Recommendations and proposed measures for the Belgian Plan for Rare Diseases

An outline of integrated and comprehensive health and social policy actions for patients with rare diseases

Phase I

Fund Rare Diseases and Orphan Drugs

managed by the King Baudouin Foundation

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A plan for integrated general actions in health care and social policy for patients with rare diseases

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(overview of members on page 76)

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INTRODUCTION

In Belgium there are an estimated 60,000 to 100,000 people who need special care because they suffer from a rare disease, i.e. a disease with a prevalence of less than 5 per 10,000. The number of rare diseases is estimated at between 6,000 and 8,000, most of which are chronic and life-threatening or highly debilitating conditions. Due to the rare nature of their condition, patients are often diagnosed very late or not at all and in many cases treatment is not optimal. In addition, the development and dissemination of special medicines for a rare disease is not a given. The Fund Rare Diseases and Orphan Drugs managed by the King Baudouin Foundation was tasked with playing a coordinating and managing role by the Belgian Minister for Social Affairs and Public Health, Laurette Onkelinx, and the Belgian National Institute for Sickness and Invalidity Insurance (RIZIV/INAMI) in setting up a Belgian Rare Diseases Plan. More specifically, the Fund was commissioned to draw up a policy action plan for rare diseases, i.e. a plan for integrated, general actions in the areas of health care and social policy for patients with rare diseases. This document sets out an initial series of recommendations and proposed measures for developing the Belgian Rare Diseases Plan.

This document is the result of cooperation between the members of the Management Committee of the Fund Rare Diseases and Orphan Drugs, managed by the King Baudouin Foundation, and five topic-based Working Groups (patient registration & databases; analysis of hidden costs and roadmap for patients; Centres of Expertise & cooperation at national level; information for care providers, patients and the general public; access to and costs of diagnosis, medication, treatment and patient management). For the composition of the Management Committee and of the Working Groups, see Addenda 4 and 5.

This document was approved at the meeting of the Management Committee of the Fund Rare Diseases and Orphan Drugs held on 30 March 2010. It does not necessarily reflect the individual opinions of the members of the Management Committee or of the organisations to which they belong.

This document submitted to Laurette Onkelinx, Minister for Social Affairs and Public Health, on 11 May 2010. It does not necessarily reflect the Minister's viewpoint.

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EXECUTIVE SUMMARY

Context

Patients with a rare disease could be described as health care 'orphans' in so far as they are often diagnosed very late or not at all, they can hardly count on medical and other support and there is little scientific research in this area. According to the European definition, a disease is 'rare' when it has a prevalence of less than 5 per 10,000. The number of rare diseases is currently estimated at between 6,000 and 8,000, most of which are chronic, degenerative diseases that are highly debilitating or even life-threatening. Naturally, this has a negative impact on the quality of life of patients with a rare disease and those around them. However, for patients in Belgium and the rest of Europe, there is new hope for a better life.

Towards a better approach to rare diseases: the European impetus

Rare diseases have been a high priority for Europe in the last few years. Accordingly, the European Council has issued a Recommendation to all member states to develop a rare diseases plan or strategy by 2013. It expressly states that it is important to take a coordinated and structural approach at European level, and that community solutions should serve as the key to a successful approach. The measures developed should enable all patients, without distinction, to be diagnosed and appropriately treated within a reasonable period of time. In addition to improving health care, work also needs to be done on research into diagnostic testing and updated treatments. The measures should ensure that patients can fully benefit from the growing number of medicines available, and from correct information about diseases and their treatment. France, Spain and Portugal are just some of the countries that have already drawn up a national rare diseases plan.

Belgium's strategy

In Belgium, rare diseases are often not diagnosed until years after the initial symptoms appear. For 78% of patients, late diagnosis is responsible for at least one adverse consequence. In 1% of the cases, it can even lead to early death. According to patient advocacy organisations, the development of a treatment, access to (often expensive) medical and paramedical care and the organisation of care as a whole are real problems that must be addressed. On 23 September 2008, Laurette Onkelinx, the Belgian Minister for Social Affairs and Public Health, announced a Belgian Plan for Chronic Diseases: the first step towards a better approach to rare diseases, which are often chronic. In addition, on 12 February 2009, the Chamber of Representatives approved a resolution on "an action plan for rare diseases and orphan drugs".

The Fund Rare Diseases and Orphan Drugs, managed by the King Baudouin Foundation, was commissioned to draw up a Belgian Rare Diseases Plan. Representatives of patient advocacy organisations, medical and paramedical

workers, RIZIV/INAMI, health insurance funds, the pharmaceutical industry and the medical/paramedical and social services, and representatives of the medical and political authorities involved in health policy are all working together and have organised themselves into topic-based working groups.
The Belgian Rare Diseases Plan aims to bring together all resources and knowledge in order to create a framework enabling better diagnosis and general care for patients, providing access to validated information, and improving the knowledge, independence and quality of life of patients and those around them. The challenge is huge: ensure better care for all patients coping with the fact that not only are they sick, but they have a rare disease. The first phase of the Belgian Rare Diseases Plan contains 11 measures that can be implemented in the short term. These measures are divided among 4 action areas.

The Belgian Plan for Rare Diseases

Area 1. Organisation of clinical expertise to improve patient health outcomes

22% of Belgian patients with a rare disease consult more than 5 doctors, and 7% consult more than 10, before a correct diagnosis is made. Moreover, 44% were first given another diagnosis, resulting in inappropriate treatment in 75% of the cases.

— Measure 1. Create Centres of Expertise and Coordinating Centres for Rare Diseases

— Measure 2. Create a National Platform for Rare Diseases

Three new structures are proposed in order to combine national expertise while encouraging networking at European level: Coordinating Centres and Centres of Expertise will be set up under the auspices of a National Platform. They each play a different, yet complementary role.

The Centres of Expertise bring together clinical and scientific expertise for one specific rare disease or a group of rare diseases. The Coordinating Centres for Rare Diseases are an access point to health care for patients with an extremely rare disease who cannot be diagnosed in the Centres of Expertise, or at least not within a reasonable period of time. They also monitor patients who cannot be treated in a Belgian Centre of Expertise. To gain approval, the Centres of Expertise and the Coordinating Centres must meet a series of European criteria that guarantee high-quality care for patients. Centres of Expertise and Coordinating Centres register patients, contribute to research and clinical studies, help to draw up guidelines for 'good practices' and improve social support. Structural cooperation with the peripheral services is developed (GPs, specialists, home care services, etc.) as is interaction with patient associations.

The National Platform for Rare Diseases will be an autonomous entity responsible for various tasks, including coordination between the Centres of Expertise and the Coordinating Centres, and the harmonisation of procedures for diagnosis and treatment. The National Platform will cooperate with the relevant European authorities and stakeholders.

Area 2. Codification and inventory of rare diseases

The absence of epidemiological data is a major obstacle to the proper planning of health care and general medical and social care for patients with rare diseases.

— Measure 3. Create a National Registry for Rare Diseases

The creation of a National Registry for Rare Diseases makes it possible to identify the number of patients with a rare disease, collect epidemiological data, and track patients in connection with basic research, clinical tests and new treatments. The National Registry will be connected to existing and future disease-specific registries.

Area 3. Increase awareness, inform stakeholders and empower patients

— Measure 4: Create a national portal website with validated, up-to-date information

— Measure 5: Support for Orphanet Belgium

Informing, raising the awareness of and empowering patients, health care workers and the general public are some of the most important conditions governing the success of the Belgian Rare Diseases Plan. Consequently, it is necessary to set up a centralised information system for rare diseases. This can be done via a portal site that is easily accessible to patients, professionals and laypeople. The information will be available in at least Dutch and French, and will be available to patient advocacy organisations. The portal site will supplement the basic information provided by Orphanet Europe and Orphanet Belgium.

Area 4. Access to and direct and indirect costs of diagnosis, medication, treatment and patient management

It is estimated that 2,000 people with a rare disease currently receive treatment with orphan drugs specifically for their disease. But for the vast majority of patients, treatment consists of drugs designed to alleviate their symptoms. Lastly, there are also patients for whom therapy is being developed.

The costs of diagnosis, treatment and general care are a heavy burden for patients and their families. Multiple measures must be introduced to change this situation.

— *Measure 6. Change the system to allow DNA samples – instead of patients themselves – to be tested abroad.*

At present, DNA tests abroad can only be reimbursed if patients themselves travel abroad. Measure 6 aims to ensure that DNA samples can be sent to specialist laboratories abroad and that patients can receive appropriate reimbursement.

— *Measure 7. A coordinated approach for non-DNA diagnostic tests*

There is little or no expertise in Belgium for carrying out tests for a number of very rare diseases. Nevertheless, more such testing will be necessary in the future. An inventory of tests which are available/unavailable in Belgium must be drawn up in order to prepare the measures that might be devised at a later stage in the Belgian Rare Diseases Plan.

— *Measure 8. Set up a system for early access, including early temporary reimbursement of orphan drugs*

— *Measure 8a. Belgium should play a leading role in boosting EU-level initiatives on early access*

As soon as a Marketing Authorisation Application (MMA) for an orphan drug is submitted to the European Medicines Agency EMA, patients must be able to benefit from early temporary reimbursement. This gives patients access to treatment an average of 18 to 24 months earlier than normal. This system also encourages the pharmaceutical industry to develop new molecules. Therefore it must also be encouraged at European level.

— *Measure 9. Ensure that raw materials for treating rare diseases can be used legally*

— *Measure 9a. Belgium should propose a change in the criteria used to grant 'orphan drug' designation when appropriate raw materials are available and used*

At present, certain non-approved raw materials are used in connection with a treatment. After analysis of these raw materials and the awarding of a certificate, it should be allowed to use them legally for treatment.

— *Measure 10. Produce a detailed inventory of off-label use of drugs for patients with rare diseases*

Patients with rare diseases sometimes use drugs in ways that are not in line with the approved indications (this is known as 'off-label' use). An inventory of such drugs makes it possible to prepare relevant measures.

— *Measure 11. Support home treatment with orphan drugs under clear conditions*

This measure is designed to improve patient compliance and quality of life.

A Plan in development

Various measures proposed in Phase I of the Belgian Rare Diseases Plan will be followed up in Phase II. In Phase II, measures will be developed to improve the situation and education of patients, encourage research, promote training for professional health care workers, and help foster the creation of national and international networking.

Impact of the proposed measures

The implementation of the above measures for Phase I of the Belgian Rare Diseases Plan will have a significant impact on the estimated 15,000 patients with a rare disease who will be newly diagnosed during the first 5 years, and on the quality of life of patients already diagnosed.

If the proposed measures are successfully implemented, this will – in addition to various savings – generate an extra health insurance cost estimated at between €9 million (during the first year) to €30 million per year (after 5 years, most successfully scenario). Such expenditure will be linked mainly to the Centres of Expertise. The implementation of the Belgian Rare Diseases Plan also implies a budget of around €1 million for the costs of running it, setting up international networks, communication and evaluation.

THE BELGIAN PLAN FOR RARE DISEASES … IN A NUTSHELL

Objectives and ambition of the Belgian Plan

1. Main objectives:
   - increase the rate at which patients with a rare disease are diagnosed
   - increase the quality of the care (medical and non-medical) patients receive
   - stimulate the development of and access to new treatments (better than existing, or new for those diseases where no treatment exist)
   - increase the knowledge base on rare diseases
   - improve the quality of life of patients and families

2. Additional objectives:
   - create higher awareness among all stakeholders, which should lead to faster diagnosis and increase access to expertise
   - identify and concentrate expertise
   - identify patients and create links with experts
   - ensure treatments are performed according to best practice principles
   - ensure patient management is performed in multidisciplinary environments (as a condition for high quality)
   - create the conditions to set up clinical trials for innovative treatments
   - adapt the administrative processes to get adequate social and financial support from public instances

3. Supporting objectives:
   - organise links between all stakeholders at national level
   - organise links between the Belgian RD system and other countries (avoid duplication, ensure contribution by Belgium to international initiatives and tools)

An integrated and comprehensive plan

4. A national Plan consists of a set of integrated and comprehensive health policy actions for rare diseases to be developed and implemented at national level.[1] The Belgian Plan has well specified objectives and actions to be supported by a budget, implemented within a time frame, and evaluated with specific indicators.

'Integrated' refers to the fact that strategies should be developed in such a way as to identify complementarities, maximise synergies and avoid duplications. 'Comprehensive' refers to the fact that the actions foreseen in the Plan should fulfil all main patients' needs (e.g. quality of care but also social services).

1 EUROPLAN, RD national plans recommendations, Draft December 2009.

Target population of the Plan

5. The target population of the Belgian Plan is every individual, of either gender, at any time of his/her life, affected by a rare disease, considered in the context of his/her family and the community at large, and independently from his/her disability level.
The organisation of service delivery (i.e. Centres of Expertise and Coordinating Centres for Rare Diseases) is aimed at improved diagnosis, treatment and management of patients suffering from rare diseases, *with special emphasis on ultra rare diseases, but excluding rare cancers*.
All other proposed measures are intended for all patients with rare diseases, including rare cancers.

6. Definition of a rare disease – Rare diseases, including those of genetic origin, are life-threatening or chronically debilitating diseases which are of such low prevalence that special combined efforts are needed to address them. As a guide, low prevalence is taken as prevalence of less than 5 per 10,000 in the Community.[2,3]
The definition of rare diseases includes genetic diseases, rare cancers, auto-immune diseases, congenital malformations, toxic and infectious diseases and others.

7. Definition of an orphan drug – An orphan drug is a medicinal product that is intended for the diagnosis, prevention or treatment of a rare disease (as defined above) for which there is no satisfactory Community-authorised method of diagnosis, prevention or treatment of the condition in question or, if such method exists, that will be of significant benefit to those affected by that condition.

8. While 5 in 10,000 seems very few, in a total population of 10,000,000 Belgian citizens, this could mean as many as 5,000 patients for a single disease. However, it is important to underline that the number of rare disease patients varies considerably from disease to disease, and that most rare diseases only affect a few dozen patients or sometimes even less. Often, the complexity of the disease increases with its rarity.

9. Orphanet and Eurordis estimate that between 6,000 and 8,000 distinct rare diseases exist today. However, not all diseases in the Orphanet list of rare diseases are life threatening or debilitating and other groups of patients with a rare disease are already diagnosed and treated according to high standards within the existing health care system. The (medical and other) needs of these patients for diagnosis and treatment with more expertise or special and dedicated treatment regimes is relatively low. Therefore these patients do not necessary fall under the scope of the new structures (i.e. the establishment of Centres of Expertise and Coordinating Centres for Rare Diseases) proposed in the Belgian Plan.

10. The exact number of patients and families who will benefit from this Plan is hard to estimate, as long as there are no formal registries for rare diseases. While the prevalence of congenital anomalies is about 3% of the newborns, those surviving and suffering from chronic severe and/or life threatening rare diseases can be roughly estimated at between 60,000 and 100,000 patients in the total population of Belgium. This is likely to be the size of the target population of the Belgian Plan for Rare Diseases.

2 *Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 'On orphan medicinal products'.*

3 *Useful information on rare diseases from an EU perspective, European Commission Health & consumer protection directorate-general, http://ec.europa.eu/health/ph_information/documents/ev20040705_rd05_en.pdf*

11. The Plan aims to treat 10,000 to 15,000 patients with rare diseases – on top of the nearly 4,000 who are currently being treated in the existing reference centres (centres with an RIZIV/INAMI contract) – in dedicated Centres of Expertise and Coordinating Centres for Rare Diseases during the first 5 years of its implementation.

Eight areas – two phases – 11 measures in phase I

12. The Belgian Plan for Rare Diseases is divided in two stages: the current phase will focus on areas for which early implementation of policy actions is possible. The second stage of the Plan is due to launch in mid-2011.

13. The first phase of the Belgian Plan will focus on four action areas:

- Area 1 – Diagnose and treat with expertise in order to improve patient outcome
  - — Measure 1: Create Centres of Expertise and Coordinating Centres for Rare Diseases
  - — Measure 2: Create a National Platform for Rare Diseases

- Area 2 – Codify and inventory rare diseases
  - — Measure 3: Create (a) central patient registry(ies) for rare diseases

- Area 3 – Increase awareness, inform stakeholders and empower patients
  - — Measure 4: Create a national portal website for rare diseases
  - — Measure 5: Support for Orphanet Belgium and (partial) translation of Orphanet in Dutch

- Area 4 – Access to and direct and indirect costs of diagnosis, medication, treatment and patient management
  - — Measure 6: Change the system to allow DNA samples – instead of patients themselves – to be tested abroad
  - — Measure 7: Organise a coordinated approach for non-DNA diagnostic testing
  - — Measure 8: Set up a system for early access, including early temporary reimbursement of orphan drugs
  - — Measure 9: Ensure that raw materials for treating rare diseases can be used legally
  - — Measure 10: Produce a detailed inventory of off-label use of drugs for patients with rare diseases
  - — Measure 11: Support home treatment with orphan drugs under clear conditions

14. Phase two of the Belgian Plan will focus on policy actions within these 4 areas for implementation at a later stage and on other areas, including (but not limited to):

- Area 5 – Status of the patient with a rare disease
- Area 6 – Research on rare diseases
- Area 7 – National and international networking
- Area 8 – Education and training of health professionals

A detailed overview of actions in phase II is described in the chapter entitled 'Preliminary agenda of Phase II of the Belgian Plan'.

