chapters of this report.

KEY POINTS FROM THE CONSULTATION PROCESS

Prevention, Diagnosis and Care

- Better access to specialist care and improvements in accurate and timely diagnosis were considered the areas which could bring most benefit to rare disease patients in Ireland.
- Awareness of rare diseases was a cross-cutting issue – this lack of awareness was evident at all levels of the healthcare system, as well as in respect of access to public and private services and entitlements both within the clinical setting and beyond.
- Lack of awareness and understanding of rare disease created significant vulnerability at many stages of the patients' journey, most particularly for those seeking a diagnosis and navigating the healthcare system in the absence of any clear care pathway.

4.1 Prevention, screening and diagnosis – Current situation

4.1.1 Primary prevention

In keeping with the approach set out in the policy framework *Healthy Ireland: A Framework for Improved Health and Wellbeing, 2013-2025* (Department of Health, 2013) and in *Future Health – A Strategic Framework for Reform of the Health Service, 2012-2015* (Department of Health, 2012), the first approach to any disease, including rare disease, is health promotion and prevention. Since about 80% of rare diseases are genetic in origin, it is acknowledged that prevention is not possible at this time for many rare diseases, given the current state of scientific and medical knowledge. Where family members are known to be at risk of being carriers of genes for certain rare diseases, pre-conception genetic testing and counselling can inform them about the risks involved in becoming pregnant. (Issues related to genetic testing services more generally are covered later in this chapter.) Beyond this, adherence to guidelines on preparation for a healthy pregnancy along the lines advised to the general population – including in relation to healthy diets and lifestyles, folic acid supplementation and good maternal ante-natal care – has a role in the prevention of a small number of rare conditions. Evidence-based, high-quality pre-conceptual care is important for women at higher risk of having babies with rare congenital anomalies (e.g. women with diabetes or epilepsy). EUROCAT and EUROPLAN (2013) have produced

a report entitled *Recommendations on policies to be considered for the primary prevention of congenital anomalies in national plans and strategies on rare diseases*.

The Steering Group recommends:

- 16.** With respect to **pregnancy**:
- Where family members are known to be at risk of being carriers of genes for rare diseases, they have appropriate access to pre-conception genetic testing and counselling, which can inform them about the risks involved in becoming pregnant;
 - Making evidence-based, high-quality pre-conceptual care available to women at higher risk of having babies with rare congenital anomalies (e.g. women with diabetes or epilepsy);
 - Women are supported regarding preparation for a healthy pregnancy, including healthy diets and lifestyles, folic acid supplementation and good maternal ante-natal care, which can have a role in the prevention of a small number of rare conditions.

4.1.2 Screening

One of the key early points in the lifecycle at which the possible presence of a rare disease may be indicated is at the newborn stage. Ireland commenced a National Newborn Screening Programme for phenylketonuria (PKU) in 1966. The success of this programme was followed by the introduction of screening for other prevalent treatable conditions preventing mental retardation: homocystinuria in 1971, Maple Syrup Urine Disease and galactosaemia in 1972, and congenital hypothyroidism in 1979 (*see Appendix 3*). Newborn screening for cystic fibrosis commenced on 1st July 2011. Newborn screening is now carried out for a total of 6 conditions.

KEY POINTS FROM THE CONSULTATION PROCESS

Newborn Screening Programme

- Newborn screening was seen as a very positive contributor to the early diagnosis of rare diseases in Ireland.
- The introduction of newborn screening for cystic fibrosis was widely endorsed.
- Responses recognised the need to support the further development of the National Newborn Screening Programme through the National Rare Disease Plan for Ireland.
- Appropriate follow-up, referral and support of parents experiencing bad news from newborn screening was emphasized.
- Ante-natal screening for rare disease or anomaly featured in several responses and may need to be considered within the National Rare Disease Plan.

The HSE recently established and implemented a governance structure within the Integrated Services Directorate (ISD). The composition of the governance group has been expanded to include a consultant paediatrician with a special interest in inherited metabolic disorders. However, as yet, there is no patients' advocate. The governance group has agreed to consider a proposal to expand the National Newborn Bloodspot Screening Programme to include two additional disorders initially – Medium Chain Acyl CoA dehydrogenase (MCAD) deficiency and Glutaric Aciduria type 1 (GA1). Key performance indication has been proposed and the tendering process for a dedicated newborn screening laboratory information system has been completed to conform with the Data Protection Commissioner's requirements. Follow-up work on this is being progressed.

Ireland does not currently have a national framework in rare diseases screening options and policies, other than for the Newborn Screening Programme. It is generally accepted that consideration of specific conditions amenable to screening (e.g. specific conditions with very high prevalence in the Irish Traveller community) would need to comply with the general Wilson and Jungner (1968) criteria for screening, i.e. that the condition should be an important health problem, there should be an accepted modality of treatment available and treatment should be cost-effective.

The European Council (EC) Recommendation of 8 June 2009 on 'Action in the field of rare diseases' (2009/C 15/02) proposes (in Paragraph 17d) that Member States 'gather national expertise on rare diseases and support the pooling of that expertise with European counterparts in order to support the development of European guidelines on diagnostic tests or population screening, while respecting national decisions and competences'.

On foot of an EC tender process, the EU Executive Agency for Health and Consumers (EAHC) evaluated population newborn screening practices for rare diseases in EU Member States with the objective of developing a decision-making matrix that could be used by Member States to progress and systematically expand (or contract) its newborn screening mandates. The final report was published in 2012 (Burgard *et al*, 2012). A number of the recommendations of relevance include (1) establishment of an EU governance body to advise national policy-makers; (2) newborn screening (NBS) to be offered to all infants in the State, universal screening the preferred option; (3) a national plan should be in place for a 5-year period; (4) health systems should cover cost of NBS; (5) this should be an informed process; (6) the national NBS panel should be expanded step by step according to Member State requirements; (7) programme evaluation should be performed annually and be made publicly available; and (8) databases recording long-term outcomes should be established.

The EC requested the European Committee of Experts on Rare Diseases (EUCERD) to consider this 2012 report and an Executive report (Vittozzi *et al*, 2012), and to issue their proposals for the next steps. EUCERD has issued an Opinion on potential areas for European collaboration and submitted it for further consideration to EU Member States, the European Commission and any third parties involved.

Strengths of current National Newborn Screening Programme

- The clinical outcomes of the current National Newborn Screening Programme in Ireland are continually audited and are exemplary as evidenced by international peer review.
- The laboratory services are accredited by CPA (UK) to ISO 15189 standards and the laboratory participates in a range of external quality assurance programmes, including ERNDIM, UKNEQAS and Region-4-Genetics Collaboration (Mayo Clinic, National Institutes of Health).
- The programme is monitored by its Clinical Director, who reports to the NNBSG Governance Group.

- The programme for the existing conditions meets the targets in the EAHC 2011 report, for example, on expectancy for sample delivery, numbers and turnaround times.

Weaknesses of current National Newborn Screening Programme

- Newborn screening is an essential public health responsibility, not currently mandated by law and lacking the appropriate legislative framework in Ireland.
- There is no health economics evaluation of newborn screening.
- There is a lack of patients' advocacy groups, in particular for newborns, and a lack of public understanding of the merits and public health consequences of appropriate newborn screening for the Irish population.
- Difficult economic conditions and a health system under reform and re-organisation present considerable challenges to the Newborn Screening Programme.

4.1.3 Diagnosis

Timely diagnosis of rare diseases is essential. Without accurate diagnosis, patients and families cannot access effective treatment/therapy or manage their condition appropriately.

Since about 80% of rare diseases are genetic in origin, effective genetic services have a vital role to play in relation to diagnosis. They help bring clarity for the patients and families concerned, as well as providing a foundation for the development of healthcare policies, service planning and resource allocation within the health and social care systems. This same is true of access to appropriate diagnostic tests for rare diseases of non-genetic origin where these have been developed.

KEY POINTS FROM THE CONSULTATION PROCESS

Diagnosis

- Delays in diagnosis were the predominant concern among respondents. About one-third considered the quality of diagnosis to be 'poor' or 'very poor', which raised issues for both patients and their health service providers.
- Other concerns were a lack of interest in rare disease symptoms and insensitive or ill-informed communication of the diagnosis by clinicians.
- Poor recognition that travel to specialist centres abroad expedited diagnosis.
- Supporting GP skills in appropriate referral and better access to specialist diagnostic services are both needed.
- Improving diagnosis of rare diseases was considered important, involving additional time, effort and clinical skills in history-taking and physical examination by the clinician, rather than repeated tests.
- Absence of a system to document, analyse or compensate patients for misdiagnosis was highlighted.

Genetic testing

The National Centre for Medical Genetics (NCMG) at Our Lady's Children's Hospital, Crumlin, provides diagnosis and genetic counselling for all genetic rare diseases referred to it. It was opened in 1994 with the objective of providing a clinical and laboratory genetic service for those affected by, or at risk of, a genetic disorder and is the only centre in Ireland providing such a service. The NCMG is organised into three divisions: Clinical Genetics, Cytogenetics and Molecular Genetics.

NCMG processes approximately 13,000 cytogenetic and molecular genetic tests each year and tests for 19 specific gene defects. The cytogenetic and molecular genetic laboratories are externally accredited by CPA UK, a development facilitated by, inter alia, an extension to the NCMG opened in 2007. EU regulations now require laboratories to seek accreditation from their own national accreditation body and so, in compliance with this, the NCMG laboratories will be applying to the Irish National Accreditation Board (INAB). When a genetic test is not available from a laboratory in Ireland but is clinically indicated, DNA samples are sent to specialised laboratories abroad (with 740 'send out' tests listed in the NCMG database). All tests done at NCMG meet international standards. For tests done abroad, the quality of genetic testing meets international standards if sent via the NCMG who ensure that any outsourcing is done in accredited laboratories, with an appropriate audit trail. Difficulties can arise where non-accredited providers send tests out without referring to specialists in the area or to standard guidelines. This practice can give rise to cost-inefficiencies and can also be a significant risk issue. A more appropriate national funding perspective in relation to genetic testing would help to mitigate this.

Initially, the NCMG had 18 staff and provided a limited service for the Greater Dublin area and the East coast area. Over time, the NCMG has obtained further resources and has been able to extend its coverage to additional areas within the Republic of Ireland. It has always aimed to provide an equitable clinical service nationwide and runs outreach genetic clinics in Cork, Galway and Limerick. Notwithstanding these developments, the NCMG has not been immune to considerable staffing and funding challenges in recent years.

A report submitted in late 2012 to Clinical Leads in Paediatrics indicated a waiting time of 12-24 months for referral to NCMG. Long waiting times impact on, for example, immediate access for linked programmes such as the National Centre for Inherited Metabolic Disorders (NCIMD). It is important that genetic counselling be offered to and provided for those individuals and families that require it and would benefit by it. Within the Republic of Ireland (RoI), however, it has to be acknowledged that although the NCMG aims to promote services in a clinically appropriate manner, a considerable challenge persists in terms of under-resourcing of clinical staff. The Royal College of Physicians UK recommends a minimum of 3 consultant geneticists per million population and the Association of Genetic Nurse and Counsellors UK (AGNC) recommends one full-time genetic counsellor per 100,000 population. Applying these ratios to the Irish (RoI) population would imply a total of 14 WTE consultants and 46 genetic counsellors (NCMG, 2010). The Northern Ireland Genetics Service has 6.5 WTE consultants, 1 trainee registrar, 6.5 WTE genetic counsellors and 1 WTE family history nurse for a population one-third the size of the Republic. Ireland has the lowest population ratio of genetics staff of 10 European countries studied (*see* <https://www.eshg.org/111.0.html>).

Strengths of the current genetic testing system

- Testing done through the NCMG meets international standards.
- The Disability Act Part IV, passed by the Oireachtas and signed into law in 2005, states that genetic testing shall not be carried out unless the consent of the person has been obtained. In addition, genetic tests cannot be used in relation to employment, insurance, pensions or mortgages.

Weaknesses of the current genetic testing system

- A report submitted in late 2012 to Clinical Leads in Paediatrics indicates a waiting time of 12-24 months for referral to NCMG. Due to funding challenges and unfavourable consultant:patient ratios, there is lack of an appropriate method of tracking patients without an appropriate database or specific disease registries.
- Difficulties have arisen in the last two years with funding challenges and excessive untimely access to appointments according to required standards. This has resulted, inter alia, in non-accredited providers sending tests out without referring to specialists in the area or to standard guidelines, giving rise to cost-inefficiencies and risk issues.
- The model of funding is on a local model basis. NCMG do not have a ring-fenced budget. Long waiting times impact on, for example, immediate access for linked programmes such as the National Centre for Inherited Metabolic Disorders (NCIMD).
- In addition to delays in diagnosis that may arise from resource challenges in established testing programmes, for ultra-rare diseases, the very rarity of the condition in a relatively small population such as Ireland poses particular diagnostic challenges. This is due to lack of knowledge among GPs, other health professionals and parents about the signs and symptoms and the appropriate treatment pathways. Many patients and families affected have an undesirably long wait for a correct diagnosis and a worrying number receive an incorrect diagnosis before their final diagnosis is made. However, more recently the NCMG has developed a UCD-linked microsite (www.ucd.ie/medicine/rarediseases) which provides practical advice to community practitioners regarding testing and the referral process in general for genetic rare diseases.

4.2 Treatment and care – Current situation

KEY POINTS FROM THE CONSULTATION PROCESS

Quality of care

- Almost one-third of respondents to the online consultation rated the quality of care as 'poor' or 'very poor'.
- Rare diseases brought unique challenges to the doctor–patient relationship, for example, addressing limited clinician knowledge on the rare disease, 'patient experts' and the appropriate use of information from many sources including the Internet.
- Many responses revealed complex care needs among rare disease patients that required multidisciplinary input.
- Rare disease patients commonly required a high level of coordination between health and disability services.
- Many issues are relevant to both specialist and general health services.
- Meeting the needs of rare disease patients with chronic, multi-morbid and/or disabling rare diseases appeared to be particularly challenging.
- Appropriate support for care (including respite) provided in the home for significantly disabled rare disease patients was also emphasized, including respite.

