EUROPLAN
European Project for Rare Diseases National Plans Development
Coordinated by the Italian National Centre for Rare Diseases
Italian National Institute of Health
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VSOP DUTCH GENETIC ALLIANCE

EURORDIS
Rare Diseases Europe

THE NETHERLANDS

EUROPLAN NATIONAL CONFERENCE

FINAL REPORT

14-15 November 2013, The Hague

EUCERD
Joint Action

FOREWORD

The EUROPLAN National conferences are aimed at fostering the development of a comprehensive National Plan or Strategy for Rare Diseases addressing the unmet needs of patients living with a rare disease in Europe.

These national plans and strategies are intended to implement concrete national measures in key areas from research to codification of rare diseases, diagnosis, care and treatments as well as adapted social services for rare disease patients while integrating EU policies.

The EUROPLAN National conferences are jointly organised in each country by a National Alliance of rare disease patients' organisations and EURORDIS – the European Organisation for Rare Diseases. For this purpose, EURORDIS nominated 10 EURORDIS-EUROPLAN Advisors - all being from a National Alliance - specifically in charge of advising two to three National Alliances.

EUROPLAN National conferences share the same philosophy, objectives, format and content guidelines. They involve all stakeholders relevant for developing a plan/strategy for rare diseases. According to the national situation of each country and its most pressing needs, the content can be adjusted.

During the period 2008-2011, a first set of 15 EUROPLAN National Conferences were organised within the European project EUROPLAN. Following the success of these conferences, a second round of up to 24 EUROPLAN National Conferences is taking place in the broader context of the Joint Action of the European Committee of Experts on Rare Diseases (EUCERD) over the period March 2012 until August 2015.

The EUROPLAN National Conferences present the European rare disease policies as well as the EUCERD Recommendations adopted between 2010 and 2013. They are organised around common themes based on the Recommendation of the Council of the European Union on an action in the field of rare diseases:

1. Methodology and Governance of a National Plan;

2. Definition, codification and inventorying of RD; Information and Training;

3. Research on RD;

4. Care - Centres of Expertise / European Reference Networks/Cross Border Health Care;

5. Orphan Drugs;

6. Social Services for RD.

The themes "Patient Empowerment", "Gathering expertise at the European level" and "Sustainability" are transversal along the conference.

A National Plan – and now?!

Dutch EUROPLAN Conference

November14th and 15th, 2013

Worldhotel Grand Winston, Den Haag/Rijswijk

CONTENT

GENERAL INFORMATION

Country	The Netherlands
Date & place of the National Conference	14 & 15 November 2013
Website	http://www.vsop.nl/nl/wat-doen-wij/zeldzaam/nationaal-plan
Organisers	VSOP
Members of the Steering Committee	Mr. Jan Benedictus, NPCF Mr. Bert Boer, CVZ Ms. Silvia van Breukelen, VSOP Ms. Martina Cornel, VUMC, Orphanet Mr. Jeroen Crasborn, Achmea Mr. Gerard Engel, FBG Mr. Jacob Hofdijk, Casemix Ms. Jolanda Huizer, ZonMw Mr. Cor Oosterwijk, VSOP Mr. John Roord, VUMC Ms. Liesbeth Siderius, SSSH Ms. Melanie Schmidt, NFU Mr. Cees Smit, expert-patient Ms. Anne Speijer, VSOP Mr. Anton de Wijer, Stichting Beter
Names and list of Workshops	WS 1 Implementation of the Dutch National Plan WS 2 European collaboration WS 3 Research and diagnostics WS 4 Quality of health care and life WS 5 Strengthening the patients' voice WS 6 Realisation of centres of expertise WS 7 Access to orphan drugs and health care
Workshop Chairs (and Rapporteurs, where applicable)	WS 1 Chair: Ms. De Visser Rapporteur: Ms. Monissen WS 2 Chair: Mr. Van Ommen Rapporteur: Mr. Oosterwijk WS 3 Chair: Mr. Wagemaker Rapporteur: Mr. Engel WS 4 Chair: Ms. Vroom Rapporteur: Mr. Dekkers WS 5 Chair: Ms. De Knecht – van Eekelen Rapporteur: Mr. Crasborn WS 6 Chair: Ms. Stoyanova - Beninska Rapporteur: Ms. Knoers WS 7 Chair: Ms. Rademaker Rapporteur: Mr. Van der Zeijden
APPENDIX	**List of participants and Programme**

GLOSSARY

AWBZ	Law Concerning Reimbursement of Special Health Care Needs
CBG: College ter Beoordeling van Geneesmiddelen	Medicines Evaluation Board
CvZ	Health Insurance Board
EUCERD	European Union Committee of Experts on Rare Diseases *(replaced by the EC Expert Group on Rare Diseases)*
FBG	Forum Biotech and Genetics
Gezondheidsraad	National Health Council
Het Kwaliteitsinstituut	Quality Institute
NFU	Dutch Federation of University Medical Centres
RVZ	Council for Public health and Health Care
SKMS, Kwaliteitsgelden Medisch Specialisten	Foundation Quality funding for Medical Specialist
Stuurgroep Weesgeneesmiddelen	The Dutch Steering Committee for orphan drugs
STZ, Stichting voor Topklinische Zorg	Foundation for top clinical care hospital.
Tweede Kamer	House of Commons
VSOP	Dutch National Alliance for Rare Diseases
VWS	Ministry of Health, Welfare and Sport
WMO	Social Support Act
ZonMw	The Netherlands Organisation for Health Research and Development
ZonMw Klankbordgroep NPZZ	Dutch Sounding Board of the National Plan for Rare Diseases
Zorginstituut Nederland	Health Care Institute of the Netherlands
ZVW, Zorgverzekeringswet	Health Insurance Act

MAIN REPORT

PLENARY REPORT – OPENING SESSION

The program components of the conference were preceded by three videos, with two patients with a rare disorder and a mother of a child with a rare condition: Mr. Michael van der Linde has Haemophilia A., his little brother is also affected by a rare condition, namely Duchenne Muscular dystrophy. Ms. Sigrid Hendriks works as policy advisor at the VSOP and found out that she has Cushing's syndrome. The eldest son of Ms. Irene Caubo has Neurofibromatosis Type I.

VIDEO 1: TAKE US SERIOUSLY! The Netherlands has one million people with a rare condition. In this video, among other things, the question is asked where the expertise and therapists are located. This does not only go for The Netherlands, but for all of Europe. There needs to be more awareness of rare disorders. The availability of a treatment depends on the country and practice shows that Dutch patients are not stimulated to seek treatment abroad. These negative points ask for more cooperation and coordination within Europe. Michael van der Linde emphasises the need for scientific research. Not easy, since there are sometimes very few patients, which makes research more difficult. Therefore, also in the field of research, international cooperation is of great importance!

VIDEO 2: MORE WORK, BETTER LISTENING! In this second video, it is made clear that many rare disorders begin with a-specific symptoms. Sometimes the correct diagnoses is made after searching for years. Accidentally, or because of their great perseverance, patients sometimes find the right diagnosis. More cooperation, coordination and better communication (exchange of information) between health care providers can shorten the diagnostic search. Patients indicate that various care aspects affect their quality of life. It is not only a fast diagnosis and quality of care. For example, a preconception advice affects the quality of life of the patient with a rare condition, as well as posterity. The above mentioned aspects of care not only affect the quality of life of the patient, but also his whole surroundings; in particular the own family!

VIDEO 3: ON THE WAY TO THE BEST CARE FOR RARE! In the last video Ms. Irene Caubo addresses the impressive number of health care providers that is involved in caring for her son with neurofibromatosis type I. In the past, she asked her GP to coordinate the care for her son, as this was too much of a burden for her, next to the care for her son. The GP did not take up the coordination because he was questioning the necessity. As a mother, because of the number of health care providers, the variety of care and the large number of institutions involved, it is almost impossible to coordinate all the care. The development of a centre of expertise for the rare condition of her son is underway. The family looks forward to such a centre of expertise that not only provides the best care, but also will coordinate it. Michael van der Linde experiences himself that a good orphan drug can be crucial for the quality of life of a patient with a rare condition. It makes a big difference in the daily functioning: if not taken the patient is bedridden, but if taken, the patient can fully participate in society.