LOOKING AFTER THE VULNERABLE …STATUS OF RARE DISEASES IN BELGIUM

15. Currently, people affected by a rare disease cannot rely on a coherent strategy for care and support. Due to the rarity of their conditions, health professionals often have limited or no experience in diagnosing, supporting and treating them. If appropriate services are existing, lack of communication, coordination and familiarity often makes these services hard to access for patients and their relatives. Moreover, some conditions occur so infrequently that the cost of developing and bringing to market a medicinal product to diagnose, prevent or treat the condition would not be recovered by the expected sales of the medicinal product. Under normal market conditions the pharmaceutical industry would be unwilling to develop medicinal products for rare diseases.[4]

Characteristics of rare diseases [5]

Rare diseases are characterised by a broad diversity of disorders and symptoms that vary not only from disease to disease but also from patient to patient suffering from the same disease. Relatively common symptoms can hide underlying rare diseases, leading to misdiagnosis.

- *Rare diseases are often chronic, progressive, degenerative, and life-threatening*
- *Rare diseases are disabling: the quality of life of patients is often compromised by the lack or loss of autonomy*
- *High level of pain and suffering for the patient and his/ her family*
- *Often there is no existing effective cure*
- *There are between 6,000 and 8,000 rare diseases*
- *75% of rare diseases affect children*
- *30% of rare disease patients die before the age of 5*
- *80% of rare diseases have identified genetic origins. Other rare diseases are the result of infections (bacterial or viral), allergies and environmental causes, or are degenerative and proliferative.*

4 *Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 'On orphan medicinal products'.*

5 *Characteristics of rare diseases, website of Eurordis, http://www.eurordis.org/content/what-rare-disease*

16. Several organisations [6] [7] [8] [9] have investigated the needs of Belgian patients with a rare disease (and their families) and the difficulties they experience. Summarised, these needs fall into the following categories:

- **more knowledge and recognition** – rare diseases are not recognised by doctors; scientific knowledge is often limited or non-existent; societal recognition is low, etc.
- **faster diagnosis and better information** – delayed and incorrect diagnosis; lack of specialised diagnostic centres or no timely referral to such centres; unequal and limited neonatal screening in Belgium; etc.
- **better access to high-quality treatment and organisation of the care system** – lack of centres of expertise; low cooperation between various health care providers; deficient availability of new medicines, paramedical and psycho-social care; etc.
- **lower costs of diagnosis and treatment** – price of orphan drugs and specialised medical devices; high costs for other medication (incl. D-medication) and cosmetics; social costs (disability and labour); hidden costs; etc.
- **lack of epidemiological data and registration of patients**
- **status of the patient with a rare disease** – difficulties with administrative status; reduction of educational, professional and social opportunities; isolation and social exclusion; limited support for patient advocacy organisations; etc.

Need for diagnosis and treatment in multidisciplinary expert centres

17. Belgium has a number of centres which deal with rare disease patients. These consist of 8 Centres for Human Genetics and 25 multidisciplinary reference centres dispersed over 13 different locations: 6 centres for neuromuscular disorders, 7 centres for cystic fibrosis, 4 centres for refractive epilepsy and 8 centres for hereditary metabolic diseases. The latter 25 centres have a contract with RIZIV/INAMI.

18. Apart from these reference centres, expertise on rare diseases is available in many Belgian university and peripheral hospitals, but the expertise is not well known to the public or to general practitioners, the departments within these hospitals may not interact amongst themselves or with similar expert centres in Belgium or abroad, and many of the services are fragmented, lack structure and official recognition. As a result, patients may lose many crucial years before being diagnosed or treated. Furthermore, regionalisation of the neonatal screening has resulted in different approaches in the regions and different procedures for monitoring the identified families.

6 *Knelpuntennota Zeldzame Aandoeningen, Vlaams Patiëntenplatform.*

7 *Website of the Rare Diseases Organisation Belgium, www.RaDiOrg.be*

8 *The Voice of 12,000 Patients: Experiences & Expectations of Rare Disease Patients on Diagnosis & Care in Europe, Results by Country, Belgium, Eurordis.*

9 *Rare diseases and patients need, VPP, LUSS, Radiorg, presented by Claude Sterckx and Lut De Baere.*

The diagnosis battle [10]

- *Before obtaining the correct diagnosis, another diagnosis was given to 44% of Belgian patients with a rare disease resulting in inappropriate treatments in 75% of patients, including medical (36%), surgical (12%) and psychological or psychiatric (7%).*
- *For 78% of Belgian rare disease patients, delays in diagnosis were considered responsible for at least one deleterious consequence, including death (1%); cognitive, psychological or physical problems, birth of another affected child, inappropriate lifestyle and behaviour, lack of confidence in medicine.*
- *During the quest for diagnosis, 22% of Belgian rare disease patients consulted more than five physicians before receiving the correct diagnosis, 7% consulted more than ten physicians.*
- *Diagnosis is expensive for Belgian patients and is rarely free (14% compared to 54% overall in Europe).*
- *A total of 22% of Belgian respondents obtained their diagnosis without receiving complete information on the disease. No psychological support was received by 60% of patients (which is low compared to 91% of respondents who expected this type of support but still represents the best value in the survey).*
- *The genetic nature of the disease was explained to families in 88% of cases, with details about the possibility of other cases in the family in 67% of cases. Genetic advice resulted in the diagnosis or identification of a carrier in the family in 36% of cases. A total of 30% of Belgian families considered the conditions of the announcement to be poor or unacceptable.*
- *In Europe 1 out of 4 patients with Ehlers Danlos syndrome waited for more than thirty years before being given the right diagnosis.*

The medical need [11]

- *Belgian patients need an average of 9.5 different kinds of medical services related to their disease.*
- *Hospitalisation occurred in 47% of patients for an average total duration of 20 days in recent years.*
- *Access to eight services considered essential for each disease was easy in 77% of cases and difficult in 12% of cases and impossible in 11% of cases. This was mainly due to lack of referral (53%), unavailability (18%), personal cost (10%) and location of the structures, including a location too far away (13%), no one to go with (12%) and difficulty in travelling (15%).*
- *The medical services responded to patients' expectations fully (61%) or partially (27%), poorly (9%) or not at all (3%), which were comparable to overall results elsewhere in Europe.*

10 *The Voice of 12,000 Patients: Experiences & Expectations of Rare Disease Patients on Diagnosis & Care in Europe, Results by Country, Belgium, Eurordis.*

11 *The Voice of 12,000 Patients: Experiences & Expectations of Rare Disease Patients on Diagnosis & Care in Europe, Results by Country, Belgium, Eurordis.*

Need for European networking

19. The establishment of Centres of Expertise for rare diseases in member states of the EU should coincide with the roll-out of a European network of dedicated centres for rare diseases. It is unrealistic to imagine that each country will have a Centre of Expertise for each of the rare diseases. As such, further collaboration at European level in rare disease patient care is necessary and Europlan recommends, citing the Council recommendation, 'fostering the participation of CE in the European reference networks respecting the national competences and rules with regard to their authorisation and recognition'.

Need for research

20. The expert centres should foster biomedical (fundamental, translational and clinical) and other research into rare diseases. In Europe, research into rare diseases is too scarce, too scattered and lacks funding. It should be a priority area for public funding, and the Council recommendation on rare diseases indicates the need for research at national, European and international level through collaboration programmes. Research in the field of rare diseases requires more international collaboration and coordination than research into common diseases, and multicentre studies are needed in order to reach a critical mass of patients for clinical trials and adequate numbers of biological samples.

In comparison with other countries, national measures to promote research on orphan drugs are relatively limited in Belgium. FRS-FNRS is a partner in E-Rare (ERA-Net for research programmes on rare diseases)[12], but otherwise no formal research or support programmes are developed, as is the case in France, Italy and the Netherlands.[13]

Need for patient registration

21. The available epidemiological data on most rare diseases are inadequate to give firm details on the number of patients with a specific rare disease. One of the main problems in planning healthcare and social care for patients with rare diseases is that the burden of most of these diseases is invisible to the health systems, due to misclassification and the lack of appropriate coding. Furthermore registries can form the cornerstone for more scientific research on rare diseases.

12 http://www.e-rare.eu/The-Project/The-Project.html

13 *Policies for Orphan Diseases and Orphan Drugs, Belgian Health Care Knowledge Centre, 2009.* http://www.kce.fgov.be/index_en.aspx?SGREF=13035&CREF=13647

Belgian rare disease registries

Belgium does not have a central registry for patients with rare diseases. Some smaller databases and registries have been set up by individual researchers or centres. On the Orphanet website 19 Belgian rare disease registries (or contributions to international registries) are listed.[14] Other, larger and more institutionalised registries – i.e. the cancer registry or the CF registry – could serve as examples for a more centralised registry. The current Belgian registries mentioned on Orphanet are:

- *ACROBEL: the Belgian registry for acromegaly, epidemiology and quality of care*
- *Antwerp registry of congenital anomalies – contributes to the EUROCAT network*
- *Belgian alpha-1 antitrypsin deficiency registry – contributes to the Alpha One International Registry (AIR)*
- *Belgian cystic fibrosis patient registry (BMR-RBM) – contributes to the EUROCARE CF and the ECFS registries*
- *Belgian familial adenomatous polyposis registry*
- *Belgian patient database for Wilson disease – contributes to the EuroWilson registry*
- *Belgian patient registry for neuromuscular diseases*
- *Belgian patient registry for rare bleeding disorders – contributes to the RBDD international registry*
- *Belgian registry of primary immunodeficiencies – contributes to the ESID European registry*
- *Belgian rituximab therapy registry for immune anaemia and thrombocytopenia*
- *Belgian severe chronic neutropenia patient registry – contributes to the SCN international registry (SCNIR)*
- *Belgian sickle cell anaemia registry*
- *Belgian systemic sclerosis cohort*
- *ENRAH – Belgian contribution to European registry for first phase alternating hemiplegia in childhood*
- *EUNEFRON – registry of the European network for the study of orphan nephropathies*
- *EURECHINOREG – Belgian contribution to the European registry of human alveolar echinococcosis*
- *Hainault and Namur registry of congenital anomalies – contributes to the EUROCAT network*
- *LCH: Belgian Langerhans cell histiocytosis registry*

Need for centralised and validated information sources and for support for patient advocacy organisations

22. Patients with rare diseases and their families experience major difficulties in getting information and finding their way within the healthcare and social security system. Similarly, healthcare professionals facing rare diseases do not have easy access to information, and available information is scattered and scarce, with lack of guidelines and validated evidence.

14 *Patient registries in Europe, October 2009, Orphanet.*

23. Orphanet[15], the most relevant international E-information tool on rare diseases is represented in Belgium. Orphanet includes information aimed at health professionals, patients and society at large. As such Orphanet constitutes the reference source for ongoing rare disease initiatives, research, clinical trials, guidelines and orphan drugs. Orphanet data are accessible in 5 languages (including French and English) but not Dutch.

24. Close to 150 specific patient advocacy organisations are currently active in Belgium on the topic of rare diseases.[16] A number of these associations have websites. Some belong to regional platform organisations like the Vlaams Patiëntenplatform (VPP)[17] and the Ligue des Usagers des Services de Santé (LUSS).[18] The Rare Diseases Organisation Belgium (RaDiOrg)[19] was founded in January 2008. RaDiOrg is a coordinating alliance of approximately 80 specific patient advocacy organisations and is the official representative of Eurordis[20] in Belgium. Its mission is to increase public awareness of the existence of patients with a rare disease, to enhance the quality of care, to inform the patient and his/her relatives, to provide social support for patients and to stimulate research into the aetiology and treatment of these diseases. RaDiOrg created a web site to encourage the dissemination of information on rare diseases in Belgium. Under the High Protection of Her Royal Highness Princess Astrid RaDiOrg organises the yearly Rare Disease Day (end of February).

Need for accessible and payable medication and treatment

25. Pharmaceutical treatments for rare diseases are less likely to be produced by private companies because the market is small. Both in the US and in the European Union incentives have been created to promote research and development on orphan drugs. To qualify for the special regulatory arrangements for orphan drugs, a drug has to obtain orphan status through the orphan designation procedure at EMA, the European Medicines Agency. Afterwards, when the drug is ready for release onto the market, marketing authorisation can be requested through the centralised procedure at the EMA. Between 2000 and March 2010 more than 725 medicinal products under development received European orphan drug status[21], 58 received marketing authorisation[22]. About 30% of these were in the field of oncology and 27% in the field of endocrinology and metabolic disorders. With only a few dozen orphan drugs available, only a small part of the need for treatment of rare diseases is covered.

26. Each EU member state negotiates pricing separately with the pharmaceutical companies. Despite the incentives developing and registering orphan drugs, access to orphan drugs in the EU member states varies widely. Delays in the availability of orphan drugs have been reported in different member states, with countries with smaller populations usually suffering the longest delays.

15 *The portal for rare diseases and orphan drugs, www.orpha.net*

16 *Information from RaDiOrg and Orphanet, www.radiorg.be/onze-leden/organisaties, consulted on 2 December 2009.*

17 *www.vlaamspatientenplatform.be*

18 *www.luss.be*

19 *www.radiorg.be*

20 *www.eurordis.org*

21 *http://ec.europa.eu/enterprise/sectors/pharmaceuticals/documents/community-register/html/orphreg.htm, consulted on 19 March 2010.*

22 *Orphanet Report Series – List of Orphan Drugs in Europe, January 2010, http://www.orpha.net/orphacom/cahiers/docs/GB/list_of_orphan_drugs_in_europe.pdf*

27. Reimbursement of orphan drug is a particularly difficult topic. Given the increasing number of orphan drugs and the high costs of orphan drugs, budgets spent to orphan drugs continue to increase. This increasing cost creates an additional upward pressure on health care budgets and may challenge the limits of solidarity between citizens. Especially since health economic evaluations using standard methods (i.e. incremental cost effective ratio – ICER) usually find that orphan drugs are hardly cost-effective. On the other hand the ethical and social dimension of orphan disease treatment has to be recognised and addressed.

28. For many rare diseases, no specific pharmaceutical treatment exists at this time so that access to certain non-pharmaceutical medical and paramedical services and products, including devices, is important. Access to these services and products should be optimised as well.

Orphan drugs in Belgium

Regulation and orphan drug reimbursement decisions at Belgian level are taken by the Minister for Public Health and Social Affairs, pursuant to receiving advice from the Drug Reimbursement Committee (DRC), the Finance inspector and approval by the Minister for the Budget. Orphan drugs follow the same procedure as Class I pharmaceutical products, i.e. products for which the company claims a therapeutic added value. However, unlike for Class I pharmaceutical products, no pharmacoeconomic evaluation has to be submitted for orphan drugs.

Budget

NIHDI expenditure on orphan drugs in Belgium is estimated to have been about €66 million or over 5% of total hospital drug budget in 2008 and further estimates indicate the future cost will be well above 10% of hospital drug budget five years from now. Orphan drugs account for probably 2% of total drug reimbursement expenditures by NIHDI in 2009, and are estimated to represent close to 4% in 2013.[23] As of March 2010 the Belgian NIHDI reimburses 37 orphan drugs.[24]

Prescription and reimbursement

In Belgium prescription of orphan medication is the exclusive responsibility of a specialist physician. The prescription and individual reimbursement of orphan drugs is subject to conditions. The treating specialist physician must first obtain the approval of a Medical Advisor of the patient's sickness fund to prescribe the medicine. The Medical Advisor can, but is not obliged to, request the advice of the College of Medical Doctors for Orphan Drugs (CMDOD). In practice, all sickness funds have agreed to refer all requests to the CMDOD. Separate sub-Colleges exist for separate products. It is the DRC that decides whether or not such a sub-College is to be established. Individual reimbursement decisions are taken on a case by case basis by the CMDOD.[25] On December 1, 2009, there were 20 colleges for 20 orphan drugs (see table).[26]

Compassionate use, medical need, solidarity fund

If a medicinal product is not yet on the Belgian list of reimbursed pharmaceutical products, the patient may be able to benefit from a compassionate use or medical need programmes by the company or in case the drug is already available on the market, request reimbursement through the Special Solidarity Fund (SSF). Conditions for compassionate use or reimbursement through the SSF are defined by law. In 2007, orphan drugs accounted for about 35% of the SSF's total budget.[27]

The functioning and the efficiency of the Special Solidarity Fund – does the fund enable all social security affiliates to access necessary care and related financial coverage? – was assessed by the Belgian Health Care Knowledge Centre.[28]

Distribution

In Belgium orphan drugs are distributed through hospital pharmacies only. In some other countries orphan drugs can also be delivered through community pharmacies.

Need for clarification of the status of the patient

29. Major and arbitrary disparities exist in the allocation of financial aid, income support and reimbursement of medical costs patients receive. Treatment costs for rare diseases are often high. A significant proportion of these expenses is born by the families, generating potential inequalities. Travel costs to specialised centres are high in terms of time off work and financial cost.

30. It is also important to underline that, in a family where a child has a rare disease, most often one of the parents – usually the mother – either completely stops or significantly reduces work remunerated outside home. As a consequence, while expenses increase dramatically, income is considerably reduced. In the case of an adult rare disease patient who is well enough to be able to work, working hours must be adapted to allow for medical visits and appropriate care. In terms of logistics, much remains to be done to ensure real equality between a disabled and a healthy citizen.