- Respondents highlighted the consequences of inadequate care pathways, care coordination and continuity of care – multiple trips to emergency departments or primary care, additional carer stress and diminished outcomes for patients.
- Issues relating to access to and eligibility for physiotherapy, occupational therapy and speech/language therapy services were frequently highlighted.
- Appropriate infection control and age-appropriate hospital facilities for in-patients with cystic fibrosis were seen as critical components of optimal care for this group.
- The transition from childhood to adult rare disease services was seen as a major barrier to achieving good care outcomes.
- The lack of understanding of rare disease patients outside the health services was highlighted, for example, in the domains of education, employment and disability. This would indicate a need to prioritise holistic packages of care, with interdisciplinary input.
- Lack of care pathways was perceived as a barrier to achieving good care outcomes.

Currently, the Department of Health has no specific list of national Centres of Expertise for rare diseases nor does it set standards for specific units to be considered ‘national’. However, the Department does recognise that particular centres have particular expertise and would give specific funds to support those specialist services. The HSE is responsible for these services and supports Centres of Expertise and laboratories, including 8 cancer centres: the National Centre for Medical Genetics (NCMG), which provides a comprehensive service for patients (both adults and children) affected by or at risk of a genetic disorder; the National Centre for Inherited Metabolic Disorders (NCIMD), a tertiary care referral centre for the investigation and treatment of patients suspected of having a metabolic genetic disease, linked to the Newborn Screening Programme; and the National Centre for Hereditary Coagulation Disorders (children and adults).

While these centres receive specific funds via their host hospitals to provide specialised services for individuals with rare diseases, this funding is not ring-fenced and the services have not been protected from significant staff losses at the NCMG and ongoing at Our Lady’s Children’s Hospital, Crumlin. The NCMG does not have a ring-fenced budget.

There are currently 14 centres for management of cystic fibrosis listed for Ireland in the Orphanet registry (www.orphanet.ie). Rare cancers are seen as part of the remit of the 8 designated cancer centres in the *Strategy for Cancer Control in Ireland* (National Cancer Forum, 2006). Patients with alpha-1 antitrypsin deficiency receive diagnosis and management at Beaumont Hospital as a main reference centre and many rare neurological conditions are seen at different tertiary-level centres throughout the country.

As mentioned in Section 4.1.3, collectively the National Centre for Medical Genetics (NCMG) provides diagnosis and genetic counselling for all genetic rare diseases referred to it. The Steering Group for the National Rare Disease Plan, together with feedback from the public consultation, has proposed that Ireland works to EUCERD’s (2012a) recommendations for designated Centres of Expertise and participates in European Reference Networks (ERNs) (*see Section 4.4.3 below*). EUCERD recommends provision of management and multidisciplinary care of rare disease patients at designated Centres of

Expertise, including the provision of psychosocial care and the development of healthcare pathways for patients (applicable to specific genetic rare diseases, e.g. Marfan Syndrome, Tuberous sclerosis, DiGeorge Syndrome, William Syndrome). While NCMG provides diagnostic access, it does not offer follow-up management and multidisciplinary care for the above specific single gene disorders, in comparison to the practice in Belfast and many European Reference Centres, since it does not have the staffing capacity to manage patients, to provide follow-up care to patients in general or run specific multidisciplinary clinics. The only multidisciplinary clinics currently held are for Neurofibromatosis, which is funded through charitable donations (Neurofibromatosis Society).

The National Centre for Inherited Metabolic Disorders (NCIMD), located at the Children's University Hospital, Temple Street, and the Mater Misericordiae University Hospital, Dublin, is the tertiary care referral centre for the investigation and treatment, care and support of children and adults suspected of having a metabolic genetic disease in Ireland, with links to the National Newborn Screening Programme. This specialised centre plays a major role in preventing and treating disability in the Irish population. The development of outreach services from Temple Street Children's Hospital, as the national tertiary hospital, to regional hospitals is an important component of a national integrated paediatric service network. The first outreach clinic was conducted in Limerick University Hospital in 2012 and there is a clinic planned for Mercy University Hospital, Cork.

NCIMD is the only recognised centre for treatment of more than 250 rare genetic metabolic diseases in Ireland (mainly paediatric-based). It provides treatment and care for over 1,800 patients nationally. As noted in Chapter 3, Ireland has a higher incidence of inherited metabolic disorders than the UK and USA, and the current linked national newborn screening, in addition to improving the quality of life of people with PKU, reduces economic costs through prevention of severe mental retardation and disability. In its 2006 review, the Irish Health Service Accreditation Board (IHSAB) identified NCIMD as the Centre of Expertise for paediatric metabolic care.

The IHSAB (2006) recommended immediate development of a centre of expertise for adult patients with treatable hereditary metabolic diseases (HMDs). An NCIMD publication (Morrissey *et al*, 2013) has indicated that there are approximately 900 known adult patients with treatable HMDs, with also major under-ascertainment of cases in the absence of a national registry and adequate coding systems. A reasonable estimate of the referral basis is of at least 2,000 cases of adults with treatable HMDs in the Irish population, which will require a designated national Centre of Expertise for multidisciplinary care.

Since September 2011, with funding and recruitment challenges, assessment of new HMD patients or provision of 'send out' laboratory tests for investigation of HMD adults is no longer available at Temple Street Children's Hospital. A large cohort of existing adult metabolic patients (more than 800) require immediate transition to an age-appropriate adult specialist centre from the paediatric programme which cannot be considered an appropriate centre of expertise for adult patients.

The opportunity to expand this service fully to meet the population need will depend on further supports in the areas of headcount and budget for related laboratory testing, basic administrative and multidisciplinary posts.

KEY POINTS FROM CONSULTATION PROCESS

Waiting times

- Opinions varied substantially on the current waiting times for assessment by an appropriate rare disease specialist.
- Responses from the consultation exercise suggest that between 1 in 4 and 1 in 5 of rare disease patients wait over a year for assessment by an appropriate rare disease specialist.
- Respondents felt that an appointment with a specialist should follow within 3 months of referral by a GP.
- Respondents considered that assessment should occur within 3 months, including genetic counselling for potentially affected family members in families where a genetic disease has been detected.

The National Centre for Hereditary Coagulation Disorders, based at St. James's Hospital, Dublin, provides care to many hundreds of children and adults with hereditary coagulation disorders. It is frequently cited as an exemplary centre of expertise since it provides timely access to care with local expertise and a staffed registry. On the recommendation of the Lindsay Tribunal (2002), the National Haemophilia Council was approved by Government in 2004 (Statutory Instrument No. 451), with its principal function to make recommendations to the Minister for Health and Children and health service agencies on all aspects of the care and treatment of people with haemophilia, to include 'the funding for such services each year, ensuring that funding is sufficient to provide the range of services required and to advise on a quality management system'.

While healthcare pathways may be well defined for some rare disorders (e.g. hereditary coagulation disorders), for many conditions and for ultra-rare disorders, there may not be sufficient local expertise in Ireland. For example, for the single gene disorders Marfan Syndrome (estimated prevalence of 1 in 5,000 of population), Neurofibromatosis (estimated prevalence of 1 in 4,000 of population) and 22q Deletion Syndrome, there are no management centres listed in Orphanet for Ireland, whereas in France for Marfan Syndrome there are 3 reference centres and 7 'competence centres'; there are 47 centres in total for Neurofibromatosis; and 49 centres in total for 22q Deletion Syndrome.

Informal collaborations for clinical care and clinical investigation exist between Dublin and Belfast and European centres for many genetic and metabolic rare diseases, as national centres, such as NCMG and NCIMD, refer to international databases for care pathways and review (e.g. Dyscerne, Decipher, ESDN, OMIM, Unique and Genetests, etc).

In keeping with the model of integrated care outlined in *Future Health – A Strategic Framework for Reform of the Health Service, 2012-2015* (Department of Health, 2012), services for patients with rare diseases 'must be planned and delivered with patients' needs and wishes as the organising principle'. In the case of rare diseases, better outcomes for patients and more efficient use of resources will necessitate integrated and coordinated service planning and delivery across a range of health and social services, such as hospitals, primary care, specialised community services, social care and beyond into the education and labour sectors. (The issue of services other than clinical services is addressed in Section 6.7 of Chapter 6, on delivering a holistic package to respond to the needs of rare disease patients and their carers.)

The Irish EUROPLAN Conference 2011 recommended that a national electronic healthcare record be developed for rare disease patients because it was seen by patients as a key need in their interaction with services (EUROPLAN, 2011).

Information for patients, families and health professionals is a critical component in the provision of an accessible and quality service for rare diseases. A 2008 study by Rehab Care reported that 75% of GPs surveyed had difficulties in providing patients and families with information on rare diseases. In addition, the Steering Group for this National Rare Disease Plan identified that Irish rare disease patients themselves, along with general medical specialists, commonly do not know where specific expertise exists and it may be many years before a centre is identified (usually by 'word of mouth') that has expertise to treat a specific condition. The diagnostic journey for very many patients is frustrating and prolonged, often with unnecessary consultations and treatments.

The Task Force on Rare Diseases published *An Easy Guide to Rare Diseases in Ireland – A Resource for the Media and the Public*. There is currently no helpline or dedicated office for rare diseases in Ireland. Some disease-specific helplines are funded through public/private partnerships. Given that information for patients, families and health professionals is a critical component in the provision of an accessible and quality service related to rare diseases and the acknowledged difficulty in accessing such information, including for service planning, the Irish EUROPLAN Conference 2011 recommended that a Central Office for Rare Disease Information should be established, without delay, to act as a national point of reference for enquiries relating to services, diagnostics, information regarding clinical trials, links to established databases such as Orphanet, and expertise for all rare diseases.

The establishment of an office is a key point identified by the Steering Group and the Rare Disease Patient Alliance. Implementation will be required for effective roll-out of the Rare Diseases Clinical Care Programme. The existence of a functional, rare disease-specific comprehensive nationwide information system and a resourced (ideally State-funded) helpline is one of the EUCERD's Key Performance Indicators (June 2013) for rare disease national plans (*see Appendix 5*).

Summary of strengths and weakness of current system

Strengths of current system

- Well-trained medical and paramedical staff.
- Commitment of relevant staff to provide a quality service.
- Very active and committed patients' support groups (e.g. GRDO, IPPOSI, MRCG).
- Good linkages and cooperation with international colleagues and European Reference Networks (ERNs).
- Major opportunities for epidemiological research with population base and high prevalence of genetic recessive disease in Irish population.
- Strong Pharma base for collaboration in Ireland.

Weaknesses of current system

- Challenges around staffing levels and lack of recognition of some of the main reference centres.
- Lack of ring-fenced budgets and national funding. No health economics evaluations apparently ever performed to illustrate predicted cost savings (e.g. for newborn screening) of treating rare diseases.
- Lack of understanding and education of the public at large in rare diseases, including local managers given responsibility for funding.
- Barriers to IVF treatments.

- No linkage of databases, no registries and lack of central office to coordinate activities, such as contact point for Orphanet according to its standard operating procedure.
- No research infrastructure funding provided for essential core activities of Centres of Expertise, such as management of databases, registries, outcome studies.
- Lack of protected time for staff in this area and unfavourable patient:physician ratios.
- Lack of funded programme for trainees in this area and HSE embargo on recruitment eliminates trainee opportunities to facilitate shared care at community level and make cost-efficiencies.
- Lack of IT linkages across hospitals to facilitate data sharing and development of e-medicine.

Genetic testing and screening recommendations

The Steering Group recommends:

- 17.** The HSE Governance Committee/Group on Newborn Screening within the Integrated Services Directorate be expanded to **include a patients' advocate**. The Committee should consider the population benefits of newborn screening, including whether programmes need to be expanded or modified, and the need for carrier screening. The Department of Health should also provide a policy framework for population-based screening programmes.
- 18.** The Department of Health consider addressing the need for a **review of legislation** that indirectly impinges on the Newborn Bloodspot Screening Programme.
- 19.** Governance arrangements for **'send out' genetic tests be strengthened**. This should include clinical guidelines for 'send out' tests and yearly audits of the quality and diagnostic yield of tests sent out from non-hospital sources in order to minimise wastage. A national funding perspective is required to maximise quality and cost-efficiency. Centres involved in testing should develop and use guidelines regarding the most commonly tested conditions.

4.3 Services for patients with rare diseases – EU context

The European Union (EU) has recognised that because of their low prevalence, their specificity and the high total number of people affected (estimated at between 27 and 36 million in the EU), rare diseases call for a global approach, based on special and combined efforts to prevent significant morbidity or avoidable premature mortality, and to improve the quality of life and socio-economic potential of affected persons.

The European Council Recommendation of 8 June 2009 on 'Action in the field of rare diseases' (2009/C 15/02) proposes, inter alia, that Member States:

- identify appropriate centres of expertise throughout their national territory by the end of 2013, and consider supporting their creation;
- foster the participation of centres of expertise in European reference networks respecting the national competences and rules with regard to their authorisation or recognition;
- organise healthcare pathways for patients suffering from rare diseases through the establishment of cooperation with relevant experts and exchange of professionals and expertise within the country or from abroad when necessary;

- support the use of information and communication technologies such as telemedicine where it is necessary to ensure distant access to the specific healthcare needed;
- include, in their plans or strategies, the necessary conditions for the diffusion and mobility of expertise and knowledge in order to facilitate the treatment of patients in their proximity;
- encourage centres of expertise to be based on a multidisciplinary approach to care when addressing rare diseases.

The recital (Paragraph 14) to the Recommendation states that ‘the Community added value of ERNs [European Reference Networks] is particularly high for rare diseases by reason of the rarity of these conditions, which implies both a limited number of patients and a scarcity of expertise at European level within a single country. Gathering expertise at European level is therefore paramount in order to ensure equal access to accurate information, appropriate and timely diagnosis and high-quality care for rare disease patients’.