FIRST CONFERENCE DAY

WELCOME AND OPENING

Mr. Lekkerkerker opens the conference. He is former Chairman of the 'Stuurgroep Weesgeneesmiddelen' (the Dutch Steering Committee for orphan drugs) and President of the ZonMw Klankbordgroep NPZZ (Dutch Sounding Board for the national plan for rare diseases). He recalls the presentation of the National Plan for Rare Diseases (NPRDs) to the Minister of VWS (Health, Welfare and Sport) on 10 October 2013. Now, the emphasis is on how the parties involved cooperate further with the recommendations of the NPRD. In June 2009, the Council of EU (health) Ministers recommended to the member States the establishment, by the end of 2013, of a national plan or strategy. The Minister of VWS has asked the Stuurgroep Weesgeneesmiddelen in 2010 to initiate such a plan. From 2012 on, the coordination was in the hands of ZonMw (The Netherlands Organisation for Health Research and Development). The goal was, based on input from all field parties, to develop a realistic and practical plan for the short and longer term with proposals for various measures, health care, research and education. The timetable ranged from March 2011 till October 10, 2013:

- **March 2011:** Stuurgroep Weesgeneesmiddelen meeting, first draft with four topics
- **December 2011:** discussion in four working teams
- **April 2012:** hearing and call for input from stakeholders
- **August 2012:** first version, broad consultation) with stakeholders
- **April 2013:** second version, recommended six topics, written commentary round for all stakeholders
- **May 2013:** third version, followed by adoption
- **October 2013:** presentation to the Minister of VWS

The NPRD contains six chapters, which are all classified in the same way. First: what is already there? What runs well? Secondly, what is missing? And thirdly: Recommendations. It is important that the parties responsible have been identified and the first responsible party clearly is designated. The NPRD has, as discussed with the Ministry of VWS, no financial section.

Ms. Maria Martens is President of the VSOP and member of the House of Lords for the CDA (Christian Democrat Party). Also Ms. Maria Martens welcomes the attendees, in particular the foreign guests. She points out that without European cooperation there would not have been a NPRD. A lot of hard work has been put in and we can all be happy with the result. The discussion during this conference will not be about the details of the plan, but on the implementation and execution. What are the tasks of the leading parties? How can the plan lead to better care and quality of life for people with a rare condition? In order to make the patient the centre of this conference, each session will start with a patient video 'The voice of the patient'. Ms. Martens expresses her appreciation to the parents and patients who tell their story in these videos. Lastly, Ms. Martens also thanks the various sponsors of the congress for their support.

PLENARY PRENTATIONS

THE NPRD: AN IMPRESSIVE PIECE OF WORK -MR. FRED KRAPELS

Mr. Fred Krapels is Deputy Director curative care (CZ), Ministry of VWS (Health, Welfare and Sport)

Mr. Krapels speaks on behalf of the Minister of VWS (Health, Welfare and Sport). The Government is usually not concerned with ' rare (diseases) '; in fact, there is no mention of rare since 6-8% of the Dutch population has a rare condition; a million people. In 1996, the Dutch Government already consulted all interested parties on how rare diseases can be addressed. A few years later, the former minister, Ms. Borst, founded the Stuurgroep Weesgeneesmiddelen (Steering Committee for Orphan Drugs) and at the Ministry of VWS, the department for Medicines and Medical Technology (GMT) became responsible for this file. Gradually, it became apparent that a broader approach was needed. The familiarity with orphan diseases among professionals, health insurers and the general public, increased. Important is the European agreement in 2009 to gather and disseminate knowledge on rare diseases in Europe and realize a broad European approach. Europlan, the '*European Project for Rare Diseases National Plans Development*', was set up for this purpose. In this context, networks of centres of expertise will be set up: Rare Disease European Reference Networks (RD ERNs). The Orphanet database provides a good basis for the designation of the centres. The Minister of VWS has appointed ZonMw to coordinate the preparation of an NPRD. The ZonMw NPRD Klankbordgroep (Sounding Board) has delivered an “impressive amount of work” according to the Minister. We now have a clear plan that is a thorough and an elaborate basis for further measures. The conference gets a scoop: as Mr. Krapels speaks, a letter from the Minister of VWS on the NPRD is presented to the Tweede Kamer (The House of Commons). He goes into detail on a number of points from this letter:

IDENTIFYING CENTRES OF EXPERTISE

On the recommendation from the NPRD to VWS on the designation of centres of expertise: for VWS, this is an essential point, but the government will not take this role itself. Mr. Krapels reports that the Minister has asked the NFU (Dutch Federation of University Medical Centres) to take on the management task. Quote: *'A main task for the implementation of the NPRD is the development of a network of centres of expertise. These centres bring together knowledge and expertise in the field of rare diseases, develop protocols and guidelines, coordinate research and ensure adequate reference of patients within and outside The Netherlands. The centres must comply with the standards set by the European Union to such centres to be compatible with the European network for rare diseases (European Reference Networks). I have requested, and found willing, the NFU to take on the coordination, the design, implementation and maintenance of the national network' (letter to the House of Representatives, 14 November 2013, p. 3).*

The NFU can take on this task because the UMC's (University Medical Centres) already have much knowledge and many centres of expertise within the UMC’s meet the criteria. In alignment with Orphanet, the European website for rare diseases and orphan drugs, the NFU has identified which centres in the UMC’s have what expertise for which rare diseases. The Minister finds such an inventory a first step towards transparency and continuity. That is why she does not accept the recommendation of the NPRD to appoint the centres of expertise on the basis of the Wet op Bijzondere Medische Verrichtingen (WBMV: Law on Exceptional Medical Procedures). There will be no legal designation. In 2014 the Minister will send a memo to the Tweede Kamer (House of Commons) about the positioning of the University Medical Centres and their new tasks, in particular those in the field of rare diseases. The Minister will organize two annual meetings with relevant parties to establish a national network of centres of expertise and to monitor the implementation of the NPRD. Therefore, the NFU has no exclusive right in the field of implementation of the NPRD and the role of the centres of expertise.[1]

[1] Post-conference note: per September 2014, on request of the Minister of Health, NFU and VSOP started the assessment of about 370 candidate-Centers of Expertise in the Netherlands, including the opinion of related patient organization. In November 2014, no bi-annual meetings had taken place yet.

SCREENING

A second recommendation from the NPRD is the evaluation of the range of blood spot testing and, where necessary, make adjustments. The Minister has asked the Gezondheidsraad (National Health Council) for advice in 2012, this advice is expected by the end of 2014.

ADAPTION WMO

A 3rd recommendation is the adaption of the Wet Medisch-wetenschappelijk Onderzoek (WMO: Law on Medical-Scientific Research) in such a way that research can be performed on mentally disabled people. A change in the law has been send to the Tweede Kamer (House of Commons).

CROSS-BORDER CARE

The NPRD calls for the implementation of European legislation on cross-border care. This has happened last October with the Dutch transposition of the EU directive patients ' rights in cross-border care.

POLITICAL AGENDA

Mr. Krapels stresses that rare disorders are now firmly on the political agenda, but the Government cannot do this alone. It calls on all parties in the field to address this now. The great interest in this conference gives us confidence in the future! At the end of his speech, Mr. Krapels congratulates the VSOP with the organization of the conference.

DISCUSSION

Question: How do individual, small patient organisations maintain contact on a professional level with the NFU regarding the centres of expertise? *Answer:* It is unknown what the representation of patient groups in the half-yearly consultations will look like. Mr. Krapels admits that the fact that subsidies to patients ' organisations have been reduced, has not made it easier, moreover in the short term, further resources are not foreseen.

Question: concentration of centres of expertise is needed. Does the Minister designate the centres of expertise? *Answer*: Yes, concentration is needed, but the Minister is confident that the UMC's will be able to work this out together. Should this fail, the Minister will designate centres of expertise if necessary. It is up to the field itself to reach an agreement.

Question: Does the Centre of Expertise have to be a real centre? It can also be a network, because it is mainly about cooperation. *Answer*: indeed, and the centres have the expertise available to best organize a network.

EUROPEAN RD RECOMMENDATIONS AND UK STRATEGY - MR. GEOFFREY CARROLL

Mr. Geoffrey Carroll is Medical Director of the Welsh Health Specialised Services. He recounts how his first introduction to rare disorders in South Africa came to be. It concerned far descendants of Dutchman Gerrit Jacob van Deventer, who came to Cape Town at the end of the 17th century and who suffered from the genetic disorder Porphyria.

EUROPEAN CONTEXT

In Europe, a series of documents in the field of rare diseases have been developed. Mr. Carroll mentions the Council Recommendation on an Action in the Field of Rare Diseases (2009/C 151/02, 8 June 2009), the Directive on the application of patients ' rights in cross-border healthcare (2011/24/EU, 9 March 2011) and the Rare Disease EUCERD recommendations on European Reference Networks (ERNs, 31 January 2013).