31. The social aspects and implications of rare diseases must also be kept in mind: services to support families and patients have to be organised and developed. These include day care services, respite centres, emergency units, socialisation and rehabilitation centres, summer camps, education services and professional training. The problems that arise when the life-long carer and/or parent of a rare disease patient dies or can otherwise no longer fulfil that role have to be tackled and brought to the attention of national and European decision-makers. Current experiences in this field have to be evaluated and valid organisational and managerial models defined. It should be stressed that the challenges and problems in relation to social services last for the whole life of a rare disease patient and become so important that medical aspects of the disease can be given second-line priority.

23 *Policies for Orphan Diseases and Orphan Drugs, Belgian Health Care Knowledge Centre, 2009.* *http://www.kce.fgov.be/index_en.aspx?SGREF=13035&CREF=13647*

24 *List of reimbursed orphan drugs, http://www.inami.fgov.be/inami_prd/ssp/cns2/pages/OrphanCns.asp*

25 *http://www.riziv.fgov.be/drug/nl/drugs/orphan_drugs/colleges.htm#3*

26 *List of reimbursed orphan drugs with college,* *http://www.inami.fgov.be/inami_prd/ssp/cns2/pages/OrphanCns.asp?qs_MnuTypSea=3*

27 *Policies for Orphan Diseases and Orphan Drugs, Belgian Health Care Knowledge Centre, 2009.* *http://www.kce.fgov.be/index_en.aspx?SGREF=13035&CREF=13647*

28 *http://www.kce.fgov.be/index_en.aspx?SGREF=5219&CREF=16778*

Social needs of Belgian patients

Two patient platforms (VPP and LUSS) assessed the needs of patients with rare diseases, including their social needs and hidden costs.[29] Recently, Ms. Onkelinx, Minister for Social Affairs and Public Health, conducted a similar inquiry for chronic diseases through their representative patient advocacy organisations. In addition, Eurordis assessed social services for patients with rare diseases in Belgium by surveying patients and their families.[30] Information on social services was collected for eight different diseases with a total of 255 families responding:

- *Amongst the 48% of families that required social assistance, 1% failed to meet with a social worker, whereas 78% met with one easily and 22% with difficulty.*
- *Compared to the European situation, such assistance was provided more frequently by associative and insurance structures, with 60% of Belgians being satisfied with assistance and 16% not at all satisfied.*
- *As a consequence of the disease, 14% of Belgian patients had to move house. Of these, families most frequently moved to a more suitable house (58%), but also to be nearer to disease specialists (12%) or to be closer to a relative (19%).*
- *As a consequence of their disease, 36% of patients had to reduce or stop their professional activity. In 26% of cases one member of the family had to stop work to take care of a relative.*

On September 23, 2008, Ms. Laurette Onkelinx, Minister of Social Affairs and Public Health, announced a Belgian National Plan to improve the quality of life of patients with a chronic disease.[31] This plan includes action areas such as 'administrative simplification for persons with a chronic disease' and 'integration of persons with a chronic disease into an active social life'. These initiatives will also influence the status and the life of patients with rare disorders, which in most cases are also chronic disorders.

29 *VPP Knelpuntennota Zeldzame Aandoeningen and LUSS Costs of chronic diseases.*

30 *The Voice of 12,000 Patients: Experiences & Expectations of Rare Disease Patients on Diagnosis & Care in Europe, Results by Country, Belgium, Eurordis.*

31 *Prioriteit aan de chronisch zieken!, Programma voor de verbetering van de levenskwaliteit van personen met chronische ziekten, 2009-2010 – Priorité aux malades chroniques!, Programme pour l'amélioration de la qualité de vie des personnes atteintes d'affections chroniques, 2009-2010.*

THE CONTEXT OF THE BELGIAN PLAN FOR RARE DISEASES

International context

32. In past years, the work done at European level in the field of rare diseases and the experience of these countries where initiatives for rare diseases exist has shown that a global and specific national approach and European collaboration and common development of solutions are the key factors in improving the health and social care of patients with rare diseases. **The Commission Communication on rare diseases and the Recommendation from the European Council states that Member States should establish and implement plans and strategies for rare diseases by 2013[32] in order to improve equity of and access to prevention, diagnosis, treatment and rehabilitation for patients suffering from rare diseases**. It should defragment the current offer of services, enable patients and health professionals to provide and use best practice care, encourage research into novel diagnostic techniques and treatments, raise public and political awareness about rare diseases, and so on.

National context

33. On February 12, 2009 the Belgian House of Representatives adopted a resolution submitted by Yolande Avontroodt, Katia Della Faille, and Herman De Croo concerning 'an action plan on rare diseases and orphan drugs'[33].

34. The Fund Rare Diseases and Orphan Drugs, hosted by the King Baudouin Foundation[34] and bringing together the various stakeholders involved in all aspects of rare diseases as well as the development and availability of orphan drugs, was commissioned by Ms. Laurette Onkelinx, Minister for Social Affairs and Public Health to play a coordinating role in the establishment of a Belgian National Plan for Rare Diseases.

35. On September 23, 2008, Ms. Laurette Onkelinx, Minister for Social Affairs and Public Health announced a Belgian National Plan to improve the quality of life of patients with a chronic disease.[35] Most patients with a rare disease will benefit from the initiatives to be developed under this Plan. The National Plan for Rare Diseases will therefore also assess which measures, taken broadly for chronic disease patients, will benefit patients with a rare disease, and will propose specific measures for rare disease patients.

32 *Council Recommendation, on an action in the field of rare diseases (2009/C 151/02).*

33 *Voorstel van resolutie betreffende een actieplan inzake zeldzame aandoeningen en weesgeneesmiddelen, ingediend door de dames Yolande Avontroodt, Katia Della Faille en de heer Herman De Croo.*

34 www.weesziekten.be, www.maladiesrares.be

35 *Prioriteit aan de chronisch zieken!, Programma voor de verbetering van de levenskwaliteit van personen met chronische ziekten,*
2009-2010 – Priorité aux malades chroniques!, Programme pour l'amélioration de la qualité de vie des personnes atteintes d'affections chroniques, 2009-2010.

Area 1 – Diagnose and treat with expertise in order to improve patient outcome

The issues …

… delayed diagnosis

36. After the appearance of the first symptoms, the diagnosis of a rare disease can take from 5 up to 30 years. This delay is common for patients with a rare disease and can have tragic consequences. Diagnosis is the basis for appropriate health care and access to treatment. Several bottlenecks have been identified in the pathway leading to diagnosis of a rare disease, from the lack of recognition of symptoms by health care professionals to the limited availability of laboratory testing.[36] It is therefore an area where appropriate health care policies can make real changes.

… non-optimal treatment

37. After the diagnosis comes the fight to be heard, informed and directed towards competent medical bodies in order to get the most adequate existing treatment. For the vast majority of rare diseases, no protocol exists for good clinical practices. Where it does exist, the completeness of dissemination may not be optimal: not all healthcare professionals are always adequately trained, not all EU countries have adopted and shared the protocols. Additionally, the segmentation of medical specialities is a barrier to the multidisciplinary care needed by patients suffering from rare diseases.

The Plan – summary for Area 1

38. **Creation of Centres of Expertise and Coordinating Centres for Rare Diseases**

The creation of a limited number of high-quality medical bodies (Centres of Expertise and Coordinating Centres for Rare Diseases), at national or sub-national level, with up-to-date expertise in rare diseases is a critical condition for the provision of proper management of rare disease patients. These bodies should incorporate national capacities in medical expertise and establish the prerequisites for specific diagnosis, systematic research, optimal information transfer and competent patient care.

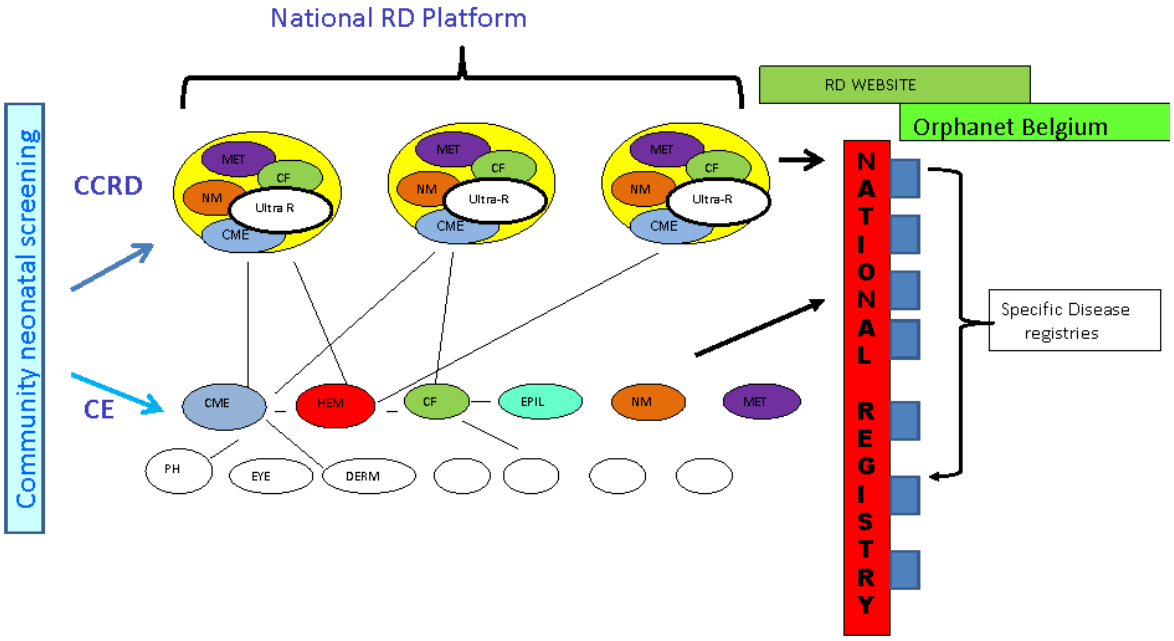
36 *EUROPLAN, RD national plans recommendations, Draft December 2009.*

39. **Creation of a National Platform for Rare Diseases**
Coordination and recognition of the Centres of Expertise and the Coordinating Centres for Rare Diseases can take place at the level of a National Platform for Rare Diseases. Furthermore, the Platform will interact with the partner who hosts the registry for rare diseases (see Area 2), Orphanet Belgium and the Belgian portal website on rare diseases (see Area 3), interact and network with organisations in Europe and worldwide, have links with neonatal screening centres, identify laboratories providing tests not available in Belgium, and interact with international parties involved in orphan drug development (EU, EMA, FDA, etc.) and other treatments, and so on.

Expert centres across Europe [37]

As of 2008, 132 Centres of Expertise for one or more rare diseases have been established in France. In the first term of the French National Plan the creation of these centres has proven to have a positive impact on patient satisfaction and to lead – in the opinion of patients – to better treatment and reimbursement mechanisms.
In Denmark, reference centres are selected by the National Board of Health after consultation with the learned societies, administrative authorities and patient advocacy organisations. In 2003, Rare Disorders Denmark carried out a survey of 900 rare disease patients. Those receiving care at a reference centre were more satisfied with their treatment overall.

37 *EUROPLAN, RD national plans recommendations, Draft December 2009.*

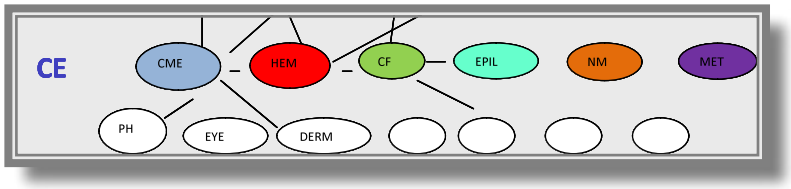


General concept – a triplicate structure

40. It is proposed that three structures be created: Centres of Expertise (CE), Coordinating Centres for Rare Diseases (CCRD) and a National Rare Disease Platform (NRDP). The CE and CCRD should fulfil several criteria to become certified.

Measure 1: Create Centres of Expertise and Coordinating Centres for Rare Diseases

Centres of Expertise



41. Centres of Expertise have expert clinical and scientific knowledge on a specific rare disease (e.g. cystic fibrosis) or on a group of rare diseases (e.g. neuromuscular diseases, metabolic diseases, genetic disorders). No Centres of Expertise are planned for rare cancers at this stage.
The tasks of Centres of Expertise are to develop, apply and promote current best practice diagnostic techniques and treatment and to develop new guidelines; to register patients in the national register; to refer to a Coordinating Centre for Rare Diseases all patients for whom the Centre of Expertise is not able to provide a diagnosis; to network with peripheral services (e.g. GP, peripheral specialist, home care, etc.) and with European expert centres; to teach and train physicians and paramedical personnel; to conduct scientific research (basic, translational, clinical) at international level; to interact on a structural basis with rare disease patient advocacy organisations and with the general public; and to report on their activities to and interact with the National Platform for Rare Diseases.

42. To become certified, Belgian or foreign Centres of Expertise need to fulfil a number of criteria. Some of the criteria are considered essential, others are optional/informative or should be developed during future evaluation rounds. The essential criteria imply:

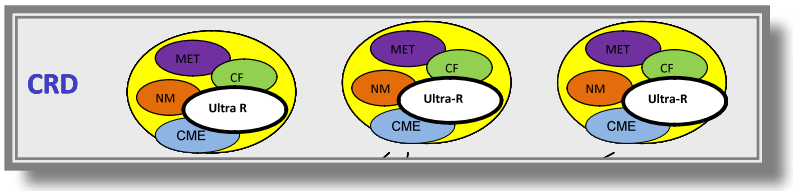
- The presence of national/international networking with other expertise centres (funded or not).
- The presence of basic/translational/clinical research concerning a specific (group of) rare disease(s). The last three years are taken into consideration.
- Conduct multidisciplinary consultations.
- Follow best practice guidelines, apply clinical pathways if possible and participate in the development of new ones.
- Have a minimal number (disease or group of disease specific) of hospitalised/ambulant patients treated by the centre.
- Have a minimal number of permanent FTE dedicated to the (group of) rare disease(s), averaged over the last three years.
- Be able to conduct specific diagnostic tests for the (group of) rare disease(s);
- Have a system in place for outcome measurement.
- The Centre of Expertise will maintain structured contacts with patient organisations.
- Publication citation score of the permanent staff in the expert team.
- Have a minimum number of medical doctors in training, attend a minimum number of specialised conferences, be a member of specialised international scientific societies.
- Register patients in the national registry, update the information on a regular basis and advise on the development of secondary platforms (see Area 2).

- Be involved in clinical studies for new medicines.
- Be involved in post-marketing surveillance of new diagnostic and therapeutic products and treatments.
- Be structurally involved in giving information and advice on rare diseases to the public (including patients and families) through some form of helpline, but not excluding patient advocacy organisations from providing such help for their specific disease or group of diseases (see Area 3).

A full list of proposed criteria is included as an addendum to the Belgian Plan.

43. Centres of Expertise should be re-evaluated on a regular basis (e.g. every five years). At certain times, new candidates can apply to become a Centre of Expertise. In principle, they can focus on (groups of) rare diseases for which there are already existing Centres of Expertise, as well as diseases which do not yet have such centres.

Coordinating Centres for Rare Diseases



44. The existence of a number of Centres of Expertise for specific rare diseases or groups of diseases will not in itself resolve the lack of sufficient early diagnosis for large groups of rare disease patients, especially those patients with an ultra-rare disease or with a disease for which there is no Centre of Expertise. These patients will benefit from centres which are able to provide a **Multidisciplinary Rare Disease Consultation (MRDC)**. For these types of consultations the establishment of Centres for Rare Diseases are proposed.

45. The Coordinating Centres for Rare Diseases will be composed of a number of Centres of Expertise. The Coordinating Centres for Rare Diseases function as an entry point into the system for rare disease patients who cannot be diagnosed at a Centre of Expertise.

46. Coordinating Centres for Rare Diseases perform a multidisciplinary and integrated evaluation of the patient's medical condition and should be able to accept any patient with an unknown or presumed diagnosis. Experts from the collaborating Centres of Expertise are closely involved in the multidisciplinary Rare Disease Consultation (MRDC). The MRDC is managed by a medical coordinator (e.g. an internist for an adult rare disease patient or a paediatrician for a child with a rare disease).

47. Once a diagnosis is definite, the patient should be referred to the appropriate Centre of Expertise, if available. The Coordinating Centre for Rare Diseases remains responsible for following up patients who do not get a final diagnosis, patients for whom there is no Centre of Expertise available and patients who are followed up and treated in a European Centre of Expertise outside Belgium. The Coordinating Centre for Rare Diseases should report annually on its activities to the National Platform.

48. Coordinating Centres for Rare Diseases share a number of tasks with their collaborating Centres of Expertise. These include registering and following up patients in the national registry, teaching and training physicians and paramedical personnel, interacting with rare disease patient advocacy organisations and the public, conducting research on rare diseases, and building national and international expertise networks.