In addition to the Council Recommendation, there have been a number of other related developments at EU level that support work on rare diseases, specifically relevant to the theme of this chapter. These include the following:

- To aid the European Commission with the preparation and implementation of Community activities in the field of rare diseases, the European Union Committee of Experts on Rare Diseases (EUCERD) was formally established via the European Commission Decision of 30 November 2009 (2009/872/EC). EUCERD has, inter alia, developed and adopted recommendations on the following: (a) quality criteria for centres of expertise (CoEs) for rare diseases (EUCERD, 2012a); (b) Rare Diseases European Reference Networks (RD ERNs) (EUCERD, 2013b); and (c) core indicators for rare disease plans/strategies (EUCERD, 2013c).
- Directive 2011/24/EU of the European Parliament and of the European Council on the application of patients’ rights in cross-border healthcare (9 March 2011) has the aim of clarifying and simplifying rules and procedures, and providing better information on patients’ rights. The Directive, while much broader in scope than rare diseases, makes specific reference to rare diseases, in particular Articles 12 and 13:
 - o Article 12 states that ‘the Commission shall support Member States in the development of European reference networks between healthcare providers and centres of expertise in the Member States, in particular in the area of rare diseases.’ It then goes on to list a number of objectives, of which such networks must have at least three.
 - o In Article 12(3), Member States are encouraged to facilitate the development of the European reference networks by:
 - (a) connecting appropriate healthcare providers and centres of expertise throughout their national territory and ensuring the dissemination of information towards appropriate healthcare providers and centres of expertise throughout their national territory;
 - (b) fostering the participation of healthcare providers and centres of expertise in the European reference networks.
 - o Article 13 deals specifically with rare diseases and states that ‘the Commission shall support Member States in cooperating in the development of diagnosis and treatment capacity, in particular by aiming to:

- (a) make health professionals aware of the tools available to them at Union level to assist them in the correct diagnosis of rare diseases, in particular the Orphanet database and the European reference networks;
 - (b) make patients, health professionals and those bodies responsible for the funding of healthcare aware of the possibilities offered by Regulation (EC) No. 883/2004 for referral of patients with rare diseases to other Member States even for diagnosis and treatments which are not available in the Member State of affiliation.'
- o Article 12(4) states that 'the Commission shall adopt a list of specific criteria and conditions that the European reference networks must fulfil and the conditions and criteria required from healthcare providers wishing to join the European reference network'. The Commission has established a Cross-Border Healthcare Expert Group on Delegated Acts under Article 12(4)(a) on the application of patients' rights in cross-border healthcare: European Reference Networks.
- o Article 20 states that 'the Commission shall by 25 October 2015 and subsequently every 3 years thereafter, draw up a report on the operation of this Directive and submit it to the European Parliament and to the Council'.
- o Under Article 21, Member States are obliged to bring into force by 25 October 2013 the laws, regulations and administrative provisions to comply with Directive 2011/24/EU. A call relating to the establishment of ERNs from the EU is anticipated in 2014. Member State countries are expected to nominate Centres to the ERNs as appropriate.
- EUROPLAN, the European Project for Rare Disease National Plan's Development, is a 3-year project involving all Member States and funded for the period 2008-2011 under the first Community Action Programme in the field of Public Health. It is aimed at supporting countries in the development of their national plans and strategies.

The support activities of EUROPLAN are continuing in the context of the EUCERD Joint Action: Working for Rare Diseases No. 2011-22-1 from March 2012 for a 3-year period. An Irish EUROPLAN Conference took place in January 2011. In 2013, EUROPLAN with input from EUORDIS finalised a set of core indicators for national plans/strategies, which has been adopted by EUCERD as its recommendation on indicators (EUCERD, 2013c). This recommendation is the fruit of an agreement between Member States on a common set of indicators and a commitment to the collection of those indicators every year across the EU. This will allow for a streamlined and aligned follow-up of the national plans/strategies among Member States in the areas defined in the Council Recommendation.

4.4 Improving services, care and supports for patients with rare disease in Ireland

4.4.1 Care pathways

Due to the complexity of the various rare conditions and to provide efficient formal guidance and support to care coordinators, it is recommended that a **rare disease care pathway** be developed. This would provide for high-quality care and would assist in guiding patients through care and social services, increase efficiency of State resources and reduce waiting times for accessing support and social services.

It is recommended that this pathway should:

1. Identify appropriate consultants and medical care professionals and support centres.
2. Provide information, educational and social entitlements appropriate to the condition, including, among others:
 - Medical/GP card;
 - Long-term Illness card;
 - Carer's Benefit/Allowance;
 - Domiciliary Allowance;
 - educational grants and support services;
 - Disability benefits, including housing adoption grants, disability driver/passenger benefits;
 - contact details for counselling and psychological services.
3. Where standards of international best practice exist for the care of a person with a rare disease, these should be implemented. If no international standard is available, a template needs to be created. The template should outline the treatments, therapies and required specialists as standard. It should also take account of guidance developed by the European Reference Networks. In addition, the care pathway should also include oral/dental health needs, particularly in the paediatric dentistry domain.
4. The transition from paediatric care to adult care needs to be managed effectively and seamlessly. At present, transition for those with rare conditions occurs on an *ad hoc* basis, with resultant stress, fear and worry for patients and families. At this highly sensitive time, teenage patients and their families need additional support. This should be coordinated centrally by a lead professional throughout the process. Guidelines for this process are required for both patients and staff. Protocols and associated training for staff are also essential to ensure that this support is accessible to all patients with rare diseases.

The Steering Group recommends:

20. The National Clinical Programme for Rare Disease through a National Office for Rare Diseases **develop the clinical and organisational governance framework** that will underpin care pathways and access to treatment for rare disease patients, particularly in the context of the transition from paediatric care to adult care.

4.4.2 Centres of Expertise

It is against the above backdrop of EU developments, as well as wider developments in the Irish healthcare system generally (*see below*), that the Steering Group addressed the issue of how the current situation regarding screening, diagnosis, treatment and care for rare diseases in Ireland might be improved. Core aspects of the approach involve the development of Centres of Expertise (CoEs) in rare diseases and participation in European Reference Networks for rare diseases (RD ERNs). The EU has agreed quality criteria relating to the CoEs (EUCERD, 2012a). These CoEs and associated healthcare pathways will need to be aligned with the planned reorganisation of Irish hospitals.

CoEs are care centres that bring together a group of multidisciplinary, specialised competencies, from offering consultations, medical examinations, genetic testing and counselling and social services to facilitating inclusion in research protocols and clinical trials as a patient-centred service, ensuring timely diagnosis and appropriate follow-up care.

The rationale for developing CoEs is well established. Rare disorders require highly specialised multidisciplinary medical teams and social service providers. Concentration of expertise in a physical or virtual structure brings together competencies and reduces healthcare costs by contributing to shorter delays in diagnosis, less adverse consequences, a reduction in misdiagnosis and unnecessary treatments. In the current economic climate in Ireland, the economic considerations of treating rare diseases (and preventing in many instances life-long disability and chronic disease) need to be considered carefully when reorganisation of services may be required. To be taken into account are the hidden costs of inaccurate and missed diagnoses and mismanagement (outside appropriate reference centres), the costs of prolonged morbidity and loss of Revenue income. There are a number of new and rapidly evolving treatments for patients with rare diseases, a number of which are life-saving and are approved by Member States in the EU. These include enzyme replacement therapy, which will require delivery in appropriate centres of reference to meet quality assurance standards, cost-effectiveness and adequate use of resources.

KEY POINTS FROM THE CONSULTATION PROCESS

Centres of Expertise

- The development of a new clinical care programme in the HSE dedicated to rare diseases was widely endorsed.
- The core functions of Centres of Excellence were seen as treatment and delivery of appropriate care and support, and development of care plans in partnership with relevant providers.
- Where no suitable service is available in Ireland, access to European Reference Networks was seen as important.
- Respondents generally considered that the State should reimburse costs associated with treatment and follow-up abroad.

As already mentioned, EUCERD has, on 25 October 2011, adopted Recommendations on Quality Criteria for Centres of Expertise for Rare Diseases in Member States (EUCERD, 2012a). This EUCERD work is complementary to work on these issues by the Cross-Border Healthcare Expert Group on the Delegated Acts under Article 12(4) of Directive 2011/24/EU.

4.4.3 Participation in European Reference Networks

While healthcare pathways may be well defined in Ireland for some rare disorders (e.g. hereditary coagulation disorders), through well-established CoEs, for many conditions and for ultra-rare disorders, there may not be sufficient local expertise in Ireland. For such situations, the development and use of European Reference Networks (ERNs) is particularly relevant.

The use of ERNs may be described as the ‘networking of knowledge and expertise’ through either physical or virtual expertise and/or reference centres and teams of experts. These are fundamental to address the issue of rare diseases at both European and national levels. The goal of an ERN is the improvement in the overall quality and management of care of a single rare disease or a group of rare diseases by complementing, supporting and providing added value to the existing services and expertise at national level. Such networking activity between national CoEs promotes the sharing and mobility of expertise, rather than patients themselves. Ireland participates, or has participated, in the

following Pilot European Reference Networks for rare diseases: Dyscerne, EPNET, EPI, Care-NMD, EN-RBD and the Paediatric Hodgkin Lymphoma Network. At the Irish EUROPLAN Conference 2011, it was agreed that strong collaboration exists in this area among the scientific communities and the patients' groups with European groups. There is some participation among clinicians in pilot ERNs, but this is not well coordinated and is better in some disease areas than others. ERNs can improve knowledge by sharing and creating mutual databases and registries of information and resources. This can increase cohorts for research studies and clinical trials, and develop standards of care for national CoEs.

EUCERD's (2013b) Recommendations on Rare Disease European Reference Networks (RD ERNs), already mentioned, state that 'the overall vision of RD ERNs is that they will provide the framework for healthcare pathways for RD [rare disease] patients through a high level of integrated expertise. ERNs will enable networking of centres on a European level and promote that the appropriate healthcare professionals have access to the tools and guidelines provided by the reference network and to the knowledge of the networks. This will cover in a step-wise approach all rare disease patients, including those in the process of seeking a diagnosis or in whom a final diagnosis is not possible' (see http://www.eucerd.eu/?post_type=document&p=2207).

European Commission services have been working with Member States to prepare the implementing measures setting the criteria for the ERNs and healthcare providers to fulfil in order to be established and designated as European Reference Networks and Centres of Expertise respectively. The ERNs are to be based on voluntary participation by healthcare providers who will participate and contribute to the networks' activities in accordance with the legislation of the Member State where the provider is established. It is envisaged that where a national centre does not meet the criteria for designation as an EU Centre of Expertise, there will be provision for it to be designated as an Associated National Centre of the relevant ERN, subject to certain criteria and conditions.

The Steering Group recommends:

21. National **Centres of Expertise (CoEs)** in Ireland be identified for groupings of rare conditions, based on clinical need and built on foundations already established. There is an urgent requirement for the HSE to map out CoEs and healthcare pathways, and to acknowledge the different role and competencies of CoEs and centres providing care at local level, such mapping to be aligned with the re-organisation of Irish hospitals into hospital groupings. It is also important that broader clinical guidelines take account of the requirements of rare diseases. The potential for cooperation on an all-Ireland basis should be realised. The designation of CoEs should be in accordance with the EUCERD quality criteria for CoEs.
22. The HSE **integrate CoEs into national funding planning**, with provision for adequate staffing for multidisciplinary care, as well as sustainable research infrastructure for clinical investigation in addition to competitive research.
23. The Department of Health and the Health Service Executive (HSE) encourage and support the national Centres of Expertise (when so designated) to **seek recognition as EU designated Centres of Expertise** or associated national centres in European Reference Networks for Rare Diseases (RD ERNs) according to the timeframe, framework and standards currently being developed at European level through the complementary work of EUCERD and the EU Cross-Border Healthcare Directive 2011/24/EU.

4.5 Care Services

4.5.1 Respite care

The complex and multisystemic nature of some rare diseases, as well as the fact that in some cases more than one family member (parent and/or siblings) may have the condition, means that access to respite care can be an important factor in reducing stress and improving quality of life for families/carers of people with rare disease.

There are several different models and approaches to services offering respite care for illnesses and conditions in general in Ireland. These include:

- centre-based respite care (day care centres);
- residential respite care;
- home care;
- in extreme cases, respite care facilities in acute hospital settings are necessary;
- short-term overnight care (e.g. occasional or intermittent overnight care in the home).

In some cases, the respite care provided for other illnesses and conditions in society is appropriate to the needs of people with rare diseases. However, for some rare diseases, special training or adaptations may be needed. Currently, there are only a small number of centre-based respite day care centres for a tiny number of rare conditions. In Spring 2013, Liam's Lodge in Tralee, Co. Kerry, was opened as Ireland's first dedicated national respite and training centre for genetic and rare disorders (*see* www.liamslodge.com). The intention is to give the whole family of a child with a genetic or rare condition some time together in a relaxed and safe environment that understands their situation and needs. The project is also in talks with TCD, UCD, UCC and the Tralee Institute of Technology regarding their accreditation of the centre's training programmes for medical professionals, medical students and professional/non-professional care providers.

The Steering Group recommends:

- 24. Residential respite care be available for children with rare diseases.**

4.5.2 Palliative care

KEY POINTS FROM THE CONSULTATION PROCESS

End-of-life care

- Respondents emphasized the need to develop appropriate provision for the end-of-life phase of rare disease patients' journeys.
- A significant proportion of responses focused on end-of-life issues for children with terminal rare diseases, including hospice and respite services.
- Bereavement issues also featured in many responses. For some families with rare genetic disease, the bereavement process was complicated by affected children observing their parent dying from their disease or families with more than one child affected.

Palliative care is an approach that improves the quality of life of patients and their families facing the problems associated with life-limiting illness. This is achieved through the prevention and relief of suffering by means of early identification, high-quality assessment and treatment of pain and other physical, psychosocial and spiritual problems. In recent years, the scope of palliative care has broadened and includes not only cancer-related diseases but supporting people through non-malignant and chronic illness also. The HSE vision for the future is that palliative care will be a gradual and natural increasing component of care from diagnosis to death. The aim is to ensure that patients with a life-limiting condition, and their families, can easily access a level of high-quality palliative care service that is appropriate to their needs, regardless of age, care setting or diagnosis. In order for this to happen, the provision of palliative care needs to become the responsibility of the whole healthcare system rather than just specialist services.