In Europe, the participation of centres of expertise in the ERNs is encouraged, but with due regard for national laws and regulations. The European Commission supports the Member States in the development of ERNs between care providers and centres of expertise, in particular in the field of rare diseases. The EUCERD Recommendations will be used by a committee that is drawing up criteria for setting ERNs. The relationship between ERNs and the Cross-Border

Healthcare Directive still deserves further development. Also in the field of financing there are still many ambiguities. Medical professionals could also make much better use of Orphanet: a practical app would be desirable.

ROLE OF THE ERNS

The ERNs provide a framework for the organization of the treatment of patients with a rare disorder. The national centres of expertise are members of an ERN. Within an ERN, one leading centre should be designated. An ERN must be active in the field of, amongst others, registrations, quality criteria for laboratories, development of guidelines and standards, training and education, personalised medicine, procedures for evaluation, indicators, information provision, referral across borders and ' telemedicine'. The ERNs must be created from existing and new centres to form a functional unit. It is very important that there is a passionate involved and respected leader. Cooperation will need to be sought with various national and European stakeholders such as: specialized care handlers, specialized social workers, patients ' organisations and '*expert patients'*, diagnostic laboratories and relevant research groups. According to Mr. Carroll, a centre of expertise should focus on conditions that are difficult to diagnose.

FINANCING

The financing of national centres of expertise is the responsibility of each Member State. This can create a stability problem. Specific costs for infrastructure maintenance (coordination and networking activities) of the European network should, however, be part of sustainable financing from European funds. That funding should be adequate for at least five years and is related to the number of patients, the number of centres in the network and the number of disorders that the network covers.

DIFFERENCES BETWEEN THE MEMBER STATES

There are large differences in numbers of centres of expertise that have been designated by the different Governments in Europe, ranging from 215 in Italy to 16 in Norway (and currently none in The Netherlands). Furthermore, Member States use many different systems for recognition of a centre of expertise. There is also a choice between specialized or general centres, as well as treatment or research, attention to technology and intervention. Political considerations and national or regional interests also play a part in this allocation.

CRITERIA FOR CENTRES OF EXPERTISE

A centre of expertise should use quality indicators to measure the medical outcomes, effects of orphan drugs and patient satisfaction. The UK has about 70 centres of expertise and monitoring is set up well, despite the fact that there are no European criteria. Collaboration with patient organisations is important, as well as collaboration with other centres at national, European and international level (ERN). This does not develop spontaneously: a systematic approach and coordination of cooperation between all health care services, also internationally, is necessary! The UK priorities are: quick and timely diagnoses, education and training, national screening committees, registration and care coordinators.

REGISTRIES

Mr. Carroll stresses the importance of records and data-sharing *(*Wales has appointed special consultants), for example including determining start-stop criteria in the use of (expensive) orphan drugs and other issues associated with cost effectiveness (HTA). The effects on the organization of care should be taken into account.

There are about 600 disease registries in Europe, mostly academic and related to conditions for which an innovative treatment is or will be on the market. Registries must be as flexible as possible so they can be used in the future. Registries must be both accessible to the local health care as well as for international scientific research. It is important that both patients ' organisations and industry are involved in the establishment and operation of registries. To prevent fragmentation smart clusters are necessary, for example based on genetics.

DISCUSSION

Question: How is the selection process for a centre of expertise in the UK organised? *Answer*: the choice for a centre is jointly determined by a group of practitioners. Northern Ireland, Scotland and Wales are much smaller than England and in that respect the 'customers' of English centres of expertise. *Remark:* you described how the doctor travelled to the patients and not the other way around. It is very important to organize it this way.

Comment: With modern means of communication a lot is possible. One does not need to be present physically for everything. The feeling of shared care is psychologically very important. Some have complained that there is too little contact between the local physician and the centre. The patient disappears out of the family doctor's sight. Personal contact is important.

AFTERNOON PLENARY PRESENTATIONS

CARE FOR RARE DISORDERS - MS. CARLA HOLLAK

Ms. Carla Hollak is Professor of metabolic diseases in the AMC (Amsterdam University Medical Centre). She was trained as a haematologist and gradually became involved in research into Gaucher disease, a Lysosomal Storage disease for which the first enzyme replacement therapy has been developed. She also researches other inherited metabolic diseases. The AMC is home to the Centre of expertise for Gaucher, with extensive knowledge on enzyme defects and therapeutic research, and has a European Centre of Expertise (European Working Group on Gaucher Disease) and thereby international contacts. She stresses that national and international cooperation in the field of rare diseases is an absolute condition in achieving goals, but at the same time not easy: a huge challenge. If enzyme replacement therapy is started early, patients can lead an almost normal life. It helps that there is one Centre for Gaucher in The Netherlands with clear agreements about referrals. However, late referrals still occur. This can be because of the unfamiliarity with the Centre of Expertise or stubbornness of the doctor who does not want to lose a patient. The input of industry can have a positive or negative impact; negative if activities are organised outside the Centre of Expertise or if the Centre of Expertise is not involved and there is no cooperation. Setting up one Gaucher registry has failed: because of the influence of the pharmaceutical industry there are now three registries. Should the biopharmaceutical industries work better together, scarce patients would not be distributed in the different registries of biopharmaceutical companies and therefore better data could be generated.

"LET'S SHARE OUR PATIENTS"

Mucopolysaccharidosis Type 1 is a rare Lysosomal Storage disease that involves damage to the skeleton, respiratory tract and sometimes the brain. In The Netherlands, there are 50-60 patients. Since 2003 there is enzyme replacement therapy for treatment of non-neurological symptoms. There are clear agreements about the clinical genetic diagnostics and referral via centres and the Vereniging Erfelijke Stofwisselingsziekten Nederland ESN (The Dutch Association for Inherited Metabolic Diseases). Although initially a joint protocol for treatment of MPS I patients was developed, there is distribution in two centres (ErasmusMC Rotterdam and AMC Amsterdam). As far as this is concerned, the academic world should also put its own house in order: Let's work together and allow the sharing of patients, this would be better for everyone!

FABRY DISEASE

The disorder of Fabry is caused by an X-linked deficiency of the enzyme Alpha-galactosidase A, which leads to accumulation of glycolipids in the vessel wall, heart and kidneys. There is one national centre of expertise in the AMC and referral is usually good because of the good reputation of the centre. Even here it goes wrong sometimes: for example if diagnostics do not take place in the AMC, causing a late referral to the centre. With the HAMLET-study, further improvement of international criteria for diagnostics is currently being worked on. With a ZonMw-grant, retrospective data collection of treated and untreated Fabry-patients in three EU centres of expertise has recently been set up. In 2001, the European Commission authorized two enzymes as an orphan drug: Fabrazyme by Genzyme and TKT's Replagal/Shire (the treatment costs are both about € 200,000 per patient per year). Because of this, two

pathways have been developed by two industries with the same activities, working parallel but separate from each other. A waste of time and not good for the patient [2] Inadequate funding of centres of expertise is a common and chronic problem causing that substantial tasks of a centre cannot be realized, especially in the field of research and cooperation. Their funding should therefore be organised much better. Collaboration in care and care research is the right ambition, but that takes time and money which is not provided in regular funding of care.

BUNDLING OF EXPERTISE

EUCERD recommended the following about cooperation in Centres of Expertise:

- Organisation of collaborations to assure the continuity of care between childhood, adolescence and adulthood.
- Organisation of collaborations to assure the continuity of care between all stages of the disease.
- Links and collaboration with other centres of excellence at national, European and international level.
- Links and collaboration with patient organisations where they exist.

There are some best practices, for example, the (inter) national cooperation in Gaucher disease in AMC and in Pompe disease in ErasmusMC as a Centre of Expertise. On a national level, areas for improvement of cooperation are: alertness, referral, better cooperation with one centre in the lead, one captain on the ship. International bundling of expertise is necessary to solve important questions. These questions are about genotype/phenotype, directives, diagnostics, pathophysiology, treatment guidelines and evaluation of the effectiveness of orphan drugs. The complexity and sluggishness of European and international cooperation should not be underestimated.

For the Dutch situation Ms. Hollak has the following recommendations:

- follow the criteria of EUCERD and NPRD;
- translational research must be guaranteed in a centre of expertise: care must be connected to research;
- one leading centre: when there is competition between multiple centres of expertise: let each submit a plan, then have it reviewed by external experts who appoint only one centre of expertise;
- involve the patient organisation in audits of centres;
- there should be a real estimate of all costs associated with the functioning of a centre of expertise, and it needs to be reimbursed as such;
- Centres of Expertise that include conditions for which there is an effective therapy or medicine, must adopt at least one other condition for which it there is no medicinal therapy.