49. To become certified, Coordinating Centres for Rare Diseases need to fulfil a number of criteria. Logically, many of the criteria for Coordinating Centres for Rare Diseases are the same as those for Centres of Expertise, because Coordinating Centres for Rare Diseases are composed of Centres of Expertise. But they will also fulfil other criteria:

- A CCRD will include a genetic centre and at least 3 Centres of Expertise.
- Organise a Multidisciplinary Rare Disease Consultation clinic with joint staff meetings.
- Form a national network with other Coordinating Centres for Rare Diseases, Centres of Expertise and engage in international networking with relevant expert centres.
- Conduct research into rare diseases (last 3 years taken in consideration).
- Procedures for rare diseases (e.g. clinical pathways) will represent at least 1/3 of the procedures implemented in the CCRD. The CCRD will develop new procedures for general multidisciplinary consultation.
- The CCRD will have a minimum number of hospitalised rare diseases patients and/or a minimum number of ambulant rare disease patients.
- A minimum number of FTE medical staff will be dedicated to rare diseases.
- Outcome measurements will be available.
- The CCRD will maintain structured contacts with patient organisations.
- It will present a total citation score of the team dedicated for rare diseases
- A number of medical doctors in training, attendance at conferences and membership of international scientific associations.
- The CCRD will use specific techniques and equipment to treat or diagnose patients.
- Be responsible for coordinating the inclusion of patients in the national registry and advise on the development of secondary platforms (see Area 2).
- Be involved in post-marketing surveillance of new diagnostic and therapeutic products and treatments.
- Be structurally involved in giving information and advice on rare diseases to the public (including patients and families) for example through a helpline for information, but not excluding patient advocacy organisations from providing such help for their specific disease or group of diseases (see Area 3)

A full list of proposed criteria is added as an addendum to the Belgian Plan.

50. To find a good balance between concentrating expertise in a truly multidisciplinary setting while avoiding fragmentation of resources on the one hand, and patient accessibility on the other hand, it is proposed that the number of Coordinating Centres for Rare Diseases be limited, but that at least one Coordinating Centre for Rare Diseases be recognised in each of the regions. Clearly, all recognised Centres should meet the criteria and should in the future endeavour to attain accreditation.

51. If Centres of Expertise perform according to expectations, it can be expected that Coordinating Centres for Rare Diseases will a) deal with a limited number of patients (see also budget impact calculation) and b) be able to focus their efforts on patients with ultra-rare diseases (i.e. patients who 'slip through the networks' of the Centres of Expertise).

Procedure for recognition of CE and CCRD

52. The certification of the Centres of Expertise and the Coordinating Centres for Rare Diseases is a shared national and regional responsibility. The drafting of the final list of criteria and standards for recognition and, in the longer term, the establishment of a certification and accreditation system falls under the responsibility of National Platform for Rare Diseases.

53. Existing reference centres who have a contract with RIZIV/INAMI, are expected to become Centres of Expertise under the same certification system.

Infrastructure, staffing and financing of Centres

54. In the current RIZIV/INAMI-contracted reference centres (i.e. neuromuscular disorders, metabolic disorders, cystic fibrosis) the principles governing financing are:

- medical acts are paid and reimbursed based on the nomenclature and excluded from the contract
- the contract covers the additional cost of multidisciplinarity and the cost of paramedical staff, both from the point of view of total care (diagnostics, treatment and follow-up of treatment) provided in essence at the centre; each contract therefore defines the type of paramedical staff the centres need to have and sets thresholds (e.g. one dietician per fixed number of patients for metabolic diseases).
- the contract covers a sum for individual patients that receive regular treatment (quarterly or annually); this sum is between €1,500 and €2,500 / patient / year on average (but actual average cost is lower)
- there is a threshold for the number of patients (25 or 50), which means that if a centre does not reach the threshold, the contract does not pay for any patient.

The three contracts together account for approximately 3,500 to 4,000 patients, and the cost to the health insurance system is probably €6 to €7 million.

55. Another model is the MOC or Multidisciplinary Oncological Consultation. This is reimbursed separately to ensure consensus-building among various disciplines before decisions are taken on an individual patient treatment. A similar approach could be used for the Multidisciplinary Rare Disease Consultation (MRDC). Such an approach would ensure that the additional costs carried by centres due to the multidisciplinary nature of the rare diseases are covered. However, it would not cover the costs of paramedical and non-medical staff.

56. The contract model seems adequate for the Centres of Expertise and the MRDC model could be envisaged for the Coordinating Centres for Rare Diseases. This conclusion is valid because under the present concept the Coordinating Centres for Rare Diseases would always be coupled with an institution that hosts at least one genetic centre and three Centres of Expertise. The Coordinating Centre for Rare Disease can therefore benefit from the critical mass of medical, paramedical and non-medical staff in the Centres of Expertise.

57. One other conclusion drawn from experience with contracts is that although the diseases are different, the average additional cost / patient / year is in a similar bracket (€1,500 to €2,500 / year). This gives an indication of the cost to be expected in future of setting up more Centres of Expertise.

Reimbursement of individual patients

58. Over time, once the Centres of Expertise and the Coordinating Centres for Rare Diseases are fully functional, the aim should be for all patients with a rare disease to be regularly followed up by such a Centre. These Centres are obliged to enter these patients in the National Registry for Rare Diseases (see Area 2). Entering patients into the National Registry is reserved exclusively for certified Centres of Expertise and Coordinating Centres for Rare Diseases. This procedure will give the authorities the opportunity to further streamline and facilitate the individual reimbursement of patients.

59. Furthermore, certified Coordinating Centres for Rare Diseases and Centres of Expertise should set up treatment guidelines for each rare disease and should coordinate individual treatment plans. Ideally, patients should be treated/monitored according to current best practices and along the lines of a treatment plan or healthcare pathway – at least if best practice treatment/monitored plans exist for a specific condition. Patients should regularly be evaluated – at least once a year – by such an appropriate Centre. Coordinating Centres for Rare Diseases and Centres of Expertise should collaborate with peripheral hospitals, specialists, GPs and paramedical treatment providers for the patient's day-to-day care.

60. During the decision-making process on reimbursement of an orphan drug by the competent authorities (i.e. the Commission for the Reimbursement of Medicines), expert involvement from the relevant stakeholders in working out national, transparent, specific reimbursement criteria for each orphan drug, thus harmonising orphan drug reimbursement for patients in Belgium, could be channelled through the National Platform for Rare Diseases. The decision to treat a patient based on these criteria would then over time be left up to the relevant Centre of Expertise or the Coordinating Centre for Rare Diseases, within the compensation terms set out by the Commission.

Impact of measure 1 on patients, other stakeholders and the budget

61. Impact on patients

The creation of a network of CE and CCRD has various impacts but the main impacts are at the level of

- Faster and more correct diagnosis.
- Better treatment (most adequate, higher compliance rates, etc.), resulting in longer (career) life, better quality of life for patients and for their relatives.
- Integrated patient care in a multidisciplinary environment, including paramedical and psychosocial expertise.

62. Impact on other stakeholders

GPs and local specialists will be able to identify the appropriate healthcare resource for their case easier, will have structural access to expert opinions, and will get involved in the application of treatment plans and clinical pathways.

Policymakers will be able to better allocate financial resources. Furthermore, several studies, including studies from the Belgian KCE, have demonstrated that the concentration of expertise leads to better healthcare for difficult conditions – like rare diseases.

63. Impact on the health insurance budget
The impact on the budget of the health insurance is difficult to estimate due to the diversity of diseases, the fact that the system will lead to savings (unnecessary costs of diagnosis and treatment will be saved), but also to additional costs (for instance, patients will live longer). Based on the experience of the reference centres as they exist today one can estimate an average additional cost per patient per year of €2,000. If the plan works adequately, one can expect that after 2 years of the existence of the CE, approximately 5,000 (additional) patients will have been diagnosed and will be treated annually in the network of CE and CCRD, leading to an additional cost of €10 million/year.

Measure 2: Create a National Platform for Rare Diseases

64. It is proposed that the National Platform for Rare Diseases function as a separate and autonomous body (e.g. based on the model of the National Cancer Centre or similar). It will be composed of representatives of relevant stakeholders involved in rare diseases. The current Management Committee of the Fund for Rare Diseases and Orphan Drugs, which currently has representatives of all relevant stakeholders, could form the core of the National Platform.

65. The National Platform for Rare Diseases will be involved in drafting the final list of quality criteria for all medical bodies involved in rare diseases and in implementing f the procedures for certification, review and evaluation of the Centres of Expertise and the Coordinating Centres for Rare Diseases, it will harmonise diagnostic procedures and best practice treatment.
Furthermore, the Platform should interact with the partner who will host the registry for rare diseases (see Area 2), Orphanet Belgium and the Belgian portal website on rare diseases (see Area 3), interact and network with organisations in Europe and worldwide, identify laboratories providing tests not available in Belgium, interact with international parties involved in orphan drug development (EU, EMA, FDA, etc.), and more.

66. The National Platform will also interact with neonatal screening centres since such centres are a corner-stone in the early screening and detection of many rare disease patients. However, the members of the Fund for Rare Diseases and Orphan Drugs take notice of the unequal screening, as is currently the case in the two regions of Belgium. It calls upon the agencies in question to coordinate their efforts and to come up with an equal screening procedure based on evidence-based criteria and performed in reference centres selected on the basis of quality and cost indicators, in accordance with international standards; guidelines and criteria.

67. The National Platform for Rare Diseases can create specific working groups of experts and stakeholders with dedicated tasks.

Impact of measure 2 on patients, other stakeholders and the budget

68. The major impact of measure 2 on patients and other stakeholders is that they will have an officially recognised steering platform which will deal with all aspects of rare diseases.

69. In order to be fully operational, it is proposed that two types of costs be earmarked for the National Platform: the salary of a permanent secretary of the National Platform and a budget to cover the costs of logistics and international networking. The total amount is estimated at €250,000/year.

Area 2 – Codification and inventory of rare diseases

The issues ...

... inadequate epidemiological information

70. The available epidemiological data on most rare diseases are inadequate to give firm details on the number of patients with a specific rare disease. In general, people with a rare disease are not registered in databases. Many rare diseases are summed up as 'other endocrine and metabolic disorders' and, consequently, it is difficult to register people with a rare disease on a national or international basis, or in a reliable, harmonised way.[38] One of the main problems in planning healthcare and social care for patients with rare diseases is that the burden of most of these diseases is invisible to the health systems, due to misclassification and the lack of appropriate coding.

The plan – summary of Area 2

71. In order to make epidemiologic surveillance of rare diseases possible, a National Registry for Rare Diseases should be created, supported and funded. In the first phase the main aim of this registry is to provide an indication of the number of people suffering from a specific rare disease in Belgium and an indication of which centres of expertise are dealing with how many rare disease patients. The registry should also be able to trace back the patients through the registering physician in case of new fundamental research, trials or therapies.

Measure 3: Create a National Registry for Rare Diseases

Master platform – phase I

72. The first phase of the Belgian Plan for Rare Diseases focus will be on the establishment of a general database for all rare diseases which will serve as a master platform. In the current proposal the master database will contain 14 variables. These 14 variables are common to all rare diseases. The proposed variables are:

- Unique patient code (generated by registry)
- Gender
- Age on 31 December
- Unique code of registering physician (RIZIV number)
- Unique code of the expert centre (RIZIV number)
- Unique identification number of the rare disease
- Age of onset of symptoms (national plan indicator)
- Age of diagnosis
- Postal code of residence
- Means of diagnosis confirmation (genetic, biochemical, histological)
- Additional social allowances
- Working regime (student, no work, part time, full time)
- Date of death (if applicable)
- Link to disease specific registries (if applicable)

In the second stage, existing and future disease-specific sub-platforms and databases will connect to this 'master' platform.

38 *Background paper on orphan diseases for the WHO Report on Priority Medicines for Europe and the World, October 2004.*

73. Patients should be registered at time of final diagnosis by a recognised Centre of Expertise or a Coordinating Centre for Rare Diseases. Further entries should take place at time of death and updated at regular intervals in between (at least every 2 years). The registration procedure should be web-based.
In addition, it should be discussed whether E-Health can be used as an entrance portal and as a third party for giving a unique patient code or whether the national portal website for rare diseases can function as an entry point.
Furthermore, collaboration with E-care vzw should be considered as well as with other registries in the EU and relevant European authorities (EU, EMA, etc.) (see also the chapter entitled 'Preliminary agenda of Phase II').

74. Patients have to give informed consent for registration. Registration of patients is an obligatory criterion for recognition and financing for the Centres of Expertise and the Centres for Rare Diseases. The database structure, access and content, the informed consent procedure, the registration protocols and study procedures will comply with Belgian and European legislation on privacy.

Disease coding and classification

75. In the database diseases will be coded and classified according to the (future) 11th revision of the International Classification of Diseases (ICD11).[39] Representatives of the European Rare Diseases Task Force are working, in conjunction with the World Health Organization (WHO), on a revision of the classification of rare diseases within the framework of ICD11. The process of revising the ICD was launched by the WHO in 2007 and the chair of the EU Rare Diseases Task Force was appointed as the Chair of the Topic Advisory Group on Rare Diseases. ICD 11 is due to take effect in 2014 but draft versions are expected to be available sooner.
In the mean time, the list of rare diseases published by Orphanet could be used as a reference, since it is the most comprehensive list developed today, regularly updated and forms the basis for the future ICD11 chapters on rare diseases.

Hosting and supervision of the database

76. The National Platform could subcontract the hosting of the registry to an appropriate scientific organisation. One such organisation could be the Belgian Scientific Institute of Public Health (WIV/ISP/IPH) because of its expertise in hosting the Belgian Cystic Fibrosis Registry (Belgisch Mucoviscidose Register – Registre Belge de la Mucoviscidose – BMR-RBM).

39 *Revision of the Internal Classification of Diseases, World Health Organisation, http://www.who.int/classifications/icd/ICDRevision/en/*

... an example: The Belgian Cystic Fibrosis (CF) registry [40]

The Cystic Fibrosis Registry falls within the framework of the 'CF Contract', a contract between the National Institute for Sickness and Invalidity Insurance (INAMI/RIZIV) and the Belgian CF reference centres (contracted centres) to optimise the quality of care of CF patients. The objectives of the CF registry are to collect annually epidemiological, medical and social data for as many CF patients as possible in Belgium; studying the epidemiological aspects of the disease; describing CF care in the contracted centres, with reporting, in order to advise INAMI/RIZIV on the CF contract; providing a database to be used in clinical, basic and epidemiological research; participating in European and international projects or registries (European Cystic Fibrosis Registry (ECFR))

Participation in the registry is mandatory for all Belgian contracted centres (in 2006 and 2007, N=7) but voluntary for individual registering physicians. All patients diagnosed with CF are included, after receiving their written consent. Patients are identified by a unique code (only known by the treating physician).

Future action – short term

77. Protocols and documents for informed consent have to be worked out further and a study protocol for approval by the privacy commission has to be prepared. Both already exist for cystic fibrosis.

Implementation

78. Phase 1 of Area 2 of this Plan should be implemented in the second half of 2010. The master platform is expected to be fully operational in 2011. Integration of disease-specific secondary platforms form part of the second phase of the Plan.

Impact of measure 3 on patients, other stakeholders and the budget

79. Impact on patients and other stakeholders.

Through the registry patients remain traceable and will no longer 'get lost' in the system. Registries are important tools for research, i.e. they enable researchers to monitor the natural course of the disease and they are indispensable tools for translational research and clinical trials. For policymakers, epidemiological data on rare diseases will become available, allowing better planning of appropriate healthcare and social care for patients, simplifying administrative processes and procedures, and enabling registries to deliver the necessary data for post-marketing surveillance (pharmacovigilance, clinical benefit, etc.) of orphan drugs, medical devices and other treatment options.

Running a central registry should also be considered a tool for linking existing or future registries for specific diseases.

80. As mentioned above, the IPH-WIV is one potential organisation for hosting the Registry. This institution has the expertise and has estimated the cost based on two factors: the number of variables and the potential number of patients.

40 http://www.iph.fgov.be/epidemio/epien/index20.htm

Comparing these two factors with the experience of running the registry for cystic fibrosis yields an investment budget (start-up) of below €25,000 and annual operating budget of up to €200,000.
This budget does not take into account the cost of data entry that would be decentralised in the CE and CCRD. This activity will need financing either by patient / entry (used for CF) or as part of the global financing of CE and CCRD (examples exist in contracts). Because of the limited number of patients and of variables, this cost is estimated at no more than 15% of the running cost of the registry.

Area 3 – Increase awareness, inform stakeholders and empower patients

The issues

81. Patients with rare diseases and their families experience major difficulties in getting information and finding their way around the healthcare system. Similarly, healthcare professionals facing rare diseases do not have easy access to information, and available information is scattered and scarce, with lack of guidelines and validated evidence.

82. When addressing the issue of patient involvement and partnership, it is universally accepted that 'experience witnesses' – in this case patients and their family members – can contribute considerably to the development of healthcare policy and the establishment of treatment guidelines. Patients are increasingly getting organised at EU, national and local level. We can only hope that public and private decision-makers are finally ready to invite patient representatives to join their ranks and that genuine recognition of patient expertise is a declared intention for all EU countries and not just pious lip-service.[41]

The Plan – summary of Area 3

83. In the area of increasing awareness about rare diseases, patient empowerment and information dissemination, one focal point will be the centralised availability of validated and updated information. Not only on the medical aspects of rare diseases, but on all aspects.
This is a daunting task, because information should be gathered, validated, and updated on up to 8,000 different diseases. In order to make this information continuously available to targeted audiences (patients, relatives, health care professionals, general public), this information source should be E-based (at least in first instance).
It is therefore proposed to start an official national portal website on rare diseases, to further support the Belgian contribution to Orphanet and to provide Dutch translation of all or part of Orphanet.

84. In addition, help lines and telephone information services have been developed in some member states, mostly on the initiative of the patients' associations.