Palliative care has been developed according to the guidance provided in national strategic documents (Department of Health and Children, 2005 and 2009). It is acknowledged that significant deficits remain in the current level of service provision; however, despite resource challenges, the HSE continues to work to implement strategic priorities and to address the gaps in palliative care services.

Palliative care services are organised according to a collaborative, inclusive model that incorporates care provided by generalist and specialist providers to meet population needs. When diagnosed with a life-limiting illness, most, but not all, patients have an existing relationship with a GP and a specialist consultant (e.g. a cardiologist or respiratory physician). These professionals should be able to meet effectively many of the palliative care needs of patients with life-limiting conditions. However, a significant number of patients experience unstable symptoms or complex problems as a consequence of their illness and therefore may require input from specialist palliative care services when generalist palliative care providers are unable to provide relief. There are approximately 30 adult palliative care consultants in Ireland.

Specialist palliative care services are configured to follow the patients' journey and to provide care in the place of the patients' need and choice. For example, patients in the community may receive the Community Palliative Care Team into their own homes or they may access Day Care or Out-Patient services. Patients admitted to hospital may receive services from the hospital-based Specialist Palliative Care Teams. Patients from either setting may be admitted to Specialist Palliative Care Inpatient Units (hospices) for the purposes of achieving control of complex symptoms such as pain, rehabilitation to maximise function and independence in the context of a life-limiting condition or care towards the end of life.

The budget allocation for Palliative Care in the 2013 HSE National Service Plan was €72 million. This is an indicative amount, which mostly accounts for the funding provided under Service Arrangements with voluntary hospice and home care providers. It does not, for example, include the spending on palliative care provided in acute hospitals, the approximate 170 palliative care support beds or on home care packages. Some key points are:

- In 2013, there were 157 specialist in-patient palliative care beds in 10 locations across the country. However, there is a wide regional and intra-regional variation in the availability of care and 3 geographic areas have no specialist in-patient units. Most of these services are provided by voluntary hospices under Service Arrangements with the HSE.
- All HSE Areas have Community Specialist Palliative Home Care Teams in operation. However, there is significant variability in service availability and composition of the multidisciplinary teams.
- There are 38 Acute Hospital Specialist Palliative Care Teams, which provide service to both in-patients and out-patients. Again there

is variability in service availability and composition of these multidisciplinary teams.

- Specialist palliative day care is provided in 7 locations around the country.
- There are over 170 palliative care support beds mostly located in long stay/ community units across approximately 80 locations around the country.

Most of the above services have seen increases in 2012 over 2011 in the number of patients seen and/or in the percentage seen within 7 days of referral. Although the expansion of service provision has been slow, the HSE Palliative Clinical Care Programme is making an impact on the quality of services currently being delivered through its work on referral guidelines, clinical care pathways, pain management guidelines, advanced care planning, improved access for patients with non-malignant disease, staff competencies and improved integration with primary care. The Programme has also established an Expert Advisory Group on Palliative Care Funding.

There are a number of organisations, including the Irish Cancer Society, the Irish Hospice Foundation and Saoirse Foundation Ireland, that fund a national palliative nursing service for cancer patients in their own homes at night time. The Irish Hospice Foundation also funds the same service for non-malignant patients. The night nursing service is provided to both children and adults, some of whom, particularly children, would have rare diseases.

Due to the complex and multisystemic nature of many rare, life-limiting conditions, palliative care services need to be appropriately tailored. Cystic Fibrosis Ireland with support from the Irish Hospice Foundation (2013) has developed a discussion paper on end-of-life considerations for people with cystic fibrosis. The development of a model of palliative care for rare diseases could potentially improve accessibility, although given the varied nature of the conditions, the development of such a model is likely to be challenging. Guidelines and training will be required to adequately identify and provide appropriate palliative care addressing the broad range and diversity of rare conditions.

4.5.3 Palliative care for children

In Ireland there are approximately 1,400 children living with a life-limiting condition, with approximately 490 childhood deaths per year. Of childhood deaths due to life-limiting conditions, the majority occur in the first year of life, with approximately 350 deaths per year.

A key finding of *A Palliative Care Needs Assessment for Children* (Department of Health and Children, 2005) was that the preferred location of caring for a child with a life-limiting condition is the family home, with parents receiving adequate professional support.

Although it is acknowledged at European level that Ireland has made significant progress in recent years, the health service is aware that palliative care services for children are still inadequate. These deficits are being addressed through the implementation of the recommendations of the national policy document *Palliative Care for Children with Life-Limiting Conditions in Ireland – A National Policy*, published by the Department of Health and Children in 2009. The aim of the policy is to ‘provide a framework within which a seamless service for children with life-limiting conditions and their families can be planned, delivered and accounted for by the Health Service Executive’. In Appendix III of the national policy, four groups of children are listed who are likely to have palliative care needs. While rare conditions such as cystic fibrosis, Batten’s Disease, mucopolysaccharidoses and muscular dystrophy are specifically listed, many other rare conditions are life-limiting and those affected may need access to appropriate palliative care. The policy includes four respite-specific recommendations for implementation:

- in-patient hospice beds specifically for respite should be developed as part of the children’s palliative care service;

- a range of respite services should be developed for children with life-limiting conditions who have palliative care needs;
- each HSE administrative area should plan and develop respite facilities for children with life-limiting conditions and their families;
- hospice-at-home teams should be developed by the HSE.

In March 2013, the Irish Hospice Foundation and Laura Lynn (Ireland's Children's Hospice) (2013), in partnership with the HSE, published the report titled *Respite services for children with life-limiting conditions and their families in Ireland – A National Needs Assessment* to provide a national overview of service provision and future respite requirements as part of a palliative care service for children in Ireland. The report acknowledges that a significant level of respite support is already being provided, but access is inconsistent around the country and can be dependent on diagnosis and/or geographic location. One of the conclusions of the report is that families whose child does not have a definitive diagnosis may find access to respite challenging. This latter finding is likely to be particularly relevant to some children with rare diseases.

The HSE provides significant funding for home nursing care for children with life-limiting conditions. For example, in the 12-month period October 2011 – October 2012, the HSE spend on home nursing care amounted to €8.58 million. Due to financial coding issues within the system, the total spend is thought to be significantly higher.

A programme of care for children with life-limiting conditions is being jointly funded by the HSE and the Irish Hospice Foundation, and includes the appointment in 2011 of the first Paediatric Consultant with a Special Interest in Palliative Care. The programme is also providing 8 Children's Outreach Nurses whose role is to ensure that children being cared for at home by their families have access to coordinated and supportive services. The nurses liaise closely with statutory and voluntary service providers, including local GPs, public health nurses, disability services, the Jack & Jill Foundation and LauraLynn.

Another aspect of the children's programme is the provision of structured education programmes for all healthcare staff who care for children with life-limiting conditions. This is being delivered in partnership with Our Lady's Children's Hospital in Crumlin. These programmes are helping to ensure that children and their families will have the necessary care and support provided to them, regardless of the location of that care.

As is the case with palliative care services for adults, much of the impetus for the development of palliative care services for children has come from voluntary organisations.

The Steering Group recommends:

- 25.** With respect to **palliative care**:
 - a. access is provided to appropriate palliative care for people with rare life-limiting conditions;
 - b. guidelines are developed in palliative care provision to address the complex and multisystemic nature of many rare life-limiting conditions;
 - c. the National Development Committee for Children's Palliative Care, chaired by the HSE, take account of the particular needs of children with rare disease in its ongoing programme of work;
 - d. the next National Cancer Strategy could elaborate further on how best to manage rare cancers, especially in the context of this National Rare Disease Plan, where there is a shared objective to detect and treat early patients with rare cancers.

The Steering Group notes the success of the National Cancer Control Programme and in particular the advantages for patients with rare as well as common cancers that come with this type of model for service provision, especially in the domain of managed cancer control networks and centres of expertise. The success of the All-Ireland Cooperative Oncology Research Group (ICORG) is also acknowledged. ICORG is predicated on a mission to enable Irish patients gain early access to new cancer treatments. Ultimately, clinical research offers hope to cancer patients by providing them with access to treatments that are not currently available outside of the clinical research arena. ICORG has succeeded in offering research options to over 10,300 patients in the last 15 years. Given the priority need for rare disease patients to access orphan therapies (*see Chapter 5*), the operations of ICORG provide a potential to replicate pathways to success. ICORG is cognisant that paediatric cancers constitute one of the major components of rare cancers and that screening for those most at risk of rare familial cancers should be routinely undertaken in treatment centres.

4.6 Training programme for health professionals

Provision of timely and quality services to patients with rare diseases implies the availability of informed and well-trained health professionals. The wide variety of rare diseases as well as their low prevalence present challenges in this regard. However, without competent health professionals there are risks of unnecessary delays in diagnosis and referral, misdiagnosis, no diagnosis, inappropriate treatment and management, or no treatment, with consequential suffering for patients and families, loss of productivity and inefficient use of resources. As already mentioned, a 2008 study by RehabCare found that 75% of GPs surveyed had difficulties in providing information on rare diseases to patients and families (McGarvey and Hart, 2008). Rare Disease UK (2010) conducted a survey on patients' and families' experiences of rare disease. One of the common issues identified was that patients and families worry about the level of awareness of rare diseases among healthcare professionals.

Key areas of focus for professional awareness and competency development include:

- GPs and consultants;
- community care services;
- early intervention services;
- A&E departments;
- staff in general hospitals;
- children's hospital staff.

Earlier exposure to the subject of rare diseases can only be of benefit to developing awareness and knowledge of medical and professional care providers. The UCD School of Medicine & Medical Sciences (SMMS) has recently initiated a new educational module entitled 'Rare Disorders and the Medical Healthcare Professional'.

The Steering Group recommends:

- 26.** Appropriate **modules relating to rare disease feature within all undergraduate and postgraduate programmes** of both medical professional and carer disciplines. In addition to developing competency requirements and training programmes for medical professionals and carers engaged with rare conditions, practical experience and exposure to patients with rare conditions is advantageous.

The system of training needs to be addressed for healthcare professionals through their professional bodies, with the support of all stakeholder groups. Patients' groups are already taking a lead in this by producing information pamphlets, books and giving lectures to medical students.

The Royal College of Physicians of Ireland has approved a Clinical Genetics Training Programme with specific aims to train clinical geneticists in the management as well as diagnosis of complex genetic diseases. The training programme commenced in July 2013, including biochemical genetics rotation. Staffing shortages have precluded broadening the educational base to GPs and other staff. Ireland falls short of the UK, where a website has been developed specifically to educate paramedical staff (see www.geneticseducation.nhs.uk).

It is envisaged that designation of Centres of Expertise and participation in European Reference Networks will strengthen professional competence in rare diseases through ongoing professional development by means, inter alia, of the networking and dissemination of information and diagnostic tools, being promoted under Articles 12 and 13 of Directive 2011/24/EU of the European Parliament and of the Council of 9 March 2011 on the application of patients' rights in cross-border healthcare.

Liam's Lodge, Ireland's first dedicated national respite and training centre for genetic and rare disorders, is developing a suite of training and competence development programmes with UCD for medical students, GPs and other medical professionals.

The Steering Group recommends:

27. A system of **training in rare diseases for healthcare professionals** be addressed through their professional bodies with the support of all stakeholder groups, including patients and their families. Action in this area should build on initiatives already underway or in progress (as outlined in Recommendation 26 above).

4.7 Quality and governance

Implementation in Ireland of the EU initiatives on rare diseases (i.e. CoEs and ERNs), outlined in Sections 4.4.2 and 4.4.3 above, will be taking place against the backdrop of recent wider developments in the Irish healthcare system, which provide the national context for improving services for, inter alia, patients with rare diseases. For example, the *Report of the Commission on Patient Safety and Quality Assurance* (Department of Health and Children, 2008) recommended the establishment of a national leadership role for the development and promotion of clinical guidelines and audit in Irish healthcare as part of a national clinical effectiveness and governance framework. In this framework, the Clinical Strategy Programmes and Directorate of Quality, Risk and Clinical Care have the goals of strengthening clinical leadership, improving clinical performance and ensuring care is delivered in a manner that maximises quality while minimising expenditure.

The Steering Group recommends:

28. The **establishment of a National Clinical Programme for Rare Diseases**. A key role for this clinical programme will be the mapping, development and implementation of care pathways for rare diseases.

It is envisaged that a National Clinical Programme for Rare Diseases would, over time and in collaboration with the designated reference centres, collate and assist with developing national treatment guidelines, standardise operating procedures and care pathways for many rare disorders, and also develop care pathways with European Reference Centres for those 'ultra-rare disorders' where there may not be sufficient expertise in Ireland. One of the goals of the proposed National Office for Rare Diseases would be to support local implementation of best practice since the patients' feedback from IPPOSI, the EUROPLAN Conference 2011 and other public consultations is that Irish patients seek quality care as near to home as possible.

It is envisaged that this National Clinical Programme, together with an improved central information function, would:

- facilitate timely access to centres of expertise nationally and internationally;
- provide up-to-date information regarding new treatments and management options;
- provide information regarding ongoing clinical trials for all patients affected with rare diseases in Ireland.

It is envisaged that over time such a model of care would:

- improve the patients' experience;
- provide safe quality care;
- expedite diagnosis and the correct treatment;
- improve communication and education;
- improve the interface with community partners;
- prove to be cost-efficient.

Also relevant to improvement of services, including rare disease services, are *Standards for Safer Better Healthcare*, published by the Health Information and Quality Authority (HIQA) in June 2012 and which took effect under Section 8 of the Health Act 2007. These standards, of which there are 45, are aimed at protecting patients and provide a strategic approach to improving safety, quality and reliability of health services. They are seen as a first step towards a licensing system for the Irish healthcare system, as envisaged in *Future Health – A Strategic Framework for Reform of the Health Service, 2012-2015* (Department of Health, 2012). The HSE Quality and Patient Safety Directorate is collaborating with HIQA in setting up an awareness and education campaign to provide information to front-line service providers and service users on the HIQA standards and their implementation.