DISCUSSION

Question: Is ' benchmarking ' possible with regard to existing guidelines for Gaucher? *Answer*: In Israel there is a lot of experience with Gaucher, so we should mirror ourselves on Israel for Gaucher.

Question: How are guidelines for Fabry matched? *Answer*: In The Netherlands, guidelines for Fabry have been made. We are now working within a European working group and we want to get consensus on start and stop criteria. Further European harmonisation is still in its infancy.

A NATIONAL PLAN. AND NOW?! -MS. ELIZABETH VROOM

Ms. Elizabeth Vroom is mother of a son with Duchenne muscular dystrophy and Chair of the Duchenne Parent Project. The Duchenne Parent Project has been set up to accelerate the search for a cure or treatment for Duchenne muscular dystrophy, by sponsorship, international cooperation and accelerated exchange of information. The Foundation also organizes activities around improving care, diagnostics and developing tools.

DIAGNOSIS

Without diagnosis no care. One of the first points addressed by Ms. Vroom, is why neonatal blood spotting is not used for the diagnostics of many more disorders. The current criteria that only 'treatable' diseases are included in blood spotting is a very unsatisfactory argument for parents: they want a diagnosis as early as possible. Research shows that the 'pink cloud', which parents have if they do not yet know the diagnosis but think they have a healthy child, will not last long. Around the age of 5 months, parents already start to worry about their child, but there has never been a child diagnosed with Duchenne at the Child Health Care Office.

Diagnostic delay is now around 2.5 years. Even if there is no (cure) treatment available, you can better care for your child if you know what his/ her condition is. At the moment parents conduct their own research. Formerly in the Codex Medicus, nowadays on the internet through sites like www.childmuscleweakness.org and FindZebra, a Danish ' Search engine for difficult medical cases '. Not all diseases can be dealt with in medical training, but there should be more attention to rare disorders. For example by making sure that doctors in training include at least two rare conditions in their differential diagnosis.

STANDARDS OF CARE

Based on an expert meeting, Duchenne-parents have already drawn up guidelines for optimal care in 1997. These guidelines were not accepted by doctors because they were derived from an initiative of parents. Fortunately, it is now the standard that parents or patients are involved in the drawing up of guidelines and standards, but still too often only as a ' sounding board '. Getting ' evidence ' for care standards is very difficult in rare conditions and will actually lead to a knowledge deficit. Personal experiences should be shared, disseminated and evaluated quickly.

CENTRES OF EXPERTISE

'The quality of care must not depend on your postal code'. Knowledge sharing from one centre of expertise that sees many patients is important. It is important that centres of expertise work together, nationally and internationally. For example: doctors must be 'on the road' more to gather knowledge elsewhere.

DRUG TRIALS

Important for drug development are: a national innovation climate, continuity in health care policy and connection to European policy. Active patient organisations should also be active in those areas. As an example Ms. Vroom mentions her involvement in the 'Commissie Doek' who has advised on medical-scientific research on minors, which may not benefit the minor itself directly, but possibly would benefit other minors. After four years, this advice is not yet put into the law, which puts The Netherlands behind.

*(www.rijksoverheid.nl/documenten-en-publicaties/kamerstukken/2009/11/26/advies-commissie-doek.html)

PATIENT ORGANISATIONS

Patient organisations can influence the research agenda. In clinical research, it is important to identify outcome at an early stage which can be ' clinically meaningful ' for patients. In the end, it is the most important criterion which EMA and FDA medicines use to approve drugs. Burnt patients for example, were found to find the reduction of itching a major target, but during the trial this was not scored. The involvement of patients ' organisations with data collection and registries is very important. Both natural course studies and bio banks are needed. As a patient you may think "let them develop a medicine instead of collecting data", but more knowledge is an indispensable basis for more understanding and treatment options.

FUNDING BY PATIENT ORGANISATIONS

The subsidies of 'Fonds PGO' (Dutch Patient Fund) should not be invested in research itself, but in the involvement of patients in research and clinical trials. Ever more patient organisations show that they can collect additional funding

and sponsor research. By investing 'seed money', the first research data can be collected, which is the basis for the request of further sponsorship elsewhere.

DISCUSSION

Question: How does the international registry come about? And who has access? *Answer:* National data are internationally linked. Participating University Medical Centres have partial access, another part is accessible for patient organisations.

SECOND CONFERENCE DAY

WELCOME AND OPENING

Mr. Bert Leufkens is President of the 'College ter Beoordeling van Geneesmiddelen' (CBG: Medicines Evaluation Board) and former Chairman of the Stuurgroep Weesgeneesmiddelen (Steering Committee on Orphan Drugs). Mr. Leufkens opens the second day of the conference. He stresses that the NPRD is very important from multiple perspectives. It concerns the continuity of care in the health care chain, therapy development for rare disorders and the affordability of care. It is now up to the parties in the field to carry out the NPRD and actually move forward.

Ms. Joke Lanphen is president of the Rare Diseases Forum, part of the Forum Biotech and Genetics (FBG), and General Practioner. She emphasized that it is important for a patient to have one point of contact. Therefore, a team is needed that includes not only medical expertise but also social expertise. Experience in the hospital show that sometimes there is too much focus on the protocol, whilst the person with a condition is out of the picture. The patient is the expert of his own condition. She endorses the motto 'Health services should be as nearby as possible and as far away as it should be '. Centralization increases the travelling distance between patient and clinic, but it gains a greater expertise. A good example is the 'Creveld Kliniek' for the treatment of haemophilia patients.

CENTRES OF EXPERTISE: RARE DISORDERS 'DE-ORPHANED' – MR. JAN KIMPEN

Mr. Jan Kimpen is president of the NFU (Dutch Federation of University Medical Centres). The NFU represents the eight University Medical Centres (UMC's) in The Netherlands.

EXAMPLES OF CENTRES OF EXPERTISE

As an example, the Centre for Blister Diseases in the UMC-Groningen is mentioned. In The Netherlands annually about twenty babies with the blister disease Epidermolysis Bulllosa (EB) are born. An estimated 700 people in The Netherlands are diagnosed with EB. Six times a year, a multidisciplinary EB-consultation is organized in which 20 specialties work together. The half-hour-long consultations are contiguous. Followed by a meeting of all practitioners for a multidisciplinary discussion on joint policy and further appointments, summed up in a single medical letter for the patient and/or parents and other stakeholders. In the centre, scientific research also takes place. Another example is the Pompe Centre, the Centre of Expertise at ErasmusMC. The Centre is active in generating, collecting and passing on information it deems necessary for the welfare of patients and for the understanding of the condition. At present, about 100 children and adults with Pompe disease are treated with Myozyme.

TOP REFERENCE CARE

The last-resort function of the UMC's means that the emphasis is on top referent care, innovation and development. The UMC environment is right for top referent Centres of Expertise because all University Medical Centres give top referent care. Herewith, the centres ensure the continuation of care for patients with severe, rare or difficult to treat diseases. In the UMC's, ground-breaking scientific research is carried out on the basis of which care innovation can be realized, and also education is given in relation to the latest developments. The UMC's receive additional financing from the Ministry of VWS (Health, Welfare and Sport); the so-called academic component. This guarantees the continuity of care for these patients and stimulation of care innovation. The government has however announced it will reduce the academic component budget with 70 million euro by 2015. The UMC's are a collaboration between medical schools and teaching hospitals. As a result, research and care are closely linked. Research in the faculties is fundamental and translational; clinical research takes place in the hospital where care is provided. The care is arranged in top referent care, highly complex care with low volume, low complex care with high volume and acute care. The top referent care is under the national auspices of the NFU. Not all UMC's offer top referent care. The degree of care concentration depends on criteria like the size of the patient group, infrastructure and the complexity of the condition, intensity of treatment, access for patients to quality and efficiency, contribution and linkage to scientific research, education and training.

THE UMC'S AND THE NPRD

The recommendations in the NPRD relate to many different components in the University Medical Centres, such as 'increasing the awareness of rare diseases in doctors in training ', 'define and focus centres of care for people with a rare condition' and 'focus specific scientific research'. The development of centres of expertise by concentration and division of tasks is in full swing. After all, rare disorders are part of the top referent UMC's provision of care. However, it is still not entirely mapped out where the experience is located and to which it conforms. The NFU is working in stages in mapping the Centres of Expertise. In the first phase, about 200 orphan diseases have been identified and appeared as such in January 2013. Clustering proved necessary: there cannot be thousands of Centres of Expertise. The NFU-catalogue contains chapters like neuromuscular diseases, rare blood diseases, rare cardiological disorders and rare dermatological tumours. Within these chapters, there are clusters, and per cluster it is indicated where the treatment centres are located, where the Centre of Expertise in The Netherlands is, and where the Dutch European Reference Centre is located. The indication of the Centres of Expertise is based on the criteria established by the Stuurgroep Weesgeneesmiddelen (Steering Committee on Orphan Drugs). Currently, it is being determined whether these NFU Centres correspond to those listed in Orphanet. After that, they will also be approved from the perspective of the patient. The publication of the NFU-Portal on orphan diseases is expected in December 2013.