85. In the second instance, the development of information and educational materials for patients (about compliance, empowerment, social and other benefits, etc.) and for specific target groups (e.g. teachers, social workers, etc.) should be considered, as well as ways to support general awareness of rare diseases through various activities, such as Rare Disease Day. In order to increase the empowerment of patients, the existence of specific associations that represent all rare disease patient associations should be promoted. Furthermore, the involvement of patients in decisions in the field of rare diseases, e.g. by consulting patients and patients' representatives on rare disease policies, should be improved and the activities performed by patients, such as awareness raising, capacity-building and training, exchange of information and best practices, networking, and outreach to very isolated patients to facilitate patient access to updated information on rare diseases should be supported.

41 http://www.eurordis.org/content/unity-and-empowerment-rare-disease-patients

Measure 4: Create a national portal website with validated, up-to-date information

86. Orphanet[42] could in theory provide the bulk of information on rare diseases, but there is no Dutch version and it will remain centrally managed and serviced from France. As such, very specific Belgian information (for example on reimbursement schemes, accessibility to orphan drugs and treatment, etc.) will not be found in Orphanet. Moreover, the user friendliness of Orphanet for patients and the general public has sometimes been questioned.
However, it is certainly not an option to replace Orphanet (see box further in the text) by a national Belgian website with similar content. Therefore, the suggestion has been made to set up a national portal website which provides various classes of users (patients, healthcare professionals, general public) with step-by-step information on specific rare diseases by providing links to validated existing information sources (including Orphanet).

87. The portal website should meet the following criteria:
- Be available in at least 2 languages (French, Dutch), possibly up to 4 languages (French, Dutch, German, English).
- Have a clear, user friendly structure, geared to specific target groups (patients, healthcare professionals, general public).
- Have an easy to use content management system.
- Link to validated sources of information (chronic disorders website, INAMI/RIZIV, Cancer Plan, etc.).
- Contain actual information on aspects of rare diseases not available on Ophanet.
- Patient advocacy organisations should be involved in the set up and the day-to-day management of the website.
- Should be an entrance point for the registry (protected access).
- Should ultimately develop into an extranet type communication platform between Centres of Expertise, Coordinating Centres for Rare Diseases and the National Platform.

Host organisations

88. The website should be hosted by an organisation which can adhere to the following conditions:
- Be able to guarantee continuity of the service;
- Be involved in rare diseases;
- Be located in Belgium and be familiar with the Belgian administrative and policy situation on rare diseases and orphan drugs;
- Be able to keep the information on the portal site actual in all of the languages (2 to 4);
- Keep in contact with all relevant stakeholders (Patient advocacy organisations, Centres of Expertise, Coordinating Centres for Rare Diseases, industry, administration, sickness funds, etc.) in order to gather validated information;
- Have the necessary qualified personnel, technical expertise and information sources;
- Be independent, autonomous and objective;
- Make a yearly report to the National Platform for Rare Diseases on the progress and activities;
- If service is stopped, all information and knowledge should be transferred at no cost to the successor.

42 www.orpha.net

89. The current proposal is that the portal website and Orphanet Belgium will be hosted by the Belgian Scientific Institute of Public Health, who is also a candidate to host the registry.

Help lines for rare diseases

90. Some EU member states have developed centralised help lines and telephone information services for rare diseases. Several of these initiatives have been evaluated (including Erfolijn (the Netherlands), Maladies Rares Info Services (France)). The conclusion is that the establishment and staffing of a permanent telephone help line is extremely expensive for relatively limited added value (e.g. in France €400,000/year).

91. The suggestion is that patients, relatives of patients and the general public can contact one of the Coordinating Centres for Rare Diseases or Centres of Expertise by e-mail or telephone if they have specific questions on rare diseases. The portal website can have a general e-mail address (e.g. *info@rarediseases.be*, *info@zeldzameziekten.be*, *info@maladiesrares.be*) which automatically refers questions to the Centres of Expertise or Coordinating Centres for Rare Diseases). This structural contact with patients and the public is one of the criteria to be recognised as a Coordinating Centre for Rare Diseases or Centre of Expertise.

92. Also the patient advocacy organisations have an important role to play in answering questions and organising companion contact. They are encouraged to organise structural communication on non-medical issues for patients, relatives and the general public.
Coordinating Centres for Rare Diseases/Centres of Expertise and patient advocacy organisations should inform patients, relatives and members of the general public about their specific roles.

Impact of measure 4 on patients, other stakeholders and the budget

93. Impact on patients and other stakeholders
Via the National Portal Website for Rare Diseases, patients, families and the general public have access to a centralised source of validated information on all aspects of rare diseases. Centres of Expertise/CCRD, the National Platform, governmental organisations involved with rare diseases and other stakeholders get a centralised medium to disperse information to patients and other target audiences.

94. The costs for the portal website (on the basis of two offers) can be estimated at:

- Initial website development €30,000
- Operational yearly cost (maintenance, debugging, updating and server hosting): €30,000/year
- 1 FTE for content management: €70,000/year (0.5 FTE for each community)

Measure 5: Support for Orphanet Belgium

95. While Orphanet's headquarters are located in France, Orphanet operates through a network of partner teams in the different countries that are responsible for collecting all information on expert services and research into rare diseases.
Orphanet has earned worldwide recognition as a comprehensive reference information source on rare diseases. It has approximately 20,000 visitors every day, including 300 Belgians. Though initially developed for health professionals (GP's, specialists, etc.), Orphanet's visitors are currently 2/3 professionals and 1/3 patients. The website is considered by all stakeholders to be valuable and it has become the preferred partner of DG Sanco.

The Orphanet database for rare diseases

Since 2000, the Orphanet database, currently hosted by France's INSERM, has been providing information on over 6000 rare diseases in six languages. It provides a comprehensive encyclopaedia of rare diseases; a directory of professional services in 35 countries; a directory of European centres of reference, of ongoing clinical trials, and of available guidelines; a database for orphan drugs providing information on their stage of development and availability in EU countries; and a range of other services for specific categories of stakeholders, including a facility to retrieve diagnoses through symptoms and signs and a library of recommendations for emergency situations.

For a more extensive description of Orphanet see reference [43]

96. In Belgium the Orphanet team is currently located at the Centre of Medical Genetics at UZ Leuven. Current progress on the Belgian database is limited due to insufficient funding (and thus manpower). When fully developed, however, the database can be an invaluable tool for Belgian health professionals and patients. The current limited European support should be complemented through national support. Switzerland, Italy, Spain and Germany already provide national support for the database.

97. With the current proposal, it will be necessary for Orphanet (or parts of it) to be translated into Dutch (it will be investigated whether the Netherlands is interested in a joint translation of Orphanet). Currently, Orphanet is available in French, English, German, Italian and Spanish. In a new proposal to DG Sanco, the Orphanet team has requested funding for translation into 10 additional languages. The Belgian government intends to support further development of Orphanet Belgium within the framework of this proposal in DGSanco.

98. It is proposed that the portal website and the national registry be hosted by the Scientific Institute of Public Health. Orphanet Belgium would be jointly managed by the Scientific Institute for Public Health and the Federal administration. This increases the critical mass of the scientific and administrative personnel involved.

Impact of measure 5 on patients, other stakeholders and the budget

99. Orphanet is the European source on all medical and European aspects of rare diseases which will become available with measure 5 to all Belgian citizens in the official languages of this country.

100. The costs included in the budget are:

- an investment cost of €70,000 for the translation of the patient-relevant data of the Orphanet website
- an operating expenditure of €75,000/year, which would cover a salary cost and provide for a budget of €5,000/year for translation and other expenses.

43 Rationale for a proposal for a joint action, Orphanet, September 2009.

Area 4 – Access to and direct and indirect costs of diagnosis, medication, treatment and patient management

The issues …

… improving access to diagnostic tests

101. Area 1 of this Plan, which describes the new organisation of clinical expertise on rare diseases at national level, aims to improve diagnosis and access to diagnosis of patients with rare diseases, and especially of patients with ultra-rare diseases. Because of the rarity of the disease and of the tests to be performed, it is often necessary to have tests performed in specialised labs in other countries. Very often these tests are not properly reimbursed and patients do not have equal access to these tests.

… improving access to treatment

102. Patients are affected differently by their rare disease and their clinical status depends on the availability of adequate treatment[44]. Therefore, patients can be grouped into four main categories:

- Those who can get an approved treatment with orphan drugs, thus improving the quality and/or the length of their life (estimated at 2000).
- Those who have a disease for which a treatment is being developed. This group is at least as large as the group benefiting at the moment from existing treatments, as the expectation is that the number of orphan drugs (and therefore treated patients) will double in the next five years. A small proportion of this group can already benefit from treatment through participation in clinical trials, compassionate use or medical needs programmes.
- Those who can be treated with a drug developed for another disease to improve their quality of life. The size of this group is very difficult to estimate at the present time and efforts to do so need to be recommended (off-label use).
- Those for whom no dedicated medicinal treatment exists, and who get symptom-alleviating medication, paramedical treatment, or other types of care for their disease. This is the largest group and currently represents probably more than 90% of the total number of patients.

The Plan – summary of Area 4

103. In the context of Area 4 two supplementary 'diagnostic' measures are proposed in this first phase of the Belgian Plan, one covering DNA diagnostic tests outside Belgium, the second non-DNA diagnostic testing outside Belgium. Both measures aim to make sure patients can access the right diagnostic test; should not pay more for the test to obtain a diagnosis or the confirmation of diagnosis because of the rarity of the disease (and therefore of the test); are not paying more because the test is performed abroad instead of in Belgium.

104. The Belgian Plan proposes, in phase one, a number of measures to improve the time of and access to treatment for patients as well patient reimbursement. The objectives include improving time to treatment, but also reducing as much as possible the number of individual rare disease patients in a situation where they cannot get reimbursed for a treatment unless they apply to the 'Bijzonder Solidariteits Fonds (BSF – Special Solidarity Fund)/ Fonds Spécial de Solidarité (FSS)'. The BSF should be considered a last resort for individual cases, not a solution for groups of patients.

44 In this context treatment may be an orphan drug, a medical device, a surgical procedure, ….

105. Clinical trials, compassionate use, programmes for medical needs and the Early Temporary Reimbursement (ETR) procedure proposed in this Plan are ways to provide access to orphan drugs before regulatory and/or reimbursement approval. The proposed processes have to be put in place taking the timing of the regulatory and review process into account, as well as current national and EU rules and guidelines for Compassionate Use (CU), Medical Need Programmes (MNP), pharmacovigilance etc. They also need to look at the consequences for the affected patients if, for a specific product, no sponsor is active in Belgium. Access to orphan or other drugs for other than designated rare disease indications is an important consideration which will partly be covered under off-label use below.

Measure 6: Change the system to allow DNA samples – instead of patients themselves – to be tested abroad

106. The days when all these samples could be handled as research samples and tests performed for free by 'friends/scientists/informal networks' are over. This is a service that needs to be performed in a laboratory which has the right expertise, which ideally is accredited, and which provides a service according to normal standards (within agreed turnaround time, with a full outcomes report). It is a necessary service as there are tests for thousands of rare diseases, and a fraction of these tests are performed in Belgium. Specialisation of labs for DNA tests is recommended for Belgium, but will happen as well at EU level. Such specialisation may increase the need for having to send samples abroad for testing. Volumes of tests sent abroad will therefore probably increase. At present however, the Belgian health insurance system does not allow their reimbursement, since there is no legal provision for charging the system for tests performed on samples sent abroad. Such tests can only be reimbursed if the patient travels abroad (E112) and the test is reimbursed in that country. However, sending a patient abroad is not necessarily the best solution, either for the patient (travel cost and time) or for the health insurance system (significantly higher cost).

107. Based on information from the centres, some 846 tests were performed abroad in 2007 at a cost of €430,000.

108. The recommendation formulated in the Belgian Plan is therefore:
For diagnostic[45] testing of DNA samples of patients and their relatives affected by rare disorders for which no specialised laboratory is available in Belgium that can perform such testing, it is recommended that a special financial budget be granted to the Coordinating Centres for Rare Diseases or the medical genetic centre collaborating with it, to allow coverage of the cost of such testing done in a laboratory outside Belgium (if such laboratory can be found).
The same should be true for the confirmation of screening results for relatives.

Impact of measure 6 on patients, other stakeholders and the budget

109. The impact for the patient and his/her relatives is access to the right test, reimbursed as if the test was performed in Belgium (the cost of the test is now sometimes charged to the patient and this should not be the case anymore with this system).

110. The budget impact of this measure will probably be between 0.5 and 1 million Euro.

45 *Although only diagnostic testing is mentioned, this also covers tests performed before deciding on medication, or to check the effectiveness of a treatment.*

Measure 7: Organise a coordinated approach for non-DNA diagnostic testing

111. Non-DNA diagnostic testing for rare disorders (enzymes, metabolics, etc.) are performed in specialised labs.
The genetic and metabolic centres in Belgium have reduced or stopped these activities as volumes were low and they were not economically viable. An aggravating factor is that these sometimes expensive tests are not part of the reimbursement nomenclature. As a result, the capacity to perform these tests has nearly completely disappeared in Belgium.
Present practice, and the implementation of the Belgian Plan leads to an expectation of increased needs for such tests.

112. As part of the Belgian Plan it is therefore proposed to produce an inventory of what tests are available in Belgium and what is missing.
This should lead in the second phase of the Plan to a proposal on how the testing needs can be organised at national and EU level, with a proposal for an adapted nomenclature to allow reimbursement of such tests performed in Belgium and performed abroad.

Impact of measure 7 on patients, other stakeholders and the budget
113. The budget impact has not yet been estimated but is expected to be provided in a later phase of the Belgian Plan.

Measure 8: Set up a system for early access to orphan drugs, including early temporary reimbursement

114. The proposal for future early access for patients to cover unmet medical needs through new orphan drugs is a system of Early Temporary Reimbursement (ETR): at the time a marketing authorisation application (MAA) is submitted to the European Medicines Agency (EMA), the pharmaceutical company (sponsor) can apply for an Early Temporary Reimbursement (ETR) with the Belgian authorities[46]. The authorities will review the ETR quickly, taking medical need and available evidence into account. When the ETR is granted, an agreement is signed including the commitments of all parties under the ETR. The ETR will stop when marketing authorisation is denied or withdrawn, or when normal national reimbursement enters into force or is denied. A risk-sharing plan will be part of the agreement.

115. This system has three related measures and conditions:
- Patients suffering from a rare disorder and who participated in clinical trials with an orphan medicine and experience a beneficial clinical effect on their rare disorder from the orphan medicine should, if clinically relevant, continue to receive such treatment after the clinical trial under a compassionate-use (CU) protocol or a medical need program (MNP), until a reimbursement decision has been obtained. Companies who provide orphan medicinal products in clinical trials should be prepared to ensure continuity of treatment until that reimbursement decision.

46 *During the application for ETR, provision by the sponsoring company of products as CU for those patients for which ETR is applied for is mandatory for the whole application period, estimated to be 3 months.*

- Expanded access through CU/MNP should be foreseen, as a mandatory provision for ETR (see above and footnote 46), but also beyond those patients that are/were involved in clinical trials and at the initiative of Medical Doctors, it can be provided by companies for an orphan medicine for which a marketing authorisation application (MAA) is introduced at EMA. This should be done with ethics committee approval, providing registration and collection of patient data, which is not foreseen in the present legislation.[47]
- If for an orphan medicinal product with active MAA, the sponsor is not active in Belgium, the pharmacists working in conjunction with a Centre of Expertise or a Coordinating Centre for Rare Diseases should be allowed to import the orphan medicine from another EU country, once the orphan medicine has received marketing authorisation from the EU. This is not possible under the present legislation. Criteria and a budget to cover the cost of such orphan medicines should be foreseen.

Impact of measure 8 on patients, other stakeholders and the budget

116. The impacts for the patients of these related measures are:

- Belgian patients would get access to the drug at least 12 months faster than what is now the ideal situation, and probably 18 to 24 months faster than the present average time period.
- A secondary impact is that industry will be encouraged and incentivised to develop more orphan drugs as they will be reimbursed faster, and will also be motivated to install more compassionate-use and medical-needs programmes in Belgium, allowing faster access to treatment for patients.

117. The budgetary impact of the measure is difficult to estimate, as it depends on the actual behaviour of the pharmaceutical companies. The system should make Belgium more attractive making it possible to bring medicines to market faster.
Taking into account the experience so far with orphan drugs and the expectation that approximately 10 new drugs will enter the market each year, this measure "could" generate an increase for the orphan drugs budget of €5 to 10 million in the first year. This is a one-off extra cost.

Measure 8a: Belgium to play a leading role in boosting EU-level initiatives on early access

118. The proposed system for early temporary reimbursement, should ideally be established at the EU level. That may lead to a parallel examination and decision for marketing authorisation (at EU level) and for reimbursement (at the Member State level). The Belgian Plan recommends that the EC work out an EU-wide proposal for early temporary access (and reimbursement) (e.g. through a funding of EU-wide compassionate use) for orphan medicines and to link the collection of treatment data to this access.

119. The discussions that are presently ongoing about the EU-level collection of clinical added value data about orphan drugs [48] is linked to earlier access as well. The Belgian authorities are requested to take an active part in these discussions and in a pilot project at EU level to work out the practicalities.

47 *The current national legislation does not provide for the collection of patient data during CU/MNP and may have to be modified.*

48 *Improving access to orphan medicines for all affected EU citizens, Final Conclusions and Recommendations of the Pharmaceutical Forum, page 4, bullet 'Exchange of knowledge amongst Member States and European authorities on the scientific assessment of the clinical added value of orphan medicines.', http://ec.europa.eu/pharmaforum/docs/pricing_orphans_en.pdf*

and

EAHC-tender 'The creation of a mechanism for the exchange of knowledge between Member States and European authorities on the scientific assessment of the clinical added value for orphan medicines', http://ec.europa.eu/eahc/health/tenders_H05_2010.html

120. Harmonisation of guidelines for Compassionate Use and Medical Needs Programmes is necessary to envision a more equal access to therapy by patients, and should also include a system for the collection of clinical data under CU/MN programmes.