Overall, it is envisaged that quality and governance issues in relation to rare diseases, as with other health issues, will benefit from the arrangements envisaged in *Future Health*. Of particular relevance here will be the establishment of a Patient Safety Agency (PSA), building on the existing functions of the Quality and Safety Directorate in the HSE. The PSA functions will include, among others, responsibility for the National Clinical Effectiveness Committee and oversight of the National Office of Clinical Audit. *Future Health* envisages that the health and social service regulatory and monitoring function will be maintained separately from the PSA and enhanced within HIQA, which will continue to set and monitor standards.

4.7.1 National Office for Rare Diseases

The establishment of a National Office for Rare Diseases in the HSE was a key recommendation from the consultation day and the online public consultation undertaken in 2012 for the development of this National Rare Disease Plan for Ireland. Rare diseases by their nature are challenged by the lack of a strong central clinical focus and for patients and families by the difficulty in accessing information and all that this entails. The model for such a National Office has worked well in other countries in terms of better clinical outcomes and overall cost savings.

In effect, the National Office for Rare Diseases could fulfil the following functions:

- act as a national point of reference for enquiries relating to services, diagnostics, etc;
- develop a register of people with rare disease in Ireland;
- in time, assist with and support research and population studies on rare diseases with various public partners;
- consolidate access to all known registries of rare diseases;

- potential to capture and collate data on Irish patients and orphan drugs;
- have a role in the review of Orphanet and its development in Ireland;
- provide support for the network of Rare Disease Registries, as set out in Chapter 3.

It is recommended that the National Office for Rare Diseases work closely with the HSE National Clinical Programme for Rare Disease.

The Steering Group recommends:

29. The **establishment of a National Office for Rare Diseases** to facilitate the coordination and timely access to Centres of Expertise nationally and internationally, and to provide up-to-date information regarding new treatments and management options, including clinical trials.

5. Enhancing access to appropriate drugs and technologies

5.1 Access to appropriate drugs and technologies for rare disease patients: The challenge

Rare disease patients can face challenges at many stages of their condition. Once they have overcome the challenges implicit in getting an accurate diagnosis and linking with an appropriate specialist, some patients can face an additional challenge – accessing drugs and technologies, where they exist, appropriate to their condition. There are relatively few treatment options available for the majority of rare diseases and more often than not there are none.

The issue of appropriate access to drugs and technologies includes aspects of both ‘mainstream’ as well as orphan drugs and technologies. Some rare disease patients require timely access to highly specialised drugs and technologies; many more require timely, convenient and affordable access to general prescription and over-the-counter items in the management of their condition. Barriers to access include affordability, eligibility, information, empowerment and advocacy skills, as well as geography. Issues of eligibility for State supports in meeting the costs of treatments were a concern in the consultation for this National Rare Disease Plan for Ireland. Access to appropriate medicines and treatments is a key concern. Respondents to the GRDO *Patients’ Experience Survey* (2012) report many difficulties in obtaining appropriate treatments and medicines: 41% of respondents do not consider that they have access to the best medical care for their condition, while 64% state that ‘Access in Ireland to medicines/treatments available in other countries’ would make a great difference to them.

Trying to obtain medicines can be distressing for many patients and families affected by rare disease. There is no licensed treatment available for many of them. Some patients are informed of off-label or unlicensed medicines, but often patients and families have to inform their doctors. Patients and families can experience inconsistencies in access to medicines, including orphan drugs.

Orphan drugs and technologies refer to treatments specific to rare conditions. They are defined by the European Medicines Agency Committee for Orphan Medicinal Products (COMP) principally as medicines intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting no more than 5 in 10,000 people in the European Union at the time of submission of the designation application. A core principle in the Orphan Drug Regulation (EC) No. 141/2000 states: ‘Patients suffering from rare conditions should be entitled to the same quality of treatment as other patients.’

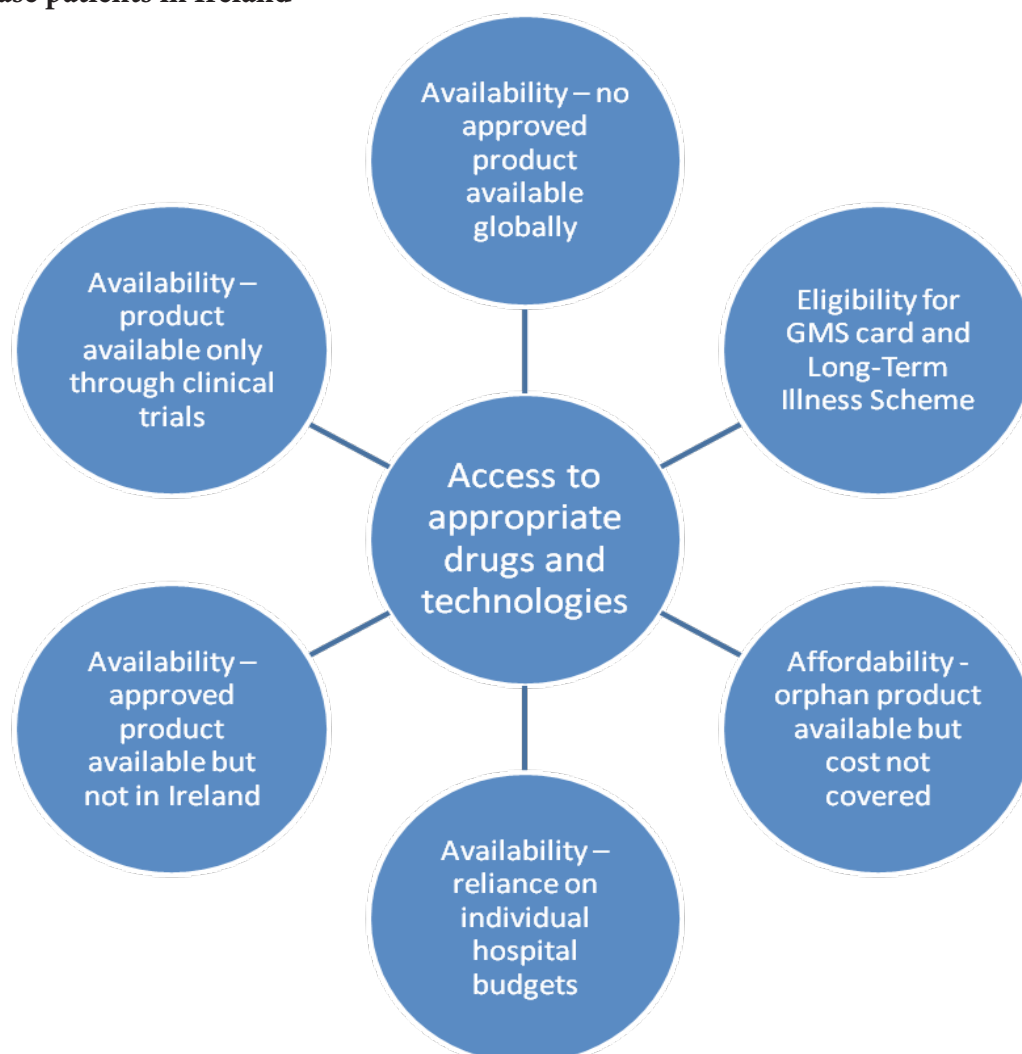
At present, orphan drugs and technologies exist for only a fraction of known rare diseases. Many rare disease patients find themselves in the position that there is no licensed treatment for their condition anywhere in the world. Enhancing the development of new orphan drugs and technologies forms a distinct goal for rare disease strategies. For patients for whom orphan drugs and technologies exist, access is dependent on that product being approved and made available in their own jurisdiction at an affordable cost (*see Figure 2*).

KEY POINTS FROM THE CONSULTATION PROCESS

Access to orphan drugs and technologies

- Many respondents did not respond to this section, suggesting that the issue of orphan drugs, while important, was not of relevance to a substantial proportion of rare disease patients and carers.
- Of those who did respond, nearly half considered that access to orphan drugs and technologies in Ireland was 'poor'.
- Concerns were raised in terms of the transparency and fairness of decisions made on the assessment of orphan drugs.
- Over one-third of respondents were unable to comment on issues relating to assessment pathways for rare diseases in Ireland, but among those who did comment, the majority favoured a new system.

Figure 2: Summary of priority issues relating to access to appropriate drugs and technologies for rare disease patients in Ireland



5.2 Orphan drugs and technologies

5.2.1 Designation of orphan drugs and technologies at European level

The European Medicines Agency is the decision-making body for market authorisation of orphan medicines in Europe. The European Medicines Agency Committee for Orphan Medicinal Products (COMP) reviews applications for products seeking 'orphan medicinal product designation'. To qualify for orphan designation, a medicine must, in the first instance, be intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition affecting no more than 5 in 10,000 people in the EU at the time of submission of the designation application. Applications are also considered for products intended for the diagnosis, prevention or treatment of a life-threatening, seriously debilitating or serious and chronic condition, and without incentives it is unlikely that the revenue after marketing of the medicinal product would cover the investment in its development.

Some conditions occur so infrequently that the cost of developing and bringing to the market a medicinal product to diagnose, prevent or treat the condition would not be recovered by the expected sales of the medicinal product. In order to address this issue and offer incentives for orphan product development, the Orphan Drug Regulation EC No. 141/2000 ensures that sponsors of medicines that receive orphan designation from the European Commission benefit from a number of incentives. This Regulation has been considered successful in promoting the development of medicinal products for rare conditions and improving quality of life and survival (EUROPLAN, 2010). The Regulation has seen the development of more than 1,000 applications for orphan drug status and the number of new applications is rising every year. In 10 years, 728 have been designated as 'orphan drugs' and 60 have received marketing authorisation, which has been estimated to benefit around 2.5-2.6 million rare disease patients. The trend suggests that around 10 new orphan medicines will be approved for marketing every year in the EU over the next 5-10 years (EURODIS, 2014).

Despite the incentives for development and marketing of orphan medicinal products provided by Regulation (EC No. 141/2000), the availability of orphan drugs within European countries and access to them remains highly variable (EUCERD, 2013a). There are many reasons for this, including that some pharmaceutical companies do not market the drug in small countries due to scarce market value and also that agreement cannot be reached in terms of reimbursement or costing of orphan drugs and technologies within the health service budgets of Member States.

5.2.2 Availability of designated orphan drugs and technologies to patients in the Republic of Ireland

Marketing authorisation of any medicinal product by the European Medicines Agency (EMA) does not necessarily result in that product being made available within all EU Member States. Individual Member States are responsible for taking decisions on the pricing and/or reimbursement of EMA-approved orphan medicines.

In Ireland, processes around pricing and reimbursement of medicines have developed from a series of framework agreements with the pharmaceutical industry (both the originator (IPHA) and generic (APMI) industry). In 2013, criteria by which decisions around the addition of medicines to the lists of items reimbursed and the mechanisms for setting prices were established on a statutory footing in the Health (Pricing and Supply of Medical Goods) Act 2013.

The HSE has a statutory responsibility to establish and maintain a list of drugs, medicines, and medical and surgical devices that may be supplied under the Health Act 1970 and to establish mechanisms to set the prices of such substances.

The HSE is required to have regard to specific criteria when making decisions on whether to reimburse a medicine or not. These criteria are:

- the health needs of the public;
- the cost-effectiveness of meeting health needs by supplying the item concerned rather than providing other health services;
- the availability and supply of items for supply or reimbursement, or both;
- the proposed costs, benefits and risks of the item to listed item relative to therapeutically similar items or listed items provided in other health service settings and the level of certainty in relation to the evidence of those cost, benefits and risks;
- the potential or actual budget impact;
- the clinical need for the item;
- the appropriate level of clinical supervision required to ensure patients' safety;
- the efficacy (performance in trial), effectiveness (performance in real situations) and added therapeutic benefit against existing standards of treatment (how much better it treats a condition than existing therapies);
- the resources available to the HSE.

The HSE is required to consider specific criteria when making a pricing proposal:

- the equivalent relevant prices (if practically available) of the item in all EU Member States where the medicine is marketed;
- the relevant prices of therapeutically similar listed items;
- the potential therapeutic benefits for patients;
- the potential budget impact;
- the ability of suppliers of the item to meet patients' demand;
- the resources available to the HSE;
- the terms of any agreement in place between the HSE and any representative body of the suppliers of drugs, medicines or medical or surgical appliances which relates directly or indirectly to the price of the item.

The HSE must review all items currently reimbursable under the General Medical Services (GMS) and other community drugs schemes (including prices) within 3 years to determine whether each item should remain on the list and, if so, the prices that should apply.

Orphan drugs and technologies are assessed through the same mechanism as other drugs and technologies in the Irish system.

Details of the actual operational processes are set out in the 2012 agreement between the Department of Health/HSE and the Irish Pharmaceutical Healthcare Association (IPHA). New medicines, including new presentations and applications, granted a marketing authorisation by the Irish Medicines Board (IMB) or European Commission become reimbursable in the Schemes within 75 days of the date of the reimbursement application to the HSE, subject to the relevant provisions in the agreement. Products that are subject to pharmacoeconomic assessment become reimbursable in the Schemes within 45 days of a positive assessment. Assessments are conducted in accordance with the HIQA (2014) *Guidelines for the Economic Evaluation of Health Technologies in Ireland*.

In the 2012 agreement, industry and the State agreed that they would accept a cost-effectiveness threshold of €45,000 per quality adjusted life year in the health technology assessment process. It was also agreed that 'exceptional' products that failed to satisfy the €45,000 threshold could be processed subject to meaningful discussions between the HSE, Department of Health, relevant clinicians and the relevant marketing authorisation holder.