DISCUSSSION

Question: according to the questioner, a large number of disorders are still missing in the NFU-list. He also struggles with the cluster format. *Answer*: grouping is inevitable. However, this list should also be seen as a provisional list.

Question: How does the NFU-catalogue relate to Orphanet? *Answer*: there is a constructive dialogue between NFU and Orphanet. It is important for the continuity that a centre does not move to a new address if its affiliated expert leaves or retires. The great importance of the NFU-list is that the NFU Boards of Directors act as a guarantor for the continuity of the centres.

Question: The letter from the Minister regarding the NPRD is not clear on what the coordinating role of the NFU entails exactly. *Answer*: The NFU coordinates the expert centres only. It is currently unclear who will coordinate the implementation of the NPRD as a whole.

Question: How will the independent testing of the quality of the expertise centres be organised? At the moment one tests each other. *Answer*: There certainly is a willingness to be tested, however there is not yet an assessment framework. We have to clearly define between centres of treatment and centres of expertise.

Question: What is the role of patient organisations in the drafting of the guidelines for the centres? *Answer*: The NFU is trying to develop guidelines in cooperation with patient organisations. Maybe, herewith also lies a task for the Dutch Quality Institute.

THE NPRD: PERSPECTIVE OF A HEALTH CARE INSURER – MR. JEROEN CRASBORN

Mr. Jeroen Crasborn is Senior Advisor Healthcare Strategy at Achmea Health Insurers. He states that the urgency of the implementation of the NPRD is not a big issue among Health Care Insurers. The question is what role the Health Care Insurers will play in determining bottlenecks and recommendations of the NPRD.

PLACE OF THE PATIENT IN THE HEALTH CARE 'MARKET'

The patient has to deal with the complex market whose content is delivered by the service provider and with the health insurance market supplied by the health care provider. Care providers and health care professionals need to determine together the health procurement market. The regulatory authorities act as a regulator to the three parties. There is no 'market' for rare disorders. Health insurers, researchers and policy makers see health especially as bodily functions. For patients health exists of many more dimensions: not only bodily functions, but also daily functioning, social participation, mental functions and experience, spiritual dimension, quality of life.

CARE COST AND DEMANDS FOR CARE

Care costs have been increasing for many years, but growth by stagnating economy means extra vigilance. In 2009, the economy crisis began, while the health care expenditures continued to rise. There is an increasing demand for care because of aging. Already 4.5 million people have a chronic illness, of which 1.3 million have multiple conditions (multi morbidity). Without intervention, the premiums for consumers and employers in the year 2030 will have at least doubled. Lack of transparency in quality and outcomes (only ca. 6% of care is transparent) obstructs the cost control. In order to be able to deal effectively with limited resources, insurers need a lot of information. Focus on quality leads to lower costs.

OTHER KEY ISSUES THAT DEMAND SOLUTIONS

- Trust between parties in the 'health care market '.
- Cooperation between all the 'players' which leads to real added value for the patient.
- Lack of a clear common social agenda on efficiency.
- How do we get operations funding to output (added value) funding?
- Not enough 'patient compliance' (lifestyle, adherence).
- A big bandwidth in standard setting resulting in a far too great, for the citizen not understandable, practice variation.
- Lack of a set of instruments to achieve good self-management.

HEALTHCARE PROCUREMENT

The health insurance companies are working to resolve these issues by contributing to the control of health care costs and boosting quality and efficiency of care by effective cooperation between healthcare providers. The performance of the provider is thereto made more transparent. Quality standards (care standards) are focused more on quality of life. It is therefore appropriate to adopt a cover of volume/rate-to outcome/result financing. A focus on cost leads to low quality, a focus on quality should lead to lower costs.

Meanwhile, projects for a great deal of conditions on the quality of care have been started by the health insurance companies. Between the worst and the best care provider, there are large differences. The collected information is used for the setting of the 'zorg inkoop pakket' (care purchasing package) that is based on quality, affordability and customer engagement. For the purchasing policy of 2014, integrated care is an important component. The "Patient-journey" is leading, there is great attention to self-management.

CARE WITHIN REACH & HELP

One of the initiatives of Achmea can be seen on the website ZorgBinnenBereik (ZBB: access to care). ZBB works for people with chronic diseases. It stimulates remote care (for example, telemonitoring and e-health) in order to improve the accessibility of health care and a higher quality of life for chronically ill patients. Another initiative is 'We Helpen' (We will Help), with the aim of making helping each other a natural thing. It is set up as a marketplace with smart features for finding and joining, organizing and sharing help, complemented by targeted information to aid workers and dependents. The help will be rewarded with credits, which can be donated to another or to the WeHelpen Fund. One can set up help around a person (oneself or another). One creates a group around himself or another and shares a calendar, log and notes. Requests for help can be posed to the whole group or to specific individuals within the group.

QUALITY PROGRAMME

Health insurers want to improve the quality of care more emphatically. Precondition is that health insurers understand the added value of the delivered care products. To this end, the information needs to say something about the medical quality, customer focus and/or efficiency. Crucial to this is unity of language. The declaration database offers many starting points for quality, but it has been found that the role for the joint development of good quality information has not yet started. To fill in their producing role, health insurance companies have joined forces to develop a clear quality of care information that is related to specific care-related disorders and preferably focused on the outcome of the entire care process and its value for the patient. When caring for rare disorders, often many care givers are involved. There is a strong need for coordination of care and for centres of expertise, because the knowledge about the disorder is often limited.

CONCLUSIONS AND RECOMMENDATIONS

Patient organisations and health insurers must work together more closely. This will stimulate the development of care pathways and care chains and thus the quality of care and healthcare procurement for people with rare disorders. It is recommended that patient organisations collaborate especially on generic aspects of rare diseases (particularly in advocacy). Consensus must be sought about the organization of care and the realization of the targets as mentioned in the NPRD. In the interest of a supportive health care, the efficiency agenda must be the agenda of all parties, also for patients themselves. Self-care/management is more than 'this you must do yourself'. 'Patient compliance and behavioural influence to 'the benefit' should get much more attention in research and approach. The funding of care must change from sales-driven to added-value-driven. It is important that patients with rare disorders join forces towards health insurance companies and healthcare professionals. Make the perspective of the patient a SMART (specific, measurable, acceptable, realistic, and time-bound) package of requirements for health insurance companies with regard to their role in the realization of the NPRD. Try to indicate as clearly as possible in which aspects rare conditions distinguish themselves from other conditions, or not, and where specific issues lie.

DISCUSSION

Question: can health insurers collectively talk with patient groups? For example, on the Law on Exceptional Medical Procedures (WBMV). *Answer*: you can do this via the trade association ZN. But this is a slow process.

Remark: Something also needs to change in the bureaucracy of the health insurance companies.

ACCESS TO ORPHAN DRUGS – MR. BERT DE JONG

Mr. Bert de Jong is General Manager Benelux of Genzyme. Genzyme is active in the development and availability of therapies that make a major difference for rare disorders (hereditary metabolic diseases, particularly lysosomal storage diseases) and multiple sclerosis. Genzyme is a member of HollandBIO, the result of a recent merger between BioFarmind and NIABA. Rare disorders form a spearhead for HollandBIO, which for example can be seen from the Working Group on Orphan Drugs, the Orphan Cafés and the information point orphan drugs (www.weesgeneesmiddelen.info).

POLICY

Dutch Governmental policy is contradictory. The Ministry of Economic Affairs is counting on the 'Top-Sector Policy Life Sciences and Health', while the Ministry of VWS and the Health Insurance Board (CvZ) discuss what could be removed from the basic health care package. The availability of innovation for the patient is therefore under pressure. For industry, a realistic price setting is important. The development costs of a drug for a rare disorder are similar to those for common conditions, but there are far fewer patients. A company should be able to make a reasonable profit. For rare disorders, the QALY (quality-adjusted life year) is not suitable; the value of the treatment for the patient is very large.