121. EU-level cooperation and harmonisation will lead to better earlier access for patients, and to decisions and significant savings through improved efficiency and cost sharing.
This measure should not generate direct budgetary impacts, and in the longer term only net savings. It does, however, imply continued attention at policy level and resources to actively participate in and eventually lead EU level initiatives.

Measure 9: Ensure that raw materials for treating rare diseases can be used legally

122. Various raw materials are currently used to treat rare diseases but for some such use is currently not legal in Belgium, because these raw materials need analysis certificates in order to ensure compliance. For the benefit of patients and to avoid a situation where a de facto illegal practice needs to be continued as there is no alternative treatment available, which implies responsibilities and risks for hospital pharmacists, the proposal is to entrust the National Platform (to be created) with the task of ensuring that such raw materials are analysed and have the adequate certificate for human use, and that such raw materials are on the reimbursement list.

123. A list of 15 such substances exists and has been prepared as part of the preparation of the Belgian Plan. The National Platform should develop a mechanism to regularly update the list.

Impact of measure 9 on patients, other stakeholders and the budget
124. The benefit to the patient is the certainty of continued treatment with a legal basis.

125. The budgetary impact is small, but a budget should be made available to the National Platform to ensure analysis is performed on each batch, and certificates can be made available.
This may be covered by an annual budget of €25,000.

Measure 9a: Belgium to propose a change in the criteria used to grant orphan designation when appropriate raw materials are available and used

126. The COMP has granted orphan drug designation to products although a raw material may be readily available on the European market, which could be used for treatment of a specific rare disease. When such designated products reach the market as orphan drugs, they may encounter difficulties in obtaining reimbursement as a much cheaper alternative exists in the form of a raw material.

127. It is therefore recommended that the European Commission prevent efforts from being made to develop orphan drugs which will be at risk of not being reimbursed based on the price difference with the existing raw material, taking the benefits of the orphan medicine versus the raw material into account. Specifically, it is asked that the COMP review article 3.2 of Regulation EC 141/2000 about whether such raw materials should be included under the definition of 'existing treatment'.

Measure 10: Start a detailed inventory of off-label use of drugs for patients with rare diseases

128. As mentioned above, a number of patients suffering from rare diseases are treated by drugs that are on the market to treat other diseases (rare or not). This is known as 'off-label' use, as the drugs are used for an indication that is not mentioned on the product label and for which the product has no marketing authorisation. This is quite normal practice for rare diseases, as specific treatments may not exist, and as it is often not economical to invest in the development of an approved medicine for a very rare indication.

129. The ultimate purpose of this proposed measure is to allow policies to be defined based on reality (to be worked out in phase II of the National Plan) so that either off-label use can be legalised or efforts to develop new drugs for these indications are supported.

130. We recommend detailed documentation of the off-label use of orphan medicines for other than approved rare disease indications, and of the off-label use of medicines in general for rare disease indications, so that relevant policy recommendations can be made and rules installed regarding off-label use.
It is also recommended that Belgium take an EU initiative to recommend such detailed documentation of off-label usage at EU level to enable potential EU policy initiatives.

Impact of measure 10 on patients, other stakeholders and the budget
131. The potential impact for patients is high, as the present practice of off-label use is not documented. This also means that additional patients could benefit from certain existing medicines.

132. The budget impact will be measured based on the result of this documentation, and therefore has not been estimated at this time.
Producing the inventory is an investment that has been estimated at €75,000.

Measure 11: Support home treatment with orphan drugs under clear conditions

133. The treatment regime of orphan drugs is often simple but may be required over a long period of time, and patient compliance may be an issue. Reimbursement of an orphan drug treatment is now nearly always linked to a treatment in a hospital setting. Home treatment may substantially improve compliance and patients' quality of life, if set up appropriately and can then be a safe and acceptable alternative for ambulant hospital treatment. Patients for whom home treatment would be an option must be able to make their own informed choice between hospital-based and home treatment.

134. Concrete measures proposed include:
- For oral forms of orphan drugs, it can be examined whether and to which extent they can be dispensed by the community pharmacist for home treatment.
- Parenteral orphan drugs with cytotoxic properties should always be prepared in the safety cabinet of a hospital pharmacy and administered in a hospital setting.
- Other parenteral orphan drugs (including ERTs, etc.) must be prepared and administered in the centre of reference /centre of rare disease for the considered rare disease at the start of treatment. Follow-up therapies may be prepared in a hospital pharmacy near the patient’s home for home treatment by a trained home nurse

- For home treatment under 1 and 3 above, patients should have the possibility to access home care services to administer such treatment. The prepared orphan drug would be collected at the hospital pharmacy and delivered, at a time agreed upon with the patient, at his/her home. The hospital pharmacist is responsible for storage, handling and compounding of the ready to use orphan drug. The community pharmacist may supply additional material such as sterile needles, syringes, antiseptic solutions etc.
- All home treatment activities are performed under the responsibility of the treating physician at the Centre of Expertise/Coordinating Centre of Rare Disease. An agreement about such home treatment needs to be signed by all parties involved (nurse, hospital pharmacist, community pharmacist, recognised service provider, treating physician and patient) which included a treatment protocol and a product-specific manual which is based on the SmPC (product leaflet).

Impact of measure 11 on patients, other stakeholders and the budget

135. The benefits are mainly for the patient and relatives. These benefits are significant both in terms of economic value (e.g. savings on travel, less loss of working time) as in quality of life for the patient.

136. Budget impact: home treatment is expected to be cost-neutral to slightly less costly than hospital treatment.

Evaluation and monitoring

137. The National Platform for Rare Diseases, as a new organ where all stakeholders are present, should play the central role in the evaluation and monitoring of the implementation of the Plan.

138. This dimension of the Plan will be further developed in phase II, but a few principles need to be clear from the start of phase I:

- the regularity of meetings of the National Platform is considered a necessity for proper monitoring
- the National Platform should create a separate working group in charge of evaluation. This working group should define the evaluation process and steer it. It should regularly review the targets, deadlines and achievements, and report back to the National Platform meetings on a yearly basis.
- The central stakeholder of the Plan are the patients. Their opinion and satisfaction should be part of any evaluation exercise.
- The National Platform should produce a yearly report on the advancement of the Plan.
- When creating separate working groups, the National Platform should, on each occasion, clearly define objectives, targets and responsibilities.
- Working groups in charge of specific measures should also be in charge of regularly reviewing indicators, defining new indicators whenever relevant.

139. The table below gives a first – non-validated – overview of potential milestones and indicators for the success of the measures proposed in phase I. These indicators are mainly 'process indicators'. In the longer term, the management of the Plan should cooperate at the EU level to review best practice and if possible also develop 'health outcome indicators'. The Europlan project plans to have a proposal of common indicators ready by February 2011.

Measure	Tentative milestones	Indicators (examples)
Measure 1: Create Centres of Expertise and Coordinating Centres for Rare Diseases	Dec 2010: launch of first call Mar 2011: CCRDs appointed Mar 2011: first set of 15 CE appointed June 2011: certification system operational Dec 2011: second set of 15 CE appointed Dec 2011: present system of contracts included in CE	Number of diseases covered Number of patients handled by Centres (CE & CCRD) Number of centres certified
Measure 2: Create a National Platform for Rare Diseases	Jan 2011: staff operational	Number and regularity of meetings of Platform Number of working groups Number of participants in working groups Presence of patients in Platform and working groups
Measure 3: Create a central patient registry	Jan 2011: database and data collection ready Jun 2011: start of data collection	Number of patients registered
Measure 4: Create a national portal website for rare diseases	Jan 2011: staff operational March 2011: portal online	Number of unique visitors
Measure 5: Support for Orphanet Belgium and (partial) translation of Orphanet in Dutch	Jan 2011: staff operational Mid 2011: Dutch version	Dutch version available Doubling the number of Belgian visitors (end 2011 compared to end 2009)
Measure 6: Change the system to allow DNA samples – instead of patients themselves – to be tested abroad	Jan 2011: new system operational	Number of samples sent abroad per year Cost charged to RIZIV/INAMI
Measure 7: Organise a coordinated approach for non-DNA diagnostic testing	June 2010: study launched Dec 2010: results available	Decisions taken – input in Phase II of Plan
Measure 8: Set up a system for early access including early temporary reimbursement of orphan drugs	Dec 2010: technical aspects defined Mar 2011: launch	Number of orphan drugs using ETR compared to not using it. Number of patients receiving early access
Measure 9: Ensure that raw materials for treating rare diseases can be used legally	Dec 2010: raw materials tested and certified	
Measure 10: Start a detailed inventory of off-label use of drugs for patients with rare diseases	June 2010: study launched Dec 2010: results available	Decisions taken – input in Phase II of Plan
Measure 11: Support home treatment with orphan drugs under clear conditions	Jan 2011: system operational	Number of patients getting home treatment

PRELIMINARY AGENDA FOR PHASE II OF THE BELGIAN PLAN

New areas

Area 5 – Status of the patient with a rare disease

140. The analysis of the rare diseases associations' responses taken from the 2008 study on chronic illnesses shows interesting elements regarding the order of priorities, the cost factors and the measures expected by people suffering from a rare illness. This statement is true when we generalise the responses but becomes even more obvious when we consider the failings and expectations mentioned for each illness. Targeted measures are thus vital.

141. The working group looking into the status of patients with rare diseases is developing a specific model for people suffering from a rare, serious disease.

Area 6 – Research on rare diseases

142. According to the Guidance Document on Recommendations for the Development of National Plans for Rare Diseases (Europlan)[49] research on rare diseases is scarce and scattered throughout the EU. However, the recent methodological and scientific advancements provide new and powerful approaches that can be used to reveal the mechanisms of many rare disorders. Nevertheless, various reasons make research on rare diseases difficult to conduct, namely: the high number and wide variety of diseases, the lack of suitable experimental models for most rare diseases, the poorly defined endpoints, the small number of patients and, above all, the limited resources.

143. Such difficulties are especially relevant for translational research, which is necessary to bridge the gap between basic research and therapy development. Clinical studies on rare diseases, which are of high added value, may also need complex collaboration among EU countries since patients enrolled and data collected in a single country may not have sufficient statistical power to draw conclusions on the efficacy of the treatment under investigation. Finally, public health and social studies on rare diseases and patients' needs are limited since these issues have received attention only recently. In conclusion, there is a strong need to foster collaborative programmes on all fields of research on rare diseases, from fundamental/basic through to social research, at national, European and international level.

144. In the second quarter of 2010 a dedicated working group within the Fund for Rare Diseases and Orphan Drugs will start on these issues. In the second half of 2010 meetings with representatives from FNRS, FWO, IWT, WIV, VIB, IRSIA etc. are planned.

49 *Guidance Document, Recommendations for the Development of National Plans for Rare Diseases, Europlan, 8 march 2010.*

Area 7 – National and international networking

145. The need for international cooperation and networking on the topic of rare diseases are important for all European countries. Such European cooperation should focus on the creation of international diagnostic and laboratory networks, networks of cooperating centres for the development of clinical guidelines, identification, recognition and certification of centres/laboratories in neighbouring countries, participation in European consortia and research projects, etc.

146. Especially for small countries these networks will be vital. Their specific situation will, especially for ultra-rare diseases, be increasingly based on the creation of agreements and frameworks with neighbouring or other countries and on European collaboration rather than on the national self-provision of health care for all patients with rare diseases.

147. A number of initiatives dealing with international networking have already been proposed in the first phase of the Belgian Plan, i.e. the foundation of the National platform, the recognition of Centres of Expertise and of Coordinating Centres for Rare Diseases which have to get involved in national and international networks. A number of administrative issues on cross-border diagnosis and treatment have also been discussed. An intensification and expansion of these measures will be further developed in the second phase of the Belgian Plan.

Area 8 – Education and training of health professionals

148. The training of professionals and development and exchange of best practices and education are a high priority in the field of rare diseases and are main determinants for a timely and appropriate diagnosis and a high quality of care. But the need for training does not refer only to clinical capacity, but also to the ability to communicate with patients. Furthermore, the provision of accurate information in a format geared to the needs of professionals is a key factor in improving diagnosis and care in the field of rare diseases.

149. For this reason the European Commission and institutions from all member states supported Orphanet, the European portal for rare diseases and orphan drugs. In the first phase of the Belgian Plan support for the continuation of Orphanet Belgium was already foreseen. In the second part of the Plan, further measures targeted in this area will be discussed.

Areas already started in Phase I

Area 4 – Access to and direct and indirect costs of diagnosis, medication, treatment and patient management

150. In the context of access to and costs of diagnosis and treatment, a number of items have already been discussed in the first phase of the Plan. Supplementary solutions will be worked out in the second phase of the Plan. These include (but are not limited to):

- **Subjects for which 'pre-recommendations' were formulated in phase I:**
  outlook for recommendations on off-label use of orphan drugs (based on phase I recommendations and concluded study)
  non-DNA diagnostic testing of samples (based on phase I recommendations and study)
  transparency of pricing of orphan drugs (based on further discussion of the results of a commissioned study done by Prof. Steven Simoens (KUL))

- **New subjects:**
  review of and recommendations for the reimbursement procedure by the CTG/CRM for orphan drugs BSF/FSS and expected KCE report
  reimbursement rules for medical devices and surgical procedures for rare disease patients
  recommendations for other medical acts which are reimbursed (physiotherapy, etc.)

- **Subjects for which collaboration with working groups from other areas is necessary:**
  global picture of rare disease treatment costs and reimbursement (including use of non-orphan drugs, medical devices, surgical procedures, research funds used for treatment, etc.) (see also Area 5 – status of the rare disease patient)
  compliance and accountability of patients
  possibilities of telemedicine
  links between the National Registry and disease registries (see also Area 2)

Area 2 – Codification and inventory of rare diseases

151. Contact will be established with the coordinators of existing disease-specific databases, protocols should be worked out for linking these databases to the National Registry and appropriate budgets will be calculated.

152. At individual member state level, a classification of appropriately coded rare diseases is needed for guiding reimbursement policies and for improving traceability of rare diseases in the health care information system. Although the national prerogatives in adopting the own health service organisation must be acknowledged, it is important that international collaboration be developed to facilitate all those activities for which EU collaboration is necessary in order to effectively cope with the challenges posed by rare diseases, e.g. collection of epidemiological information, healthcare provision, surveillance, the establishment of pan-European clinical trials and research, etc. Therefore, the scientists responsible for the Belgian National Registry will collaborate with fellow European registries and with relevant European authorities. The importance of comprehensive inventories for rare diseases at European level was noted in the Council Recommendation of 8 June 2009. Furthermore, for a number of rare diseases, treatment databases already exist under the supervision of EMA (former EMEA). Efforts will be made to evaluate how these databases can be useful for the National Registry and vice versa.

Area 3 Increase awareness, inform stakeholders and empower patients

153. Empowerment is also one of the areas addressed in the Council Recommendation of 8 June 2009. Actions in the field of rare diseases contributing to patients' empowerment is a moral duty, based on solidarity and social justice. In addition, empowerment, education and the active involvement of patients in the shaping of health care policy can increase compliance, therefore leading to a better use and higher effectiveness of health care initiatives.

154. Patient advocacy organisations play an important role in getting information to patients, doctors, and caregivers. Furthermore their contribution in generating interest and awareness in rare diseases, collecting funding for research and lobbying for better care and treatment cannot be overestimated. Therefore, further initiatives for supporting patients at national level in phase II will include: supporting patient advocacy organisations and umbrella organisations that represent the interests of all rare disease patients; creating national patient forums to discuss rare diseases including the involvement of other stakeholders in the field of rare diseases (i.e. the Rare Disease Day event and other events) and supporting activities performed by patients, such as awareness-raising, capacity-building and training, exchange of information, creation of dissemination material, networking, organisation of courses, outreach to very isolated patients; promoting the involvement of patients in the national and European scene; involving patients in the planning of research and in registry activities (including translational and clinical research – see Area 6); supporting the integration of rare diseases patients at school and at work (Area 5); further exploring services dedicated to information about rare diseases (help lines).

ADDENDUM 1 – CRITERIA FOR CENTRES OF EXPERTISE (CE)

E criteria are essential/obligatory.
O criteria are optional/informative.
D criteria: obligation to develop within a specific timeframe (3 or 5 years).