Pricing and reimbursement applications are accepted by the HSE Corporate Pharmaceutical Unit on behalf of the HSE. Health technology assessments are commissioned and carried out by the National Centre for Pharmacoeconomics (NCPE). The NCPE also facilitate meaningful discussions through IPPOSI, with patients' representatives where the relevant orphan medicinal products under review are viewed 'exceptional'. The NCPE publishes its reports on its website (*see* www.ncpe.ie). These reports provide detailed information on the potential budget impact of a medicine and assess whether it satisfies the agreed €45,000 threshold at the price sought by the manufacturer. Medicines that satisfy the threshold are approved and added to the lists of reimbursable items.

Medicines that fail to satisfy the €45,000 threshold are usually the subject of intense commercial discussions. If after all commercial discussions are concluded, the medicine still fails to satisfy the threshold, it falls due for consideration by the HSE Leadership Team, the membership of which includes clinical leadership from within HSE Senior Management. The HSE Leadership Team has established a committee called the HSE Drugs Group to make recommendations in relation to these medicines. Final decisions are signed off by the HSE Leadership Team. On occasion, the HSE may seek policy direction from the Department of Health and Government prior to progressing a decision.

Orphan drugs and technologies are assessed through the same mechanism as all other drugs and technologies in the Irish system. It is possible to argue that this ensures decisions around pricing and reimbursement of orphan medicines are not made without first considering the potential for non-provision of other services to patients with rare diseases or services to other patients. It is also possible to argue that assessing orphan medicines in the same way as other medicines may disadvantage them. It is argued by some stakeholders that the price of an orphan drug is set by a manufacturer to recoup research and development costs and attain a profit margin. High treatment costs, inability or failure to satisfy nationally agreed cost-effectiveness thresholds and uncertainty around the magnitude or extent of treatment benefit can make decision-making in this area particularly challenging.

5.2.3 Community and hospital schemes – How patients access medicines and how budgets fund them

Medicines in Ireland are provided to patients in community and hospital settings. At community level, prescription medicines are dispensed by pharmacies through the Community Drug Schemes. Section 59 of the Health Act 1970 (Statutory Instrument No. 1 of 1970) is the basis for the existing community drug schemes that cover the General Medical Services (GMS) Scheme, the Drug Payments Scheme (DPS) and the Long-Term Illness (LTI) Scheme. Arrangements are in place to provide certain High Tech medicines commenced by hospital specialists but which are suitable for self-administration via community pharmacies and to fund the provision of all new oncology medicines administered in hospitals via a single national reimbursement mechanism.

For products expected to be delivered under the Community Drug Schemes and High Tech medicines (for which there is a single fundholder, i.e. the Primary Care Reimbursement Service), decisions at a national level are made in relation to both pricing and reimbursement. This has the advantage of ensuring that once a decision is made, funding follows that decision. At present, a small number of rare diseases (including cystic fibrosis, hydrocephalus and PKU) are included in the LTI Scheme. Some data on reimbursement of orphan medicines under the Community Drug Schemes are available within the Annual Reports of the Primary Care Reimbursement Service.

Many orphan drugs and technologies can only be commenced by hospital specialists in the in-patient, day case or out-patient settings. Such a system ensures that only those with specialist expertise to fully understand the clinical indications and management of rarely used and highly specialised orphan

medicines are in a position to prescribe them. Medicines administered on an in-patient or day case basis are funded by hospitals. Nationally, hospital funding decisions are made on an annual basis as part of the HSE Service Plan process. Individual hospitals/regions are responsible for submitting business cases for funding as part of the national service planning process. This approach, whereby each orphan product is considered separately within the context of individual hospital budgets, creates substantial pressures for some hospitals and can create the potential for inequities between patients attending different hospitals, as well as in decision-making for spending on products for 'common' and 'rare' disorders. For an individual hospital, the financial impact of reimbursing a very high cost orphan treatment can be substantial. There is a need to find long-term sustainable resourcing that respects, but also goes beyond issues related to individual hospital budgets.

Through the remit of national programmes, it has been proposed to centralise the reimbursement of Enzyme Replacement Therapy for patients with lysosomal storage disorders nationally with a central procurement mechanism. This could be a model for other rare diseases. The appropriate clinical (with guidelines) and financial governance should improve the access and quality for patients who require treatment and in some cases will curtail unnecessary costs of treating patients who may not be responding. There is currently no information system that provides for a national assessment of use and cost of orphan medicines and technologies in the hospital system. Such a system could work at a national rather than a hospital level; however, resources would be required to do this. A solution to similar issues was developed in the context of funding cancer therapies within the National Cancer Control Programme. A national funding and therapeutic review process has been developed, specific to cancer technologies but within the overall HSE governance structures and decision processes. This is of relevance in terms of rare cancer patients accessing orphan medicines and technologies, but also as a potential model for the assessment of orphan medicines and technologies in the longer term.

5.2.4 Health system reform – Universal Health Insurance and orphan medicines

The Government plan to introduce universal healthcare has the potential to bring substantial benefits to rare disease patients in terms of access to primary care, acute services and treatments. Deliberations should include consideration of how best to meet the specific needs of patients with rare diseases.

5.2.5 Ireland's role in supporting the development of new orphan medicines and technologies – Clinical trials and research

Many rare disease patients find that their disease is poorly understood and there is no product available anywhere in the world to treat their disorder. In recent years, the rare disease research community is making an unprecedented effort to work collaboratively to support the development of orphan products with potential benefits in the diagnosis, cure and management of rare diseases.

The International Rare Disease Research Consortium (IRDiRC) aims to deliver 200 new therapies for rare disease by 2020, as well as the means to diagnose most rare diseases by the same year. The consortium was initiated by the European Commission and the US National Institutes for Health, and launched in April 2011.

Access to clinical trials, under the supervision of experts whether in Ireland or abroad, is a key issue for patients with rare diseases and their families. The proposed National Office for Rare Diseases would work closely with Orphanet, where recruitment for clinical trials across the EU and beyond features on its website and is updated regularly.

5.3 Towards fair access to medicines and technologies for people with rare conditions in Ireland

5.3.1 Strengths and weaknesses of access to medicines and technologies

Strengths of current system

- An established system of health technology assessment and assessment for new pharmaceutical agents exists in Ireland.
- The existing systems have been successful in supporting the access of rare cancer patients to appropriate orphan medicines and technologies.
- The system and practice of early interaction with the National Centre for Pharmacoeconomics (NCPE) has proven helpful in the planning process.
- Ireland is considering approaches in which the ‘money follows the patient’ and this will be of benefit to rare disease patients.
- A large pharmaceutical industry and skilled workforce exists in Ireland, which ensures there are pathways for treatments to enter the Irish system.

Weaknesses of current system

- There is no ring-fenced fund to support access to orphan medicines and technologies. Current budgetary approaches are fragmented and may perpetuate inequalities in access to orphan medicines and technologies.
- Rationalisation of health service resources is required under current economic conditions. The focus on increasing cost-effectiveness at system level can inadvertently disadvantage the needs of individual rare disease patients requiring complex and sometimes costly therapies. There is a need to explore new approaches in the assessment of orphan drugs and technologies that respect the patients’ right to treatment, irrespective of the rarity of their disorder. There will always be competing demands for scarce healthcare resources. This highlights the need for rigorous evaluation so that services and treatments achieve an acceptable level of cost-effectiveness and represent value for money and benefits for patients;
- Decision-making around orphan medicines can often involve difficult social and ethical considerations since there may be some uncertainty about the exact magnitude of the clinical benefit and proposed prices may be quite high. This can result in protracted price negotiations and potential delays in access.
- Adequate and equitable decision-making in terms of availability of some orphan medicines and technologies is hindered by the requirement that the cost of such products be met from within hospital budgets.
- Transparency and communication are key themes for patients and their organisations within the processes relevant to the approval, assessment and reimbursement of orphan medicines and technologies. There is no clear system supporting complaints and appeal for decisions made in the context of orphan medicines and technologies in Ireland.
- Ireland’s potential role in supporting the development of orphan medicines and technologies is underdeveloped at present.

5.3.2 Access to orphan medicine and technology development – Relevant international models

There are many examples of systems for pricing and reimbursement of orphan medicines and technologies in other EU countries and beyond. However, there is no one country that provides a natural ‘fit’ within the Irish healthcare system. It is therefore clear that any developments in this area will need to be relevant and appropriate to the structures currently in place. Valuable learning is evident

from models used in the Netherlands (<http://www.government.nl/government/documents-and-publications/reports/2013/01/24/strategy-of-the-netherlands-in-the-field-of-rare-diseases.html>), France (http://www.has-sante.fr/portail/jcms/fc_1249930/fr/medicaments), Australia (<https://www.health.gov.au/lsdp>), Canada (<http://www.cadth.ca/en/products/cdr/recommendations>) and the UK (<http://www.specialisedservices.nhs.uk/info/agnss>). The Orphan Medicines and Technologies Subgroup of the Steering Group placed particular emphasis on learning from the English AGNSS system and the work at EU level on the CAVOMP (http://www.eucerd.eu/?post_type=document&p=1446).

Findings from comparative reviews of models in European countries

A study investigating pricing and reimbursing schemes and specific orphan medicines policies in a set of European countries (<http://news.ohe.org/2010/10/21/access-to-orphan-drugs-in-the-eu/>) compared schemes in France, Germany, Italy, the Netherlands, Spain, Sweden and the UK (http://www.orpha.net/consor/cgi-bin/Education_AboutOrphanDrugs.php?lng=EN&stapage=ST_education_education_aboutorphandrugs_eur; <http://www.eurordis.org/content/europlan-guidance-national-plans-and-conferences#EUROPLAN%20%20National%20Conference%20Final%20Reports>). This highlighted the need for early involvement by key stakeholders, including clinicians, licensing bodies and industry, and the development of guidelines for licensing and reimbursement.

Learning for the Irish system from international models

Patients and their representatives believe that the system in Ireland requires development to perform in a way that is transparent to rare disease patients, their carers and the clinicians who manage their care. The system should facilitate timely access to evidence-based therapies. The system in Ireland requires considerable development to support decisions that provide balance across competing service domains, but also respect that rare disease patients have an individual right to evidence-based therapies, irrespective of the rarity of their disorder.

Key elements of effective orphan medicines and technology assessment and reimbursement systems include governance and accountability, administrative, project management and communication processes, clarity in decision-making criteria, appeal processes, reporting and audit. In the UK, the AGNSS system provided for patients' engagement and developed a separate assessment pathway for orphan medicines and technologies that were not approved or did not fulfil the criteria through the main assessment pathway. This was replaced by an HTA Group to review and evaluate the high cost of orphan medicines for people with rare diseases.

5.4 Steering Group Recommendations on access to medicines and technologies for people with rare disease in the Republic of Ireland

The Steering Group recommends

30. The HSE develop a Working Group to bring forward appropriate decision criteria for the **reimbursement of orphan medicines and technologies**. The approach should include an assessment system similar to that for cancer therapies established under the National Cancer Control Programme and link with the CAVOMP at European level.
31. The HSE undertake a **preliminary economic evaluation** of current activity and costs for orphan medicine and technologies for rare disease patients across all hospitals settings.
32. Applications for the use of orphan medicines and technologies in hospitals be dealt with in the **context of a national budget**, rather than through individual hospital budgets, and that the HSE take account of this.

33. The HSE develop a publicly available **annual report documenting the use of both existing and new-to-market orphan medicines and technologies** in Ireland and a summary of applications received and decisions relating to those applications.
34. The existing **horizon scanning between pharmaceutical companies and the HSE**, including clinical value assessment authorities, continue and be enhanced so as to improve information available regarding orphan medicines in the pipeline and the future needs for these medicines.
35. The capacity to prescribe all orphan medicines and technologies for **ultra-rare conditions be limited to specialist teams** designated through the Centres of Expertise.
36. The HSE apply a set of **guidelines on the prescribing** of orphan medicines and technologies in Ireland. The HSE should evaluate clinical outcomes regarding use of orphan medicines.
37. Clinicians should provide data necessary to the **monitoring of prescription patterns** and pharmacovigilance, so as to ensure patients' safety and high-quality healthcare.
38. Early dialogue between the HSE and companies who are running **clinical trials in Ireland** with Irish patients where license approval is imminent.
39. Sponsors could be offered an incentive to run trials in Ireland **increasing access to innovation** for Irish patients.

6. Empowering, protecting and supporting rare disease patients and carers

6.1 Introduction

Patients' empowerment is a priority theme within rare disease strategies and plans across Europe and internationally (EUCERD, 2013a). It is essentially about respecting and incorporating patients' rights and their voices into the policies and services that affect them. The WHO Regional Office for Europe, in its *Health 2020 – A European policy framework and strategy for the 21st century*, has now embedded patients' empowerment actions within the new European health policy (WHO, 2013). Empowered patients are recognised as key to success in achieving better health outcomes, as well as contributing to cost-effective care, particularly in the context of chronic disease management. They are also active participants in decision-making regarding their own disease when they are equipped with understanding of their disease and knowledge of the full range of choices and resources open to them.

This chapter is largely predicated on the European Council (EC) Recommendation of 8th June 2009 on an 'Action in the field of rare diseases' (2009/C 15/02). It declares that the World Health Organization (WHO):

'... defined empowerment of patients as a "pre-requisite for health" and encouraged a "proactive partnership and patient self-care strategy to improve health outcomes and quality of life among the chronically ill". In this sense, the role of independent patient groups is crucial both in terms of direct support to individuals living with the disease and in terms of the collective work they carry out to improve conditions for the community of rare disease patients as a whole and for the next generations.'

The Recommendation goes on to advise that:

'Member States should aim to involve patients and patients' representatives in the policy process and seek to promote the activities of patient groups.'

This led to the Council's recommendations at Section VI entitled 'Empowerment of Patient Organisations', that Member States:

'Consult patients and patients' representatives on the policies in the field of rare diseases and facilitate patient access to updated information on rare diseases.

'Promote the activities performed by patient organisations, such as awareness-raising, capacity-building and training, exchange of information and best practices, networking and outreach to very isolated patients.'