AFFORDABILITY AND COSTS

Often it is stated that society is no longer willing to pay for expensive drugs. However, an independent survey by Maurice de Hond (August 2013) with 2,000 respondents, shows that 95% of those surveyed think that people with a rare condition are entitled to treatment, even if it is expensive because of the rarity (the solidarity principle). In addition, 54% of those surveyed find a profit of 10% or more for a pharmaceutical firm reasonable. In the period 2001-2011, Genzyme's net profit was 6%. 93% of respondents think that a company has to make a reasonable profit so that new drugs can continue to be developed. The affordability of orphan drugs may not be a problem. On average, spending on orphan drugs is only a small percentage of the total budget for drug development. Although the cost of total health care expenditures ascends, the spending on drugs descends. It is expected that the expenditure for orphan drugs will level out to under 5% of the total drug expenditure. The median cost for an orphan drug per patient per year is a little more than € 32,000 (with a range of 1.251 to € 407.631). Spending on orphan drugs in The Netherlands amounts to approx. € 250 million/year, converted ± € 25 per adult Dutch person/year. That is less than 5% of pharmaceutical expenditure and less than 0.4% of health care expenditures. Spending on orphan drugs does not go at the expense of other care and a saving on orphan drugs does not have a large impact on the healthcare costs. So ... patient, do not feel guilty!

THE COSTS AND BENEFITS OF THE CARE

Per person, during their lifespan, there are € 280,000 care costs. However, benefits are € 450,000. Every euro spent on care means € 1.30 in benefits! The expenditure for orphan drugs does not constitute an acute problem, only if there is a tsunami of expensive orphan drugs, this will be different. But the reality is that there are about 70 orphan drugs registered since 2001. It is expected that the same number will be registered within the next 10 years.

CONCLUSION

There is a need for innovative medicines that make a difference, after all, there are 5,000 to 8,000 orphan diseases. Industry needs a reasonable profit to enable research. The social solidarity/willingness is there. Affordability is not an issue. Of course good start and stop criteria need to be established; the treatment should be effective.

DISCUSSION

Question: what to do about the situation that different producers each start their own database. And what to do for conditions for which there is no early diagnosis? *Answer*: building data files at European level is important. Industry needs to work together to create joint databases. We also need a concerted effort on screening programmes. *Remark:*

CvZ is not open to contact with patients. *Answer*: Genzyme is also committed to start talking with CvZ in an early stage. This was not successful with Pompe disease. Looking back at recent discussions: after four years, it is wrong to take patients off the therapy if no prior arrangements have been made.

REPORT OF WORKSHOPS

THEME 1 - METHODOLOGY, GOVERNANCE AND MONITORING OF THE NATIONAL PLAN

WORKSHOP 1 – IMPLEMENTATION OF THE DUTCH NATIONAL PLAN

In this workshop, the following two themes were addressed: Coordination and guidance of the implementation of the National Plan (NPRD), including input of the perspective of the patient, and the policy for a future-proof NPRD.

INTRODUCTION MS. JOLANDA HUIZER

Ms. Jolanda Huizer was Secretary of the Stuurgroep Weesgeneesmiddelen (Steering Committee on Orphan Drugs started late 2011) and then at the ZonMw NPRD Sounding Board. She stresses that during the development of the NPRD, all input from the stakeholders has been incorporated, making it a realistic plan. In The Netherlands this was a step in the right direction, but it was not successful in all European countries. On October 10th2013, the NPRD was presented to the Minister of VWS by ZonMw. For other plans and strategies in Europlan, she refers to www.europlanproject.eu. Now that the NFU has been appointed as director for the designation of centres of expertise, it is urgent that there is a consistent policy for centres of expertise, having regard for the provisions of title, orphan drugs and promoting timely and appropriate diagnosis and referral. Especially the assurance of the perspective of the patient is important.

DISCUSSION

Question: what are the results in other countries with the drafting of a national plan? *Answer*: the themes in other national plans are the same, but there are no common European solutions because of the difference in the organisation of health care in the different European countries. There is a specific interpretation per country.

Question: there is little regard for the social follow-up after the diagnosis is made. Since the NFU is coordinator, we are afraid that the emphasis will not be on the follow-up of care. *Answer*: Yes, in the NPRD there indeed is little indication about this follow-up.

Remark: The municipalities receive an important task in implementing the WMO (Social Support Act). It is uncertain how this turns out in relation to rare diseases.

Remark: The teaching hospitals will install client advice board. The question is what their role can be. How can we assure input from patient organisations for rare disorders?

INTRODUCTION MR. GERRIT SALEMINK

Mr. Gerrit Salemink is Medical Advisor of the Umbrella of Health Insurance Companies (ZN) and member of NPRD Sounding Board. The paradox of rare conditions is that they each have a limited impact due to the low numbers of patients, but because there are so many rare diseases, the impact of all rare diseases together is larger than those of many common chronic diseases such as diabetes. What can health insurance companies contribute to the NPRD? The health insurers do not determine what will be reimbursed in the basic package. The Health Insurance Board (CvZ) makes recommendations to the Minister and if something is in the basic package, the health insurance companies are obligated to reimburse. The idea is that the care in The Netherlands is well regulated, but the NPRD shows that certain things are missing when it comes to rare conditions, such as lack of 'awareness ', information, knowledge, education,

problems with organization and availability of care; this concerns centres of expertise as well as orphan drugs, scientific research, coherence and coordination.

CENTERS OF EXPERTISE

The inventory of the NFU reveals that an interesting mix of expertise in the University Medical Centres is present. This has often grown historically because of the individual interest of a specialist. Mr. Salemink finds that choices have to be made, creating Centres of Expertise is more than the exchange of contact information by the experts. Patient organisations and insurers can enforce this. As an example, he mentions the Paediatric Oncologic Centre: here parents and doctors choose a centre and thus the health insurance companies agreed. Nevertheless, there was pressure from other academic centres that wanted to keep paediatric oncology in their own centre.

ORPHAN DRUGS

How expensive should it be? The discussion on the reimbursement of medicines for Pompe disease and Fabry is known. Despite the very high cost of the drugs the cost effect is low because it concerns very rare disorders. The consequence of the paradox, however, is that there are more and more rare conditions defined by better diagnostics, for which orphan drugs are required. The government has a role in regulation and prepares itself thereupon. From a macro-fiscal perspective, the impact of the reimbursement for Pompe and Fabry is still limited because there are so few patients. But more medicines will lead to the diagnosis of more patients and to more costs. Price negotiation is therefore important and possible because some drugs are clearly cheaper abroad.

SUMMARY

SUSTAINABILITY OF CARE

In the NPRD it is all about the sustainability of the plan. In the workshop-discussion this is widened to sustainability in health care. The following points on this theme were addressed:

- Centres of Expertise will not resolve the boundaries between the components of care (between, for example, hospital and at home). Another financing system could be a solution.
- There is a need for shared care and provision of care by more institutions working together.
- The patient should be the starting point for funding, a tailor made budget for one patient.
- Application of the SKMS, Kwaliteitsgelden Medisch Specialisten (Foundation Quality funding for Medical Specialist) is important.
- Quality Standards of Care should be dynamic and modular.
- Networks should be supported, registration and national EPD (Electronic Patient File) is needed.
- Sustainability of the clinical pathway: what is the process after diagnosis and treatment, central coordination of all care is needed.
- Clear rules are needed by the referral specialist: unknown makes unloved.
- A centre of expertise must have a 'back up'.
- Centralization of treatment in Europe should be possible.
- Knowledge transfer must be protected so that knowledge is retained.
- Attention is needed for patients with rare disorders that are not organized and are hardly visible within the health care system.

CENTRES OF EXPERTISE

The number of centres can be limited by clustering rare disorders. That could mean that also patients' organisations have to cluster. This would also provide a solution for the participation in customer councils in teaching hospitals, which now require a lot of manpower.

UMC's

- The experience is that centres will protest if they are not selected as a Centre of Expertise.
- UMCs educate. If they lose a centre of expertise, the relevant education will also be lost with them.
- The pharmaceutical industry influences the decision making, because they preferably plan trials in expert centres.
- Good communication between European centres is important to ensure that patients can also get access to knowledge elsewhere in Europe.
- The certification of centres also include criteria for clustering: that can be both too narrow and too broad.
- Guarantee the input by patients by identifying centres of expertise, through NFU, Orphanet and VSOP.

Expertise

- There are many rare disorders that are in the hands of few experts.
- If one doctor has the expertise and he leaves the centre, the expertise also disappears. The centres of expertise must secure knowledge.
- There are objective criteria to designate a centre of expertise on the basis of the actual expertise.
- An inventory is needed of knowledge that is housed in both patient organisations and the University Medical Centres, also at a European level.
- The NPCF (Dutch) has insufficient expertise in the field of rare diseases.
- There are also centres of expertise needed for patients with the strong presumption of a rare condition but who have not (yet) been diagnosed.
- Knowledge must be passed on, both through internal and external training The NFU will be in the lead as far as the Centres of Expertise are concerned, but coordination is also needed for the implementation of the NPRD as a whole.