Certification	
E1	**National/international networking with other centres of expertise (funded or not)**
D2	Accreditation of the centre (e.g. accreditation of stem cell therapy unit [JACIE]; accreditation of laboratory facilities [BELAC])
D3	Accreditation of the hospital (e.g. ANAES [FR], NIAZ [NL], JCAH [US])
Basic / Translational / Clinical research	
E4	**Basic / translational / clinical research concerning a specific (group of) rare disease(s) (Last three years are taken into consideration)**
E5	**Number of published studies?**
O6	Basic / translational / clinical?; Phase one / phase two / phase three?
O7	Investigator-driven / Pharma-driven / Organisation-driven (= paid for by an [international] organisation)?
O8	For clinical studies: National / international?; Monocentre / multicentre?; Primary / secondary investigator?
Multidisciplinarity	
E9	**Multidisciplinary consultations**
E10	**Follow existing guidelines for rare disease (e.g. clinical pathways) (formalised – on paper – and effectively used). Participate in development of new guidelines.**
O11	Joint staff meetings
Number of patients	
E12	**Number of new cases of hospitalised and ambulant patients treated by the expertise centre (a patient can only be included if he had at least one hospitalisation or one consultation during the past year / last three years)**
O13	Source: e.g. rapport annuel de l'hôpital / Jaarverslag van het ziekenhuis; MKG / RCM
O14	Figures for the past year (and for the last three years)

Number of staff	
E15	**# permanent FTE medical staff dedicated to the (group of) rare disease(s) Average over the last three years**
O16	# FTE paramedical staff dedicated to the (group of) rare disease(s)
Outcome measurement	
D17	**Outcome measurement at the level of the centre of expertise (yes/no?; type?) (e.g. mortality rate; event-free survival; Quality of Life [QoL] measurement [can replace "tevredenheidsenquête" / "enquête de satisfaction"])**
Patient services	
E18	**Structured contact with patient advocacy organisations dedicated to the specific rare disease / group of rare diseases**
E19	**Structured patient information (e.g. patient brochures; dedicated internet sites, informational conferences)**
E20	**Open up an information channel to patients and the general public (e.g. centralised telephone number for questions, Q&A response on website)**
O21	Languages
O22	Help for family members (e.g. staying the night; psychological support)
O23	Reception
O24	Room
O25	Food
O26	Complaints (# of complaints registered; handling)
O27	Patient wellness initiatives
Scientific activity	
E28	**Citation score of the permanent team pertaining to the expertise**
E29	**Active involvement in Biobanking**
O30	Publications: basic/translational/clinical research
O31	Research funding FWO / IWT / other
Teaching activity	
E32	**# of trainees (PhD, postgrad, GSO) for the (group of) rare disease(s)**
E33	**# of specific conferences for the (group of) rare disease(s)**
O34	Organisation of conferences (by RDC/national / international) Active participation (poster / speech) (national / international)
E35	**Membership international scientific associations (~ networking)**

Technical environment	
E36	**Specific diagnostic test(s) for the rare disease Special techniques / equipment (imaging, transplantation, gene therapy, etc.) for the diagnosis / treatment of the rare disease**
O37	Development of new techniques or tests
D38	ICT environment / use of e-health
Turnaround time	
O39	Waiting time in order to get an appointment (= waiting list)
O40	Time lapse between sample taking and diagnosis Caveat: a minimum time lapse is needed to ensure sufficient quality Other regulations exist for this.
O41	Time lapse between diagnosis and treatment
O42	Number of undiagnosed patients
Other criteria	
E43	**Set up networks with peripheral hospitals, specialists, GPs, paramedical and other care providers for day-to-day care of the patient**
O44	Short-track system in case of emergency
O45	Attractiveness indices – distance between patient and hospital (e.g. postal codes of patients → MKG / RCM) – (# of second opinions)

ADDENDUM 2 – CRITERIA FOR COORDINATING CENTRES FOR RARE DISEASES (CCRD)

E criteria are essential/obligatory.
O criteria are optional/informative.
D criteria: obligation to develop within a specific timeframe (3 or 5 years).

Certification	
E1	**A genetic centre and at least 3 INAMI/RIZIV-contracted centres for rare diseases (i.e. cystic fibrosis, metabolic diseases and neuromuscular diseases). These should be located on the same clinical campus. If not, a track record of intense and functional collaboration has to be provided.**
E2	**National/international networking with other rare disease centres.**
D3	**Accreditation of the hospital (e.g. ANAES [FR], NIAZ [NL], JCAH [US])**
Basic / Translational / Clinical research	
E4	**Research concerning rare diseases that are not rare cancers (Last three years are taken into consideration)**
E5	**Number of studies? Minimum of 3**
O6	Number of rare disease patients included in the clinical studies? (ratio: # rare disease patients included in the studies / total # rare disease patients treated in the RDC)
O7	Basic / translational / clinical?; Phase I / II / III?
O8	Investigator-driven / Pharma-driven / Organisation-driven (= paid for by an [international] organisation)?
O9	National / international?; Monocentre / multicentre?; Primary / secondary investigator?
Multidisciplinarity	
D10	**General multidisciplinary consultations** **(This will become an essential criterion after the first evaluation by the national platform)**
E11	**Guidelines for rare diseases (e.g. clinical pathways) (formalised – on paper – and effectively used) Minimum 1/3 of the expertises present in the RDC?**
E12	**Joint staff meetings**
O13	Frequency of joint staff meetings?
Number of patients	
E14	**Total number of <u>hospitalised</u> rare disease patients treated by the centre for rare diseases (at least one hospitalisation during the past year / last three years)**

E15	**Total number of <u>ambulant</u> rare disease patients treated by the centre for rare diseases (at least one consultation during the past year / last three years)**
O16	Source: e.g. rapport annuel de l'hôpital / Jaarverslag van het ziekenhuis; MKG / RCM
O17	Figures for the past year (and for the last three years)
Number of staff	
E18	**Total # FTE medical staff dedicated to rare diseases Average over the last three years; only permanent staff taken into consideration**
O19	Total # FTE paramedical staff dedicated to rare diseases
Outcome measurement	
E20	**Outcome measurement (yes/no?; type?) (e.g. mortality rate; event free survival rate; Quality of Life (QoL) measurement [can replace "tevredenheidsenquête" / "enquête de satisfaction"])**
Patient services	
E21	**Structured contact with patient advocacy organisations**
E22	**Structured patient information (e.g. patient brochures; dedicated websites)**
E23	**Open up an information channel to patients and the general public (e.g. centralised telephone number for questions, Q&A response on website)**
O24	Languages
O25	Help for family members (e.g. staying the night; psychological support)
O26	Reception
O27	Room
O28	Food
O29	Complaints (# of complaints registered; handling)
O30	Patient wellness initiatives
Scientific activity	
E31	**Total citation score of the team dedicated to rare diseases (only staff with at least 20% dedication to rare diseases). Minimum to be defined**
O32	(Publications: basic / translational / clinical research)
O33	(Research funding FWO / IWT / other)

Teaching activity	
E34	**# of trainees (PhD, postgrad, GSO)** **Minimum to be defined**
O35	# PhD students # Postgraduate students (fellows) # Médecin candidat spécialiste en formation / Geneesheer specialist in opleiding (GSO) # paramedical students
E36	**# of conferences** **Minimum to be defined**
O37	Organisation by the RDC or national/international conferences? Active involvement (poster / speech) in national / international conferences
E38	**Membership international scientific associations (~ networking)**
O39	Passive or active participation (officers)?
Technical environment	
E40	**Special techniques / equipment (imaging, transplantation, gene therapy, etc.)** **Number of patients treated or diagnosed with these special techniques / equipment**
O41	Development of new techniques
E42	**ICT environment / use of e-health** **Procedure to be developed**
Turnaround time	
O43	Waiting time in order to get an appointment (= waiting list)
O44	Time lapse between sample taking and diagnosis *Caveat: a minimum time lapse is needed to ensure sufficient quality* *Other regulations exist for this.*
O45	Time lapse between diagnosis and treatment
O46	Number of undiagnosed patients
Other criteria	
E47	**Set up networks with peripheral hospitals, specialists, GPs, paramedical and other care providers for day-to-day care of the patient**
O47	Short-track system in case of emergency
O48	Attractiveness indices – distance between patient and hospital (e.g. postal codes of patients → MKG / RCM) – (# of second opinions)

ADDENDUM 3 – BUDGET IMPACT ANALYSIS

Belgium is preparing a National Plan Rare Diseases based on the EC recommendations. The plan is being developed in two phases:

- a first phase with a limited set of measures that can be implemented at short term;
- a second phase that will be a comprehensive plan.

This document covers the budget impacts of the measures proposed in the first phase of the Plan. These financial impacts are not put in relation to the impacts on patients and other stakeholders, which are described in the Plan itself. The objective of this description is to document the estimates mentioned in the plan.

The table below gives an overview of the budget impacts.

Three types of budget impacts are estimated and covered in the table:

- costs to the health insurance budget: this is the estimated net increase compared to a situation without the measure
- investment budget: these are one – off costs to get the measure implemented (e.g. design and programming of web site)
- yearly budget: this is the estimated additional yearly cost of implementing the measure. These costs are often essentially salaries and are therefore likely to increase over time.

No "overheads" are taken into account in the two last categories, only direct costs.

Table: summary of yearly costs by measure of the National Plan Rare Diseases – phase I – estimates for second year of operations.

Measure	Budget impact health insurance	Costs outside the health insurance	
		Investment budget	Yearly budget
1,1 creation of CE	15 to 20 M €	0	0
1,2 creation of CRD	0,5 to 1 M €	0	0
2, creation of National Platform	0	0	250.000
3, National Registry	0	25.000	200.000
4, Portal	0	30.000	100.000
5, Orphanet Belgium	0	70.000	75.000
6, cross-border dna testing	0,5 to 1 M €	0	0
7, non DNA diagnostic testing	0 in phase 1	75.000	0
8, early access and temporary reimbursement	5 to 10 M €	0	0
9, raw materials	p,m,	0	25.000
10, inventory off label use	0	75.000	0
11, home treatment of orphan drugs	0	0	0

The estimates for each measure are documented below. At the end of this document, there is a conclusion on the impact with a forecast over a 5 year period.

Measure 1: Creation of Centres of expertise and Coordinating Centres for Rare Diseases

Infrastructure, staffing and financing of Centres

In the current RIZIV/INAMI-conventioned reference centres (neuromuscular disorders, metabolic disorders, cystic fibrosis) the principals for financing are:

- medical acts are paid and reimbursed based on the nomenclature and excluded from the convention;
- the convention pays for the additional cost of multi-disciplinarity and the cost of paramedical staff, both from the point of view of total care (diagnostics, treatment and follow-up of treatment) provided in essence at the centre; each convention therefore defines the type of para-medical staff the centres need to have and puts thresholds (e.g. half-time dietician per 50 patients for metabolic diseases);
- the convention pays for individual patients that receive regular treatment a sum (quarterly or annually); this sum is between 1,500 and 2,500 Euro/patient/year on average;
- there is a threshold in number of patients (25 or 50), which means that if a centre does not reach the threshold, the convention does not pay for any patient.

The three conventions together account for approximately 3,500 to 4,000 patients, and a cost to the health insurance system of probably 6 to 7 million Euro.

Another model that exists is the MOC or Multi-disciplinary Oncological Consultation. This is reimbursed separately to ensure consensus building among various disciplines before decision-making on an individual patient treatment. A similar approach could be used for the Multidisciplinary Rare Disease Consultation (MRDC). Such an approach would ensure that the additional costs carried by centres due to the multi-disciplinary nature of the rare diseases are covered. It would however not cover the costs of paramedical and non-medical staff.

Preliminary conclusion – The convention model seems adequate for the Centres of Expertise and the MRDC model could be envisaged for the Coordinating Centres for Rare Diseases. This conclusion is valid because under the present concept, the Coordinating Centres for Rare Diseases would always be coupled with an institution that hosts at least 3 Centres of Expertise. The Coordinating Centre for Rare Disease can therefore benefit from the critical mass of medical, paramedical and non-medical staff in the Centres of Expertise.

A conclusion from the experience with the conventions is also that although the diseases are different, the average additional cost/patient/year is in a similar bracket (1,500 to 2,500 Euro/year). This gives an indication of the cost to be expected in the future of setting up more Centres of Expertise.

Impacts for the health insurance budget

This is extremely difficult to estimate due to the diversity of diseases, the fact the system will lead to savings (unnecessary costs of diagnosis and treatment will be saved), but also to additional costs (patients will e.g. live longer). Based on the experience of the reference centres as they exist today:

- There is a general consensus that savings are probably offset by additional costs linked to the longer life of patients; savings are therefore not estimated.
- The average cost/year/patient for the diseases covered by the present conventions gives a good indication of the additional costs generated by rare disease patients, when treated through centres of expertise.
- The forfait as used is generally considered as adequate to cover the costs of multi-disciplinarity and the costs of additional personnel.

As a conclusion one can estimate an average additional cost per patient per year of 2,000 Euro.

It is not clear how fast the CCRDs and CEs will be selected and become operational.
If the plan works adequately, one can expect between 10,000 and 15,000 (additional) patients will have been diagnosed within a five-year period and will be treated annually in the network of CEs, leading to an additional yearly cost of 20 to 30 million Euro/year in the year 2015 based on a costing mechanism comparable to what exists today. In the overview table above, a cost of 15 to 20 million is estimated for the year 2013.
As a comparison:

- the centres for Human Genetics are estimated to see in total some 10,000 patients/year for counseling. This number includes new patients, but also patients that were diagnosed in the past. It also includes family members. 80% of rare disease patients are estimated to have a genetic disease.
- the networks of RIZIV/INAMI-conventioned reference centres (neuromuscular disorders, metabolic disorders, cystic fibrosis) are treating 3,500 – 4,000 patients/year.

With regard to the CCRDs, the estimate is even more difficult to make. Two assumptions are made:

- the Multidisciplinary Rare Disease Consultation (MRDC) would be reimbursed at 150 Euro (no discussion has taken place yet on the actual content or ways to standardise such MRDC)
- two CRDs in Belgium would each see for diagnosis 1,000 patients on a yearly basis.

On top of this, each CCRD would be paid for the equivalent of 0.5 FTE medical staff, and 0.5 administrative staff to manage the coordinating role of rare disease activities per 1,000 patients.
The annual budget for one CCRD with 1,000 patients/year would therefore be 250,000 Euro.

Measure 2: Creation of a National Platform for Rare Diseases

It is proposed that the National Platform for Rare Diseases will function as a 'steering committee' within the Federal Public Service for Health, Food Chain Safety and Environment. It will be composed of representatives of relevant stakeholders involved in rare diseases. The current Management Committee of the Fund for Rare Diseases and Orphan Drugs, which has representatives of all relevant stakeholders, could form the core of the National Platform.

The costs generated by the creation of the National Platform will therefore be part of the budget of the Federal Public Service in charge. It is still considered important to foresee a separate budget for the smooth operational running of the National Platform also because the National Platform should be the organ that steers other budgets linked to measures of the National Plan. As part of the first phase of the National Plan this includes the measures linked to communication, the national registry and the analysis of raw materials. In phase 1, it also includes the supervision and outsourcing of studies.

The National Platform is expected to work at the operational level through working groups. These working groups can be linked to specific measures (e.g. the selection and evaluation of CEs and CCRDs), or to specific diseases (groups). These working groups will need professional support to be fully operational.

The National Platform should take charge of the coordination of international networking activities. A specific budget is foreseen to cover these costs (participation in and also hosting of coordination-related activities).

Three types of costs are therefore proposed to be earmarked as a minimum for the National Platform to become operational:

- the salary of a permanent secretary of the National Platform, estimated at 100,000 Euro/year.
- A budget to cover the costs of the logistics of organising meetings, estimated at 100,000 Euro/year.
- A budget to cover costs of international coordination and networking, estimated at 50,000 Euro/year.

Measure 3: Creation of a National Registry for Rare Diseases

The IPH-WIV is an organisation that could be responsible for the Registry. This institution has the expertise and has estimated the cost based on two factors: the number of variables and the potential number of patients. Comparing these two factors with the experience of running the registry for cystic fybrosis, gives an investment budget (start-up) of below 25.000 Euro and operating budget each year that could be up to 200,000 Euro.
This budget does not take into account the cost of data entry that would be decentralised in the CE and CRD. This activity will need financing either by patient/entry (as used for CF) or as part of the global financing of the CE and CRDs (examples exist in conventions). Because of the limited number of patients and of variables, this cost is estimated at max 15% of the running cost of the registry.

Running a central registry should also be considered as a tool to serve as a basis to link various existing, or to be created, registries for specific diseases.

Measure 4: Creation of a national portal website with actual and validated information

The costs for the portal website (on the basis of two offers) have been estimated at:

- Initial website development: between 22,000 and 37,000 Euro
- Operational yearly cost (maintenance, debugging, updating and server hosting): between 7,500 and 20,700 Euro/year
- 1 FTE for content management: 70,000 Euro/year (0.5 FTE for each community)

The costs included in the budget are therefore:

- an investment cost of 30,000 Euro for the initial design and set-up of the portal site
- an operating expenditure of 100,000 Euro/year, which would for 70% cover a salary cost.

Measure 5: Support for Orphanet Belgium and translation

For Orphanet Belgium support:

- 1 FTE for content management: 70,000 Euro/year (0.5 FTE for each community)

For translation of Orphanet into Dutch, several possibilities exist. Orphanet might receive European funding for translating the website (or parts of it) in Dutch. In that case no specific National Belgian funding is needed. If Orphanet does not receive this funding, different scenarios might apply, dependent on which content will be translated:

- Full translation of Orphanet: 150,000 Euro + 2,000 Euro per consecutive year
- Translation of abstracts (patient relevant information): 70,000 Euro + 1,000 Euro per consecutive year.

The costs included in the budget are therefore:

- an investment cost of 70,000 Euro for the translation of the patient-relevant data of the Orphanet website
- an operating expenditure of 75,000 Euro/year, which would cover a salary cost and provide for a budget of 5,000 Euro/year for translation and other expenses.

Comment on measures 2 to 5 with regard to staff

All three measures would imply the recruitment of staff members. These staff members need to be hosted inside another organisation in order to have a physical and social infrastructure.
Only the direct cost[50] of the staff is included, as mentioned above.