Core themes within patients' empowerment for rare disease patients include:

- Involvement of rare disease patients and carers in the design, implementation and review of national policies.
- Respectful and appropriate involvement of rare disease patients and carers in decisions relating to their diagnosis and care at all stages.
- Re-orienting the health system to become more user-friendly, patient-centred and family-centred.
- Supporting the development of information resources on rare diseases that are accessible, as well as supporting health literacy among rare disease patients and carers.

- Supporting the development of the skills of patients, their carers and the organisations that represent them to navigate the health system and bring about effective changes.
- Valuing and supporting the social inclusion of rare disease patients in wider society, including aspects of employment, education, discrimination, entitlements and disability.

In policy terms, rare diseases are often considered within the context of complex systems – for example, in the context of multidimensional healthcare systems, information and budgeting systems. However, such an approach may fail to adequately acknowledge the support system that is closest to the rare disease patient – i.e. the family. The whole family of a rare disease patient, whether children or adults, is affected by the disease of the loved one and can become marginalised: psychologically, socially, culturally and economically vulnerable (EURORDIS, 2005).

A patients' empowerment approach to rare disease seeks to value and support the abilities of carers and parents as a key determinant of patients' outcomes. This involves skills of caring, advocacy, service navigation and coordination, information gathering, and supported self-care and disease management. A patients' empowerment approach also seeks to promote equity in many domains – for example, between the rights of those with rare and more common disorders and in the outcomes experienced by rare disease patients with higher education/incomes and those who are disadvantaged.

6.2 Scope and key determinants for empowerment of patients' organisations

Patients' support and empowerment is not a separate element of this National Rare Disease Plan; rather, it is integral to every aspect of national rare disease plans. The Patient Support and Empowerment Subgroup of the Steering Group engaged with a range of stakeholders to shape this section of the national plan and to introduce principles of patients' empowerment into every aspect. Opportunities to forward concerns, experiences and suggestions were offered to member organisations of the Irish Platform for Patients' Organisations, Science and Industry (IPPOSI), the Genetic and Rare Disorders Organisation (GRDO) and the Medical Research Charities Group (MRCG), independent patients' organisations/advocacy groups, and individual patients/parents representing or affected by rare conditions.

A wider consultation process with rare disease stakeholders was undertaken, the details of which are contained in a separate report (Department of Health, 2014). Since the vast majority of respondents to the consultation were themselves rare disease patients and their carers, the findings from this process are particularly relevant to the recommendations made in this chapter.

The scope of this chapter encompasses a number of pertinent issues against the backdrop of the 2009 Recommendation by the European Council (2009/C 15/02) on the empowerment of patients' organisations. These issues, each examined in detail below, are:

- ensuring patients and carers get the right information at the right time;
- protecting patients' rights;
- developing and valuing carers;
- promoting equity for rare disease patients;
- delivering holistic packages of care for rare diseases beyond the healthcare setting.

6.3 Ensuring patients and carers get the right information at the right time

KEY POINTS FROM THE CONSULTATION PROCESS

Obtaining information

Difficulties in accessing appropriate information was a concern for patients, carers, specialists and GPs; this included the question of limited clinician knowledge of any particular rare disease. In addition, the consultation showed that the following information would be helpful:

- an evidence-based and trustworthy online source of information about the condition;
- guidance on how to access appropriate specialist services in Ireland or abroad, and on navigating the Irish healthcare system;
- guidance on how to navigate the healthcare system in Ireland with that condition;
- a summary of the main treatments available and/or if no treatments available, information on clinical trials;
- benefits and entitlements relevant to the condition;
- points of contact for others with similar conditions or experiences.

The last point ('points of contact for others with similar conditions or experiences') is particularly important given that people living with a rare disease and their families – especially parents of young children – are often the leading 'experts' in their diseases. Indeed, a lack of understanding about rare disorders can be frustrating for people seeking information and help. One of the means to address this is to develop a national information portal on rare diseases that makes the transition between information for patients and clinicians seamless.

6.4 Protecting patients' rights

KEY POINTS FROM THE CONSULTATION PROCESS

Patients' rights

- Under this theme, common concerns from the consultation included accessing information and services; eligibility and entitlement to public and private healthcare, including medical card, Long-Term Illness Scheme, life insurance and critical illness mortgage protection cover; privacy and confidentiality; and the management of delayed or misdiagnosed illness, especially given opportunities for assessment in foreign specialist centres.

Rare diseases can present unique challenges to the healthcare system and beyond, seeking to manage patients' care, including access to appropriate services and treatments, patient safety and the quality of healthcare. Other areas that are of direct relevance in the rare disease context are access to information and personalised health, along with the issues of privacy, confidentiality and consent.

The current legislative and policy environment governing these latter areas (of privacy, confidentiality and consent) offer some protection and coverage to patients with rare diseases; but of course there is always scope for improvements as policy and protection agendas are developed and advanced further in the areas of:

- access to orphan drugs;
- access to medical treatment trials;
- access to treatments outside of Europe;
- education and support;
- employment protection;
- benefit and pension protection.

Those diagnosed with rare conditions, as well as families and carers, are very frequently left in difficult situations with regard to employment and financial security. The precariousness of their situation needs to be taken into account as policy is developed in these areas.

It is essential that discrimination against a person based on their genetic heritage – be it family history of inherited disease or the results of genetic tests – is avoided and properly handled. The principles enshrined in the Convention on Human Rights and Biomedicine, the UN Convention on the Rights of Persons with Disabilities (UN, 2006) and the EU Charter of Fundamental Rights (European Parliament, 2000) are all examples of such international conventions applicable in this context.

In recognition of the challenges facing patients and their families with rare diseases, it is important that health and social benefit programmes are applied in a fair and transparent manner.

Rapid advances in genetic knowledge create special legal and ethical issues, including informed consent concerning genetic testing and genetic research; confidentiality and the duty to inform those potentially affected by genetic-related conditions; liability and risk management to avoid malpractice; privacy interests concerning identifiable genetic data; ethical analysis of public health initiatives (genetic screening, national registries); insurance and employment discrimination; sex selection; and genetic and intellectual property issues.

6.5 Developing and valuing carers

KEY POINTS FROM THE CONSULTATION PROCESS

Carers

- Carers were the most common respondent to the public consultation on the National Rare Disease Plan, representing 37% of all responses. Further supports needed from State resources in the home and in end-of-life situations for adults and children featured strongly in the consultation, as did the stress experienced by carers and the bereavement process.

Other issues expressed in submissions received to the public consultation included:

- the need for early assessment, educational assessment and psychological interventions;
- isolation;
- mental health issues affecting patients, their families and carers;
- residential facilities for the provision of respite care and appropriate long-term care;
- palliative care;
- home care.

Respondents noted that other than a small number of centre-based respite day care centres for a tiny number of rare conditions, there are no residential respite centres dedicated for those affected by rare conditions.

The *National Carers' Strategy – Recognised, Supported, Empowered* was published by the Department of Health in 2011. The four national goals for carers are to:

- recognise the value and contribution of carers and promote their inclusion in decisions relating to the person they are caring for;
- support carers to manage their physical, mental and emotional health and well-being;
- support carers to care with confidence through the provision of adequate information, training, services and supports;
- empower carers to participate as fully as possible in economic and social life.

The Steering Group and its Subgroups consider that bringing the roadmap for implementation contained within the National Carers' Strategy into reality would be hugely beneficial to carers of rare disease patients, the patients themselves and wider society. However, it is also recognised that carers of rare disease patients differ from the national profile and also that caring in the rare disease context can bring additional challenges. These unique challenges with respect to rare diseases must be taken on board when it comes to the development of further health and social protection measures.

6.6 Promoting equity for rare disease patients

KEY POINTS FROM THE CONSULTATION PROCESS

Equity

Submissions received on this aspect of the consultation raised a range of pertinent issues with respect to equity for rare disease patients, including:

- Access to treatment and services were viewed as being inequitable given that expertise for many rare diseases may not be available in Ireland.
- This brings another layer of financial and monetary inequity due to the burden of having to travel for such care to specialist centres abroad, sometimes without inadequate State support.
- The availability of such care in Ireland may also be confined to Dublin, to the detriment of people from the rest of the country.

- Equally, care may not always be fully integrated due to blurred care pathways for management and treatment of the disease.
- The lack of awareness of particular rare diseases in the healthcare system, along with the transition from childhood to adult treatment services, were other issues raised.
- Furthermore, financial inequity can occur from the incapacity of patients with rare diseases to engage in paid employment.

The health system needs to be better supported to respond to the diagnostic and treatment needs of many rare disease patients. For example, where a diagnosis is elusive or unclear, there is no system that facilitates rapid referral for assessment by an appropriate specialist in Ireland or internationally. Delayed diagnosis or misdiagnosis may have implications for life expectancy and quality of life; it also absorbs scarce resources. Where a rare disease diagnosis has been reached, there is often no established care pathway for that disease within the Irish health and social care system. Lack of recognition and clarity within the system creates inequalities in outcomes – between patients living in one region and another, as well as between patients with ample financial resources and those with none. Respondents to the public consultation felt that the health system needs to be re-oriented with respect to the management and treatment of patients with rare diseases.

Many patients and families are affected by a delayed diagnosis and sometimes by an incorrect one. This has serious implications for life expectancy and quality of life, and is an inefficient use of resources.

Chapter 4 presented recommendations relating to improvements in the diagnostic, treatment and care services for rare disease patients in Ireland. Respondents to the public consultation considered that the implementation of these recommendations form the foundation for addressing the inequity in the management and treatment of rare diseases. Key issues include the development of healthcare pathways, Centres of Expertise, working in multidisciplinary teams and equality of access to treatment as appropriate.

6.7 Delivering holistic packages of care – Rare disease beyond the healthcare setting

KEY POINTS FROM THE CONSULTATION PROCESS

Holistic care

Recurring themes that emanated from this dimension of the consultation included:

- social isolation and exclusion;
- adapting to disability;
- loss of employment and independence at a young age;
- the need for interdisciplinary packages of care that include psychological/counselling services;
- a general lack of understanding of rare diseases and their implications outside of the health system in areas such as education, employment and disability.

Rare disease patients and carers are adversely affected when their disease is misunderstood or decisions are made by the rigid application of certain qualifying criteria. Respondents to the public consultation also emphasized that the complex needs of children living with a rare condition be met within the education system. Raising awareness with teachers about the inherent complexity of rare disorders and their consequent impact on learning needs to take place within the context of teacher-training. Children with rare conditions often present with their own unique cognitive and behavioural profiles and thus require timely interventions in line with their Individual Education Plans. Emotional distress and/or anxiety levels, which often co-exist with this population of children, also require monitoring, with appropriate access to mental healthcare factored into any treatment plans. Further education for teachers could be facilitated by providing specialist training at appropriate intervals.

Currently within the Irish Education System, there are moves afoot to provide better supports for young people with disabilities to avail of higher education opportunities. An opportunity therefore exists for collaborative efforts between the many disability groups and services already working in this area and these efforts could encompass tackling employer-related issues in regard to finding employment after school/college.

The overall promotion of education and social inclusion of children with complex needs does not therefore need confinement to those children with a rare disease diagnosis. Oftentimes, the overlap with a 'disability' label is sufficient to warrant a 'whole school' approach to encourage what is, in essence, an acceptance of differences.

The Steering Group for this National Rare Disease Plan highlights the issue of improving transition supports within the education system. Research within the disability sector shows clearly that reaching the age of 18 is a precarious time in terms of finding appropriate adult services, be they medical, educational or social, or in terms of finding appropriate employment. There are valuable lessons to be learnt from the disability sector in relation to this most important time of transition in the lives of people affected by a rare disorder. A strong emphasis is required on the fact that children grow *up* and not *out* of their conditions. Needs will never disappear; they merely change over the lifespan. Recognition of these facts can both inform policy and enhance treatments and management of those affected by rare and oftentimes disabling conditions.

People with rare diseases often need support to access mainstream education, training, employment and social opportunities. Some rare disease support groups may provide limited supports in the form of family support workers, youth workers and rehabilitative therapists to assist people to live independently, reach their full potential in life and contribute positively to their community. Most of the organisations, however, do not have the resources to provide or sustain these services, and so the gap in support is often left unfilled. This applies not only to those affected by rare conditions, but also to carers and other family members who routinely require their own support, particularly in the area of psychological services.

Specialised social services are instrumental for the empowerment of people living with rare conditions, as well as improving well-being and health. For people living with a rare, chronic and debilitating disease, care should not be restricted to medical and paramedical aspects, but should also take into account social inclusion and psychological and educational development. After all, adults with rare conditions can sometimes find that they are unable to participate in work or education due to the severity of their symptoms and associated disability. Equally, many carers forego paid work in order to meet the care needs of their child, sibling or parent at home. However, for a significant proportion whose condition does not affect their ability to participate, it is the lack of support or flexibility in relation to the rare condition which excludes them from education and employment opportunities.

Filling gaps in the provision of care both to rare disease patients and their carers and family members is challenging given that resources are scarce in the voluntary and public sector. One area for consideration is therapeutic recreational programmes; these are organised recreation activities and have been operating successfully in Scandinavian countries for many years. Some are run as specific summer camps and others are *ad hoc* programmes that are planned and take into account the specific needs of children or young adults with rare diseases. Activities are centred on fun, leisure and entertainment. The benefits of participation to patients, particularly younger children, have a significant impact on the quality of life of individuals and families, and have been shown to improve health and well-being significantly.

In summary, by employing best practice principles, social services should seamlessly integrate into the patient's daily life and support psychological and educational development.

6.8 Developing the effectiveness of patients' organisations

KEY POINTS FROM THE CONSULTATION PROCESS

Patients' organisations

- The consultation noted the diverse functions of patients' organisations, such as support, information, advocacy, advice, research and fund-raising. Thus there was strong support for the involvement of patients' organisations in the National Rare Disease Plan.
- Fostering links with similar patients' organisations abroad was seen as beneficial, although the consultation showed that organisations for some people with rare diseases in Ireland may not exist.