DISCUSSION

- *Remark:* it's been a difficult process to get to one paediatric oncology centre. That gives pause for thought for future concentration.
- *Question*: The themes seem contradictory: sustainability is about the patients, with centres of expertise it is about the NFU. What can we expect from the NFU? Who will guard the input of patients? Who takes charge of the overall coordination of patient care? *Answer*: By consulting patients ' organisations, the VSOP is involved with the assessment of the quality of the candidate centres of expertise. Hopefully this leads to intensive cooperation between centres of expertise and patient organisations.
- *Question*: Not all treatment clinics for rare disorders are covered by the NFU, for example the Antoni van Leeuwenhoek hospital. What about rare cancers? Others may also be a centre of expertise? *Answer*: the Centre does not have to be a University Medical Centre, it can also be a STZ, Stichting voor Topklinische Zorg (Foundation for top clinical care) hospital.

- *Question*: comprehensive care is needed, not just medical care, which is also more than chain care. The care is paid from different sources. Then it is more about networking. How do we realize comprehensive care? *Answer*: The NPRD is mostly about *cure*. The question is indeed how *care* is secured if the NFU is leading. The connection between *cure* and *care* is a task for Het Kwaliteitsinstituut (Quality Institute). So this is a good question to ask Mr. Jan Kimpen tomorrow: he is both working for the NFU and this institute (see pages 13 and 14).

THEME 2 - DEFINITION, CODIFICATION AND INVENTORYING OF RD

This theme was not addressed separately during the Dutch Europlan Conference. Some of the sub-themes were addressed in presentations and workshops in other themes.

THEME 3 - RESEARCH ON RD

WORKSHOP 3 – RESEARCH AND DIAGNOSTICS

In this workshop, the following two themes were addressed: timely diagnosis; and coding, registries and data collection.

INTRODUCTION MR. GERARD ENGEL

Mr. Gerard Engel is secretary of the FBG. He explains briefly the role of the FBG, in particular the Rare Diseases Forum, which currently explores how a timely diagnoses can be stimulated. A lot can be gained by better cooperation between young doctors, general practitioners and paediatricians.

Mr. Gerard Wagemaker is chairman of the Dutch Association for Gene and Cell Therapy, and from 2010 to 2013 member of the EUCERD. Mr. Wagemaker stresses again that rare disorders, with 6-8% of the population and an estimated 20% of the care costs, are not so rare or insignificant. Diagnosis and subsequent registration in registries should be linked inextricably.

INTRODUCTION EDWIN CUPPEN

Mr. Edwin Cuppen is Professor of Human Genetics at the UMC Utrecht. In his presentation, Mr. Cuppen addresses current and future tools for timely diagnosis of rare disorders. While in 1990, 3,000 base pairs per day could be analysed, this has by now risen to complete analyses of 5 billion base pairs. The current application of genetic screening around childbirth, focuses on pre-conception carrier screening, prenatal non-invasive diagnostics (NIPT) for trisomy 13/18/21 and neonatal screening. In addition, genetic screening in adults is used for disease prevention, for example in hereditary breast and ovarian cancer (BRCA) and to a lesser extent for personalised medicine and pharmacokinetics. Finally, there is a place for genetic screening at molecular autopsy and the fight against aging. Mr. Cuppen then outlines the challenges ahead before a genetic passport for each person, and a standard recording of complete genome analysis (Whole Genome Sequencing, WGS) in the diagnosis of rare diseases, will be a fact:

- Awareness of opportunities (and impossibilities) by health care providers should be increased.
- Costs for WGS are still high and the cost effectiveness has yet to be determined.
- What is the place of WGS in the EPD (Electronic Patient Record)? And what are the consequences for the patient?
- Generating genome data is one thing. The interpretation of rare mutations is and remains difficult. Exchange of data (national and international) should contribute as well as link with other data (metabolomics, proteomics). There may be a role for Genetic Centres of Expertise at genome interpretation.
- To ensure that there are enough people to generate and interpret the data, there is a need for more training and specialization of health care providers and researchers, as well as more fundamental research into "unknown" genes (from mutation/gene to mechanism, and from mechanism to medication).

- Diagnosis does not automatically lead to treatment.

SUMMARY

Awareness of health care providers is one of the challenges in the detection of rare disorders. Paediatricians for example have an essential role to play. More attention and training in this medical specialty is a must. The 'DNA Passport' is already possible; it assists in faster detection of rare disorders. Why not start the diagnosis with a full genetic profile when there is the possibility of a rare disorder? Especially those with intellectual disabilities. Is genome sequencing the neonatal blood spotting of the future? Various pros-and-cons are discussed, which raises more questions than answers. In theory WGS gives more information, but also more unreadable information: what to do with the random mutations in the genome? How to deal with the 'right to know' of the child/ individual? Early diagnosis is essential for adequate care and therapy. Registration of all patients with genetic disorders (if necessary, associated with a financial incentive) with data management by centres of expertise is a prerequisite for awareness and a balanced research policy.

THEME 4– CARE FOR RDS - CENTRES OF EXPERTISE AND EUROPEAN REFERENCE NETWORKS FOR RARE DISEASES, WORKSHOP 4 – QUALITY OF HEALTH CARE AND LIFE

INTRODUCTION MS. MARJOLEIN DE BOOYS

Ms. Marjolein de Booys is Quality Care Advisor at the Quality Institute. Ms. De Booys elaborates on the development of the new Zorginstituut Nederland (Health Care Institute The Netherlands). The quality task of the CvZ is accommodated in the Kwaliteitsinsituut (Quality Institute) with the tasks: drawing up quality standards and associated measuring instruments; the care and support of the parties in providing insight into the quality of care. The current guidelines focus on one specific condition without taking multi morbidity into account. Health care thereby insufficiently connects with the questions of patients and is not focused enough on relevant outcomes for patients, namely quality of life. Patients with rare disorders strive to develop quality standards for their condition. However, given the experience with the current guidelines, the question is whether developing quality standards will be a complete solution for the problems they currently experience. People with a rare condition often have multiple problems in various fields, not only medical but also social. This requires a comprehensive approach. Het Raamwerk Individueel Zorgplan (Framework for Individual Care) can help to achieve this, because the starting point is not the disease, but the sick person itself, with all his or hers healthcare needs. By developing quality standards from the patient's perspective, and then build this in a modular way as much as possible, individual care can be realized by incorporating these modules to fit into this Framework for Individual Care.

THEME 5– ORPHAN MEDICINAL PRODUCTS

WORKSHOP 6 – ACCESS TO ORPHAN DRUS AND TO HEALTH CARE

INTRODUCTION MR. WIL TOENDERS

Mr. Wil Toenders is a Consultant on Drugs Reimbursement at ToendersdeGroot BV. Mr. Toenders: the therapeutic value of orphan drugs must be central; if after time reality shows that this is not there, then stop reimbursement. However, there is currently an unfavourable wind that causes a great deal of discussion. So there seem to be no more exceptions to be made in the event of adverse cost-effectiveness outcomes. The start and stop criteria have been tightened up and exemption is no longer automatically granted for pharmaco-economic research. The various players in this field should take their own responsibility and take action:

Patients. In the current climate, it is important that patients make themselves heard. Make sure you're visible at CVZ and VWS! Keep hammering in the background about the condition and the importance of treatment. Present evidence such as relevant outcomes and experiences of other patients and search for international cooperation.

Treating Physicians. Treating physicians may also influence and be visible at CVZ and VWS. It is important that they are working on guidelines for rare disorders and focus on concentration of care. In addition, they must give feedback on treatment results and costs, so care for rare disorders remains funded.

Pharmaceutical Companies. The role of pharmacists is to continue funding research, also in new areas. They should invest in joint registries on one indication and make sure orphan drugs are available for patients by acceptable pricing.

Health insurers can ask CVZ for a judgment, in case of doubt about the desirability of off-label use. Furthermore they should allocate a portion of the proceeds from the preferential policy towards the sponsorship of patient organisations.

ZonMw has its role in the bundling of knowledge and research in the field of rare diseases and can identify gaps in the field of research on orphan drugs and research to encourage off-label use.

Advice to CVZ and VWS: maintain the separate status for care for rare disorders (including orphan drugs), give the medicines the benefit of the doubt and give ample space to proof the efficacy of medicine in practice in the longer term. Consider whether pharmaco-economic research does contribute to the decisions in this case, also accept the use of international data.