It would be a clear advantage to host these few staff members into the same organisation:
Creating a team feeling and motivation to work towards common goals.
Sharing of expertise and capacity between the different functions.
Better management and control.
The WIV-IPH, as obvious host for the Registry, would make a natural choice. The secretary-general of the Platform could act as manager of this small team.
In case this is not possible, one should take into account there will be an additional cost for coordination and management as well as overheads.

Measure 6: Change the system to allow DNA-samples and not patients to be tested abroad

The budget impact of this measure will probably be between 0.5 and 1 million Euro.

The basis of this calculation is an inventory done by the eight Centres for Human Genetics in Belgium for the year 2007: 846 tests were performed abroad at a cost of 430,000 Euro.

The lower end of the estimate is based on 1,000 samples / year at an average cost of 500 Euro/sample.
The higher end of the estimate is based on an increase in volume to 2,000 and a similar average cost/test/sample.

This measure should be combined with measures on standardisation of quality and as part of this, of purchasing decisions for tests. The procedure to choose suppliers and negotiate prices with these suppliers needs to be "coordinated" to ensure both the quality of the test and service (e.g. only accredited labs) as the cost (price charged, cost of transport taken into account).
If this is not done, neither the cost to the health insurance system nor the quality of the service to patients will be optimal.

50 *Direct cost means the Gross salary cost and all the costs for the employer directly linked to the person employed (social security charged to the employer). No overhead costs are included (housing costs, computer, telecom, supervision, …).*

Measure 7: Organise a coordinated approach for non-DNA diagnostic testing

The budget impact will probably correspond to the cost of a study to be launched to make the inventory. This budget has not been estimated. A standard budget of 75,000 Euro is therefore included in the overview, pending the establishment of terms of reference that will allow a better estimate.

Measure 8a: Setting up a system for early access including early temporary reimbursement of orphan drugs

The budgetary impact of the measure is difficult to estimate, as it depends on the actual behaviour of the pharmaceutical companies. The system should however make Belgium more attractive to introduce medicine faster to the market.
Taking into account the experience up to now with orphan drugs and the expectation that approximately 10 new drugs would enter the market each year, this measure "could" generate an increase for the orphan drugs cost of 5 to 10 million Euro / year (or 8 to 15% taking 2008 as a basis). This would be a one-off extra cost.

Measure 8b: Belgium to take a leading role to boost EU-level initiatives in relation to early access

This measure should not generate direct budgetary impacts (on top of what is estimated for measure 6a) and in the longer term, only net savings as EU level cooperation means more efficiency. It does however imply continued attention at policy level and resources to actively participate in and eventually lead EU level initiatives.

Measure 9a: Ensure that raw materials used to treat rare diseases can be used legally

The actual cost consists in performing analysis on the raw materials and producing certificates based on this analysis. This should be a rather small cost, but a budget should be made available to the National Platform to ensure analysis is performed on each batch, and certificates can be made available.
No concrete estimate could be done at this stage (volumes are unknown), but an annual budget of 25,000 Euro should cover this type of costs and miscellaneous costs the National Platform might generate.

Measure 9b: Belgium to propose a change in the criteria used to grant orphan designation at EU level when appropriate raw material is available and used

There is no budget impact for this measure.

Measure 10: Start a detailed inventory of off label use of drugs for rare disease indications

The budget impact will probably correspond to the cost of a study to be launched to set up a system for data collection and make a first analysis of data collected. This budget has not been estimated.
A standard budget of 75,000 Euro is therefore included in the overview, pending the establishment of terms of reference that will allow a better estimate.

Measure 11: Provide the potential for home treatment with orphan drugs under clear conditions

Home treatment leads to lower costs for the patient as the patient does not have to go to the hospital. This impact is a direct financial impact (cost of travel), but has other dimensions, especially time saved that can be productive time (for both the patient and a relative, and their employers).

In terms of impact on the health insurance budget, this very much depends on how the home treatment is organized. If a nurse is travelling instead of a patient, the actual cost to the health insurance budget will be higher.
Based on the logics behind this measure and the conditions as described, one can expect the actual budget impact for the health insurance will be neutral to slightly lower. A cost-neutral impact is put as a conclusion.

Forecast

The two tables below provide a first estimate of the costs of the measures proposed over a time-frame 2010 – 2015.

They are based on two different scenarios and the analysis described above.

The key elements of the scenarios are:

- Scenario 1:
— Slower in identifying patients. This can be because of lack of "success" of the Plan in reaching patients with rare diseases, or linked to a limitation in selecting Centres of Expertise. This scenario is based on the assistance of an "additional" 5,000 patients in 2012, and slightly less than 10,000 in 2015.
— All budgets linked to the management and implementation of the National Plan are "fixed" over the period.

- Scenario 2:
— Faster in identifying patients. This can be because of a higher "success" of the Plan in reaching patients with rare diseases, or linked to less restrictions in selecting Centres of Expertise. This scenario is based on the assistance of an "additional" 6,000 patients in 2012, and slightly less than 15,000 in 2015.
— The budget available to the National Platform to perform its management and implementation tasks is regularly increasing over the period, allowing to hire more staff, or to outsource specific tasks.

- Common to both scenarios:
— No inflation effect is taken into account.
— The one-off budgetary impact of early access and reimbursement of orphan drugs is spread over two calendar years.
— A budget for studies is foreseen for the National Platform. This is only partially justified by the measures above (two studies, both scheduled in 2010), but is considered necessary as the National Platform will need to organize monitoring and evaluation of this first phase of the Plan at regular intervals.
— A fast implementation: staff operational from January 2011, and preparatory activities in 2010: prepare call for CCRDs and CEs; launch studies (measures 7 and 10) in 2010 to still have an input for the second phase of the Plan; development of registry, portal web site and translation of Orphanet.

scenario 1						
	2010	2011	2012	2013	2014	2015
Costs to the health insurance system						
1,1 creation of CE		5.000.000	10.000.000	15.000.000	17.000.000	19.000.000
1,2 creation of CCRD		500.000	1.000.000	1.000.000	1.000.000	1.000.000
8, early access and temporary reimbursement		3.500.000	3.500.000	0	0	0
6, cross-border dna testing		500.000	1.000.000	1.000.000	1.000.000	1.000.000
sub-total		9.500.000	15.500.000	17.000.000	19.000.000	21.000.000
Costs linked to the National Plan management and implementation						
2. costs linked to National Platform RD	50.000	250.000	300.000	300.000	300.000	300.000
3. National registry	25.000	200.000	200.000	200.000	200.000	200.000
4. Portal	30.000	100.000	100.000	100.000	100.000	100.000
5. Orphanet Belgium	70.000	100.000	100.000	100.000	100.000	100.000
9. raw materials		25.000	25.000	25.000	25.000	25.000
cost of studies	150.000	75.000	75.000	75.000	75.000	75.000
sub-total	325.000	750.000	800.000	800.000	800.000	800.000

scenario 2						
	2010	2011	2012	2013	2014	2015
Costs to the health insurance system						
1,1 creation of CE		5.000.000	12.000.000	20.000.000	25.000.000	30.000.000
1,2 creation of CCRD		500.000	1.000.000	1.200.000	1.400.000	1.500.000
8, early access and temporary reimbursement		3.500.000	3.500.000	0	0	0
6, cross-border dna testing		500.000	1.000.000	1.200.000	1.400.000	1.600.000
sub-total		9.500.000	17.500.000	22.400.000	27.800.000	33.100.000

Costs linked to the National Plan management and implementation						
2. costs linked to National Platform RD	50.000	250.000	300.000	350.000	400.000	400.000
3. National registry	25.000	200.000	200.000	200.000	200.000	200.000
4. Portal	30.000	100.000	100.000	100.000	100.000	100.000
5. Orphanet Belgium	70.000	100.000	100.000	100.000	100.000	100.000
9. raw materials		25.000	25.000	25.000	25.000	25.000
cost of studies	150.000	75.000	75.000	75.000	75.000	75.000
sub-total	325.000	750.000	800.000	850.000	900.000	900.000

Comment:
These scenarios and budget impact analysis take only direct effects into account. There might be indirect impacts both in terms of savings (consequence of better health) as in terms of costs (longer life of patients, more genetic tests performed as more patients identified and diagnosed).

Conclusions

The set of measures proposed in phase 1 of the National Plan implies the availability of a budget worth 1 Million Euro / year to manage and implement the Plan.

It is also expected to generate between 9 Million (1st year) and 30 Million Euro/year (5th year, highest scenario) of additional costs to the health insurance system.

These amounts have to be put into perspective:

- the Plan will also generate significant savings e.g. because of wrong or lack of diagnosis; they are not taken into account in the estimates;
- the Plan has impacts mainly on patients and their families in terms of longer life and quality of life. These impacts on patients can translate into economic benefits for society;
- they cover the measures proposed in phase I; the picture will be different with measures proposed in phase II;
- estimates are tentative due to the lack of objective information available to actually make this type of forecast:
- many of the measures still need to be fine-tuned at the technical level before a good estimate can be made
- there is no reliable source to estimate the actual number of patients suffering from rare diseases
- the highest cost comes from the setting-up of the network of Centres of Expertise. This can potentially be "managed" from a budget impact point of view by starting / stopping contracts with Centres of Expertise, and putting limitations in terms of patients that are eligible.

ADDENDUM 4 – COMPOSITION OF THE MANAGEMENT COMMITTEE OF THE FUND RARE DISEASES AND ORPHAN DRUGS – PHASE I

Chairman
Jean-Jacques Cassiman, Professor Emeritus

Vice-Chairman
Marc Abramowicz, Membre du Conseil supérieur de la Génétique humaine, Chef de Clinique Centre de Génétique Humaine, Hôpital Erasme – ULB,

Members:
Yolande Avontroodt, Volksvertegenwoordiger, Voorzitter van het Algemeen Beheerscomité van het RIZIV
Marc Bogaert, Voorzitter College van Geneesheren voor Weesgeneesmiddelen bij het RIZIV
Vincent Bours, Chef de service Département Génétique ULg
Klaartje Bruyninckx, Ilse Weeghmans, stafmedewerker en coördinator Vlaams Patiëntenplatform VPP
Lut De Baere, Voorzitster Rare Diseases Organisation Belgium (RaDiOrg.be)
Ri De Ridder, Directeur-generaal Dienst Geneeskundige Verzorging RIZIV
Marc Dooms, Lid Belgische Vereniging van Ziekenhuisapothekers, Apotheker UZ Gasthuisberg Leuven
François Eyskens, Diensthoofd Provinciaal Centrum voor Opsporing van Metabole Aandoeningen Antwerpen
Geneviève Haucotte, Secrétaire du Comité Scientifique des Maladies Chroniques et Affections Spécifiques INAMI
Viviane Gendreike, Présidente suppléante du Collège des médecins-directeurs INAMI
Pol Gerits, Adjunct van de Directeur-generaal Organisatie Gezondheidszorgvoorzieningen FOD Volksgezondheid, Veiligheid van de Voedselketen en Leefmilieu
Herwig Jansen, Coördinator Belgisch Mucoviscidose Register – Afdeling Epidemiologie, Wetenschappelijk Instituut Volksgezondheid
Céline Leto, Conseillère Cabinet de la Ministre Laurette Onkelinx (from 01/10/2009)
André Lhoir, Agence fédérale des Médicaments et des Produits de santé, Membre du COMP (EMA)
Sophie Maes, Experte Cabinet de la Ministre Laurette Onkelinx
Leo Neels, Herman van Eeckhout, Algemeen directeur en adjunct algemeen directeur Pharma.be
Gustaaf Nelis, Vera De Groof (until 01/12/2009) Intermutualistisch Agentschap
Mattias Neyt (until 30/09/2009), Expert Economic Analysis, Federaal Kenniscentrum voor de Gezondheidszorg
Claude Sterckx, Président, Ligue des Usagers des Services de Santé LUSS
François Sumkay, Agence Intermutualiste
Erik Tambuyzer, Voozitter Werkgroep Zeldzame Ziekten en Weesgeneesmiddelen Pharma.be
Marie-José Tassignon, Raad van Universitaire Ziekenhuizen van België
Chris Van Hul, Geneesheer-Expert Landsbond van Onafhankelijke Ziekenfondsen
Tinne Vandensande, Adviseur Koning Boudewijnstichting

ADDENDUM 5 – COMPOSITION OF THE WORKING GROUPS – PHASE I

Workpackage 1: Patient Registries/Databases

Chairman:
Herwig Jansen, Coördinator Belgisch Mucoviscidose Register – Afdeling Epidemiologie, Wetenschappelijk Instituut Volksgezondheid

Members:
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Corinne De Laet, Chef de Clinique Adjoint Hôpital Universitaire des Enfants Reine Fabiola HUDERF, Bruxelles
Marion Delcroix, Kliniekhoofd Interne Geneeskunde Pneumologie, UZ Leuven
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Elfriede Swinnen, Lid Orphanet Belgium, Wetenschappelijk medewerker Centrum Menselijke Erfelijkheid KULeuven

Workpackage 2: Identifying hidden costs for patients/ roadmap for patients

Chairman: Claude Sterckx, Président Ligue des Usagers des Services de Santé LUSS

Members:
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Jean-Jacques Cassiman, Professor Emeritus
Luc Detavernier, Expert Matières régionales et communautaires, Union Nationale des Mutualités Libres
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Geneviève Haucotte, Secrétaire du Comité Scientifique des Maladies Chroniques et Affections Spécifiques INAMI
Evelyne Hens, Stafmedewerker Nationaal Verbond van Socialistische Mutualiteiten
Cécile Minet, Centre de Génétique humaine, Institut de Pathologie et de Génétique, Gosselies
Gustaaf Nelis, Vera De Groof (until 01.12.2009) Intermutualistisch Agentschap
Pascale Ribaï, Centre de Génétique humaine, Institut de Pathologie et de Génétique, Gosselies
Elfriede Swinnen, Lid Orphanet Belgium, Wetenschappelijk medewerker Centrum Menselijke Erfelijkheid KULeuven,
Nathalie Vandenbroucke, Stafmedewerker Vereniging Personen met een Handicap VFG
Chris Van Hul, Geneesheer-Expert, Gezondheidszorg en Vergoedingen, Landsbond van Onafhankelijke Ziekenfondsen

Workpackage 3: Information for patients, health professionals and the public

Chairman: Klaartje Bruyninckx, Stafmedewerker Vlaams Patiëntenplatform VPP

Members:
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Lut De Baere, Voorzitter Rare Diseases Organisation RaDiOrg
Vera De Groof (until 01.12.2009) Afgevaardigde Intermutualistisch Agentschap
Tim De Kegel (until 30.09.2009) , Secretaris-Generaal Pharma.be
Marc Dooms, Belgische Vereniging van Ziekenhuisapothekers, Apotheker UZ Gasthuisberg Leuven
François Eyskens, Diensthoofd Provinciaal Centrum voor Opsporing van Metabole Aandoeningen Antwerpen
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Elfriede Swinnen, Lid Orphanet Belgium, Wetenschappelijk medewerker Centrum Menselijke Erfelijkheid KULeuven,

Workpackage 4: Centres of competence, Centres of expertise, and national collaboration (including neonatal screening)

Chairman: Jean-Jacques Cassiman, Professor Emeritus

Vice-Chairman: François Eyskens, Diensthoofd Provinciaal Centrum voor Opsporing van Metabole Aandoeningen Antwerpen

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Vincent Bours, Chef de service Département Génétique, ULg
Piet Calcoen, Medisch directeur DKV
Pieter Vandenbulcke, Afgevaardigde Vlaams Agentschap Zorg en Gezondheid
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Elfriede Swinnen, Lid Orphanet Belgium, Wetenschappelijk medewerker Centrum Menselijke Erfelijkheid KULeuven,
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René Westhovens, Ondervoorzitter Belgische Vereniging Reumatologie, Reumatoloog UZ Gasthuisberg Leuven

Workpackage 5: Access to and costs of diagnosis, medication, treatment and patient management

Chairman: Erik Tambuyzer, Voorzitter Werkgroep Zeldzame Ziekten en Weesgeneesmiddelen Pharma.be

Vice-Chairman: Marc Bogaert, Voorzitter College van Geneesheren voor Weesgeneesmiddelen bij het RIZIV

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Geneviève Haucotte, Secrétaire du Comité Scientifique des Maladies Chroniques et Affections Spécifiques, INAMI
Céline Hermans, Pharmacienne en charge des dossiers du Collège des Médicaments Orphelins, INAMI
Hilde Stoop, Afgevaardigde door de werkgroep Zeldzame Ziekten en Weesgeneesmiddelen van Pharma.be/ Bio.be
Françoise Stryckman, Conseiller Scientifique Remboursements, Direction Politique des Médicaments Pharma.be
François Sumkay, Agence Intermutualiste
Chris Van Hul, Geneesheer-Expert, Gezondheidszorg en Vergoedingen, Landsbond van Onafhankelijke Ziekenfondsen

The Fund Rare Diseases and Orphan Drugs

The Fund Rare Diseases and Orphan Drugs arose from the Steering Group for Rare Diseases and Orphan Drugs, which organised the first Belgian symposium on orphan drugs in the Parliament in 2006. The Fund is managed by the King Baudouin Foundation. It brings together all stakeholders in Belgium and endeavours to promote a coherent, consistent policy to enhance the quality of life of patients affected by a rare disease and those around them.

The Fund aims to take a structural, integrated approach to rare diseases, focusing on diagnosis and seamless care, and on research into and the development of appropriate medicines and treatments.

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King Baudouin Foundation

Working together for a better society

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