Rare diseases represent a large and diverse group of around 8,000 disorders. The majority of rare disease patients do not enjoy the benefits of having a patients' organisation in Ireland to offer them support and guidance, and to advocate on their behalf. For many conditions, particularly very rare and ultra-rare ones, there are no condition-specific support groups in Ireland. Therefore, people affected rely on international groups for information and support. More than 50% of respondents to the GRDO Patients' Experience Survey in 2012 reported either that there is no patients' support group in Ireland for their condition or that they do not know of one. However, more than 90% of respondents to the same survey said that they consider support organisations for rare disease patients 'essential', 'very important' or 'important' (GRDO, 2012). In many cases, where there are no Irish-based organisations for numerous rare diseases and those affected rely on international groups to provide support, information and advice. These international organisations cannot provide a formal voice in Ireland, which, in turn, provides obstacles to empowerment for those concerned.

There are, however, many patients' organisations in Ireland that operate specifically to support the needs of rare disease patients. Rare disease patients are also variously represented among patients' alliance and umbrella-type organisations, such as those relating to neurological, lung, kidney or heart disorders, and cancers. Disability-related organisations in the community and voluntary sector are also active in supporting many children and adults with complex needs and disabilities resulting from rare disease.

Rare disease patients' organisations in Ireland take many forms. Despite the small numbers that do exist, both for individual conditions and as umbrella groups, they play a vital role in the promotion of rare disease awareness and support. Some provide social and financial support to those affected; some are actively involved in raising funds for research and lobbying for better care and appropriate Government policies.

Many rare disease support groups function as the only specialist support and information provider on their particular rare condition and provide training and information to health and social care professionals, as well as to those affected by the condition. Online support groups or telephone contact can also be essential for those who experience social isolation due to lack of transport or carers, and for those who do not have a specific rare disease support group. The Internet offers people with the same rare disease (for which there may not be a representative patients' organisation) the possibility of establishing online support networks here or abroad. In the case of ultra-rare conditions, there is commonly no access to any specialist centre or specific support group and so the difficulties of lack of information, expertise and support are heightened.

Many rare and ultra-rare disease organisations are founded by individuals or small groups of people who are personally affected by the condition. Sustaining these organisations often places considerable additional stress on people who themselves have a rare condition or are caring for others who do. State support for these organisations is urgently required to ensure that their vital work is continued and developed, and to ensure that this work is not the sole responsibility of people already burdened with the effects of a rare condition. Of the patients' organisations that responded to the GRDO's Patients' Experience Survey, 63% receive no statutory funding and 51.9% have no paid employees (GRDO, 2012). Rare disease patients' organisations can be challenged by many factors, including, inter alia, a smaller pool of volunteers and supporters; a requirement to reach and support patients with highly complex needs/disabilities; a requirement to liaise beyond national borders in many aspects of their work; and a requirement to support patients to navigate a system that is all too often ill-equipped to understand their disease. The financial hardship associated with rare disease has been discussed earlier in this chapter. Without the support and advocacy provided by patients' organisations, many would be unable to negotiate through the system.

In addition, the lack of awareness in the health and social care system of such groups, where they do exist, hampers the reach of the groups. Patients are not automatically referred to them on diagnosis. Those affected may become isolated by not making contact with relevant organisations.

Further progress in the integration and development of patients' organisations and patients' representation is required, with particular reference to the balanced representation of rare, very rare and ultra-rare conditions in all domains. Patients and the organisations that represent them need financial, structural, and institutional support to participate meaningfully in any process that will develop the policies that ultimately affect patients and their families.

A framework with explicit provisions to ensure the participation of groups of small patients and individual patients is an urgent requirement to ensure meaningful participation in the decision-making process and facilitate real patients' empowerment.

Patients and patients' organisations should be meaningfully involved throughout the research process, from the 'idea' stage to the proven intervention, in partnership with academic research bodies and the pharmaceutical industry. Many rare disease patients' organisations in Ireland have demonstrated an impressive track record in supporting the development of research through partnerships characterised by supported access to patients, joint funding and governance arrangements. Supporting the involvement of patients' organisations in research should be supported and facilitated within this National Rare Disease Plan.

In recognition of the challenges facing patients and their families with rare diseases, it is important that health and social benefit programmes are applied in a fair and transparent manner.

A clearly defined 'Management of Change' process is recommended, as is a thorough analysis to identify the current available resources and highlight existing shortfalls. It is also of the utmost importance to ensure that those people affected by rare conditions who are currently receiving care, services and support are provided for during the transition.

6.9 Steering Group recommendations

The Steering Group recommends:

40. The **principles of patients' empowerment** be integral to all aspects of this National Rare Disease Plan for Ireland, both now and in the future, in recognition of the fact that patients and their carers require significant clinical and non-clinical support.
41. Arrangements be put in place to support the integration of the experience and expertise of rare disease **patients' organisations in the implementation and review** of this first National Rare Disease Plan for Ireland.
42. **Patients' rights to appropriate assessment and treatment be realised** through a recognised national Centre of Expertise or by linkage through the patient's healthcare provider to recognised European Reference Networks (ERNs) and in the context of the EU Cross-Border Healthcare Directive 2011/24/EU.
43. The proposed National Office for Rare Diseases provide **support and information** to patients.
44. The National Rare Disease Plan for Ireland encompass a **holistic and person-centred** view of the lives of rare disease patients and their families, one that goes beyond healthcare issues.
45. The HSE and non-governmental organisations (NGOs) provide **ongoing support** for people living with rare diseases and that they cooperate and promote awareness of rare diseases.
46. The HSE and NGOs avail of the opportunity to promote awareness of and information on rare diseases on **Rare Disease Day**.

Implementation, Monitoring and Review of the National Rare Disease Plan

The development of a National Rare Disease Plan for Ireland is welcomed by all stakeholders and recognised as an important step in the right direction. It is critical that the momentum built up over the development phase be maintained and strengthened in the implementation phase. The Plan is a high-level one and therefore many of the finer details of its implementation cannot be outlined here.

The National Rare Disease Plan is being published at a time of many wider reforms and developments in Ireland and further afield. In Ireland, the organisation of hospitals into 6 Groups and the planned licensing of hospitals are relevant. At EU level, the Directive on Patients' Rights in Cross-Border Healthcare will influence the implementation of Ireland's National Rare Disease Plan in coming years. In addition, its publication comes at a time of national economic and budgetary challenges, which have been recognised by the Steering Group when developing the plan.

The implementation of this National Rare Disease Plan shall therefore be set in the context of re-orienting current resources for the purposes of advancing these recommendations in the health service, given the prevailing financial constraints. And thus, the present budgetary environment shall be explored to identify and exploit all opportunities for progressing this national plan as the future platform to address the care and treatment of people with rare diseases. The service planning mechanism provides an accountability framework with respect to the delivery of health services. Rare disease management programmes should be specified within the HSE Service Plan mechanism.

Against the above background, it is envisaged that the National Rare Disease Plan will be implemented on the basis of the recommendations set out in the report, supported by high-level outcomes underpinned by a series of key outputs/action areas with designated lead agencies.

The Steering Group recommends

47. An **Oversight Implementation Group** of relevant stakeholders, including patients' groups, led by the HSE be established to oversee and monitor implementation of the National Rare Disease Plan's recommendations and associated key outputs. The HSE will report to the Department of Health using key performance indicators (KPIs) on a periodic basis in accordance with reporting requirements under the National Service Plan. It should be noted that the European Union has mandated EUCERD's KPIs and that Ireland will have to report on these (*see Appendix 5*).
48. There should be **an overall review of the National Rare Disease Plan** prior to development of the next plan in 2019.

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Appendix 1: Membership of the Steering Group and Subgroups

Steering Group

Dr. John Devlin (<i>Chair</i>)	Department of Health
Louise Kenny	Department of Health
Liam McCormack	Department of Health
Prof. Eileen Treacy	Health Service Executive
Mr. John McCormack	The Medical Research Charities Group
Ms. Eibhlín Mulroe	Irish Platform for Patients' Organisations Science & Industry
Mr. Tony Heffernan	Patient Representative, CEO, Saoirse Foundation (Bee for Batters)
Mr Philip Watt	Cystic Fibrosis Ireland
Dr. Helen McAvoy	Institute of Public Health in Ireland
Ms. Avril Daly	The Genetics Rare Disorders Organisation
Mr. Owen Metcalfe	Institute of Public Health in Ireland
Mr. Shaun Flanagan	Pharmacy, Health Service Executive
Dr. Catherine Gill	Health Research Board
Dr. Anne Cody	Health Research Board
Oonagh Ward	Health Research Board
Geraldine O'Dea	Irish Medicines Board
Caitríona Connolly	Department of Health (Secretariat)

Subgroups

Research and Information	<i>Chair:</i> Helen McAvoy
Centres of Expertise	<i>Chair:</i> Avril Daly
Patient Empowerment	<i>Chair:</i> Tony Heffernan
Orphan Drugs and Technologies	<i>Chair:</i> Eibhlín Mulroe
Communications	<i>Chair:</i> Philip Watt

Appendix 2: Sources of information on rare disease in Ireland

National health information systems

Hospital In-Patient Enquiry (HIPE) (compiled by Economic and Social Research Institute)
National Perinatal Reporting System (NPRS) (compiled by Economic and Social Research Institute)
National Psychiatric In-Patient Reporting System (NPIRS) (compiled by Health Research Board)
Vital Statistics – death and birth (compiled by the Central Statistics Office)
National Newborn Screening Programme (run by HSE)
HSE Health Protection Surveillance Centre
National Physical and Sensory Disability Database (compiled by Health Research Board)
National Intellectual Disability Database (compiled by Health Research Board)

Population-based registries

EUROCAT (Dublin, Galway, South, South East)
National Cancer Registry
National Paediatric Mortality Register

Specific rare disease registries

Cystic fibrosis registry
Myelodysplastic syndromes registry
Bernard-Soulier syndrome registry
Amyotrophic lateral sclerosis and motor neurone disease registry
Hurler Syndrome registry
Severe Chronic Neutropenia registry
National Alpha 1 Patient Registry
Haemophilia register (National Centre for Hereditary Coagulation Disorders)
Irish Childhood Diabetes register
Motor Neurone Disease register

Other registries

Stroke registry
Cerebral Palsy registries (West, South)
Scoliosis database
Register of patients with PAH (pulmonary hypertension)
Renal registry
National Registry of Deliberate Self-Harm
National Register of Patients with Primary Immunodeficiency
National Hepatitis C database
National Cleft database
Heart and Lung Transplant registry
Cardiovascular disease registry

Healthcare provider databases

Records held by clinical specialists operating a particular service for rare diseases
Records held by support/advocacy groups for rare disease patients
Laboratory records – pathology, genetic testing, microbiology, etc.

General or rare-disease specific cohort or longitudinal studies

Appendix 3: National Newborn Screening Programme

Table A3: Comparison of incidence in the Republic of Ireland and worldwide

Condition	Date started	Irish incidence	Worldwide incidence
Phenylketonuria	1966	1:4,500	1:12,000
Homocystinuria	1971	1:65,000	1:200,000
Classical Galactosaemia	1972	1:19,000	1:60,000
Maple Syrup Urine Disease	1972	1:125,000	1:216,000
Congenital hypothyroidism	1979	1:3,500	1:4500
Congenital toxoplasmosis	2005	<i>not available</i>	<i>not available</i>
Cystic fibrosis	2011	<i>not available</i>	<i>not available</i>

Appendix 4: Principles relating to assessment for reimbursement of orphan medicines

The 10 principles that could describe any new route for assessing pricing and reimbursement of Orphan Medicines are:

- Be transparent and accountable.
- Support rational decision-making.
- Best quality evidence which is available.
- Promote accessibility and equity and reflect societal values.
- Support improvements to economically efficient or clinically effective service provision.
- Realistic predictions of future need.
- Demonstrate how the evidence has been considered in a robust and documentable process, able to withstand legal challenge.
- Maintain consistency, but allow some flexibility in balancing the relative importance of criteria.
- Clear criteria, which should be used as a structure for the evaluation and decision-making process.
- Ensure that the criteria and the approach to using them are reviewed regularly to incorporate changes in external context.

Appendix 5: EU EUCERD Indicators to monitor National Rare Disease Plans

List of core indicators

The following list of core indicators is proposed for all EU Member States so as to monitor their national plans or strategies on rare diseases (EUCERD, 2013).

Background indicators (preparation of the plan/strategy)

1. Existence of regulations/laws or equivalent official national decisions that support the establishment and development of a Rare Diseases (RD) plan.
2. Existence of a RD advisory committee.
3. Permanent and official patients' representation in plan development, monitoring and assessment.
4. Adoption of the EU RD definition.

Content indicators

5. Existence of a national policy for establishing Centres of Expertise on RD.
6. Number of national and regional Centres of Expertise adhering to the national policy.
7. Participation of national or regional Centres of Expertise in European Reference Networks.

Information

8. Development of/participation in a comprehensive national and/or regional RD information system.
9. Existence of helplines for RD

Knowledge, classification/coding, registries and research

10. Existence of a national policy on RD clinical practice guideline development and implementation.
11. Type of classification/coding used by the healthcare system.
12. Existence of a national policy on registries or data collection on RD.
13. Existence of RD research programmes and/or projects in the country.
14. Participation in European and international research initiatives.

Therapies

15. Number of Orphan Medical Products with a European Union marketing authorisation and available in the country (i.e. priced and reimbursed or directly supplied by the national health system).
16. Existence of a governmental system for compassionate use of medicinal products.

Social services

17. Existence of programmes to support the integration of RD patients in their daily life.

Financial support indicators (implementation of the plan/strategy)

18. Existence of a policy/decision to ensure long-term sustainability of the RD plan/strategy.
19. Amount of public funds allocated to the RD plan/strategy.
20. Specific public funds allocated for RD research.
21. Public funds specifically allocated for RD research actions/projects per year since the plan started.

Notes

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Department of Health
Hawkins House
Hawkins Street
Dublin 2
Tel: +353 (0)1 635 4000
Web: www.doh.ie

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