INTRODUCTION MS. PAULINE EVERS

Ms. Pauline Evers is policy advisor at the Nederlandse Federatie van Kanperpatiëntenorganisaties (NFK: Dutch Federation of Cancer Patients Organizations) and member of the Committee on Orphan Medical Products at the European Medicines Agency (COMP at EMA). She presents on the funding of orphan drugs and the so-named compassionate use/off-label use and financing of top clinical care and treatment.

ORPHAN DRUGS

After France, the Netherlands has the broadest availability of oprhan medicinal products: 88%. In principle, all registered products in The Netherlands are reimbursed. With regard to expensive and orphan drugs that are used within the hospital, additional rules apply. CVZ determines whether they are reimbursed on the basis of therapeutic added value (is this remedy better than what is already there) and cost-effectiveness (does it offer the best value for money). When there is lack of clarity, reimbursement is conditional for a period of four years and there is always the perception that this means 'too expensive '. During this time, additional studies should demonstrate added value and cost effectiveness. The added value of the use of orphan drugs is difficult to demonstrate (small numbers of patients and heterogeneity of disease); societal benefits in the event of reimbursement of orphan drugs are insufficiently taken into account in this regulation. In reality, orphan drugs rarely meet the limits for cost effectiveness. In the NPRD, two recommendations focus on the funding of orphan drugs. To fulfil this in the right way, it is important that the patient is involved at an early stage in the assessment of added value and cost-effectiveness and in the design of subsequent research. Patients may help to demonstrate the added value of the orphan drug, and with this, the need for reimbursement.

OFF-LABEL USE

To fulfil recommendations on the off-label use of medicines correctly, it is important to connect to international developments in science and practice. Where this is a problem, it is important that patients and health care professionals work together. Practitioners must draft up treatment protocols. Industry should lower the pricing of medicines with off-label indications. After all, there is no research done on the indication for which the drug is used now.

FINANCING TOP CLINICAL CARE AND TREATMENT

A number of recommendations are made in this area in the NPRD. Of interest is that the specialised care for rare disorders, concentrated in Centres of Expertise, is going to take place. A limited number of hospitals will then claim the cost for granted top clinical care to patients with predetermined conditions. Daily care can be provided locally. It is necessary to look at the total package of which the care for rare disorders is constructed: integrated care. The claim that expensive drugs will weigh heavily on the Centres of Expertise's budget should not prevent concentration of care. Patient organisations have already called for more involvement (more dialogue) about the points above, as well as more customization. Furthermore, there are already initiatives that map out the care for a rare disorder in its entirety for example in standards of care. Also, there needs to be attention for the cooperation between patient organisations and the CvZ, for example in the development of criteria for the effectiveness of care.

SUMMARY

The directory role of VWS (Ministry of Health) must involve that the agreements are actually secured. In the field of orphan drugs, this means an integrated approach to development, compensation and use. In the field of care, this means ensuring that treatment trajectories (integrated care) are defined and that their quality is monitored. In the workshop by representatives of field parties, concrete commitments are presented:

- Achmea agrees to set up a Think Tank within the health insurers (ZN) which will deal with the non-competitive cooperation in the field of rare diseases; and funding (research linked to) off-label use in paediatrics.
- HollandBio is committed to ensure that registries in the future will be set up across companies: not with the product as a starting point, but the condition.
- The VSOP is there to ensure that CVZ will include the input of patients in its assessment process from the start (registration phase).

One calls for a funding system that takes into account individual, really necessary, health care needs. There is, after all, a wide variety of care per clinical condition. Mr. Smit, patient advocate, will check if he can take action on this, together with VSOP. All field parties in the NPRD have the responsibility to be proactive. Patient organisations are the first designated to encourage field parties to pick up that responsibility.

THEME 6– SOCIAL SERVICES FOR RARE DISEASES

WORKSHOP 4 – QUALITY OF HEALTH CARE AND LIFE

INTRODUCTION MR. HENK BELTMAN

Mr. Henk Beltman is a consultant of the program: "Aandacht voor Iedereen" (Attention for Everyone).

THE PROGRAM 'ATTENTION FOR EVERYONE'

The program ' Attention for Everyone ' is a program of the national organizations CG-Raad, CSO, Koepel Wmo-raad, LP-GGZ, Mezzo, Patiëntenfederatie NPCF, Oogvereniging, Per Saldo, Platform VG, VCP and Zorgbelang Nederland. The purpose is to advice and inform members and representatives of WMO-councils (Councils of Social Support Act) on the transition from the AWBZ (Law Concerning Reimbursement of Special Health Care Needs) guidance, and advising them about their role in doing so. The program also monitors the impact of this change for patients and care givers. Patient advocacy and WMO councils can join forces in the dialogue with municipalities. See www.aandachtvooriedereen.nl.

TRENDS

In a society with citizen participation, the citizen has room to take initiatives. The government provides a safety net for the most vulnerable citizens. In politics, this trend goes hand in hand with the reduction of public spending, limiting the AWBZ and transfer of jobs to the municipalities. In this context it is important that the Staatssecretaris (Secretary of

State) for VWS (Ministry of Health, Welfare and Sport) expects the Dutch ratification of the UN Convention on the Rights of Persons with Disabilities, which is expected in mid-2015. This will give an important contribution to the objectives of the renewal of long-term care.

LEGAL DEVELOPMENTS

There is a lot of new legislation, in which above all institutional care is being phased out. As of 1 January 2015, this concerns Jeugdwet (Youth Law), de Participatiewet (Participation Law), the WMO and Wet Langdurige Zorg (WLZ: Law for Long-term Care), which then replaces the AWBZ. Changes with respect to the AWBZ are: limitation to intensive 24-hour care; support and participation to the WMO; cure, treatment and nursing to the Zorgverzekeringswet (ZVW: Health Insurance Act). Purpose of the WLZ is that older people and people with intellectual, physical or sensory impairments, get adequate care with attention for the individual well-being.

According to VWS, residents of institutions will be able to include concrete agreements on the establishment of daily life in their care plan. Zorgzwaartepakketen (Care Burden Packages) will be eliminated or transferred to the ZVW. People will have the right to claim integration of nursing and care at home. This will strengthen the cooperation between family doctors and visiting nurses. In the end, one can remain at home longer. The municipalities will get resources for social neighbourhood teams, visiting nurses and patient support.

CONSEQUENCES OF DECENTRALISATION

For all parties, this decentralisation means a big change. Patients will have less rights and more own responsibilities with the emphasis on self-direction and self-reliance. The municipalities will have a directive role where the ‘purchase of care’ is crucial. The care institutions will have an uncertain position; they will need to regroup.

RECOMMENDATIONS TO THE MUNICIPALITIES

'Attention for everyone' has drawn up eleven points of attention for patients/clients organizations to use when forming their opinion. Support of individual clients:

1. Start with self-management of clients and strengthen their skills to make it happen.
2. Strengthen the position of the client in a ‘kitchen table talk’.
3. Support family caregivers with carefully tailored service.
4. Make sure there is good mediation or complaints regime.
   Participation and initiatives of clients and citizens:
5. Develop a vision of customer and citizen participation.
6. Involve WMO-councils and organisations in decentralisation.
7. Inform and involve clients and citizens on the effects of the decentralisation.
8. Accommodate and facilitate citizens ' initiatives.
   Quality and content of municipal administration:
9. In the purchasing policy, take into account quality criteria from the patients’ perspective.
10. Involve the implementation of the UN Convention on Disability (key policy intentions in advance to the Treaty); involve organisations of people with disabilities in relevant guidelines; set requirements for settings).
11. Monitor the implementation of the transitions and transformation from the perspective of the client.

SELF-MANAGEMENT

The concepts of self-management, own strength, self-reliance and personal responsibility are key concepts in the WMO. The changes are aimed at the encouragement of self-management. The idea is that patients get more control by self-management in their own lives and care, which improves the quality of life. The question is whether patients look at self-management in the same way and how self-management can be strengthened. Key question is: is it about

broadening freedom of choice, space to develop their own talents and possibilities (emancipation) and opportunities to get involved and to contribute to society (participation)? Or about limiting the accessibility of professional support (budget cuts)? Self-management means self-determination, not doing everything yourself. Relying on support, does not mean that someone else decides for your needs. Self-management concerns all areas of life, social roles and relationships.

WAYS TO STRENGTHEN SELF MANAGEMENT

The American philosopher Martha Nussbaum bases this on a minimum of ten capabilities with which one is capable of fully functioning: life, physical health and physical inviolability, sensory perception, imagination and thinking, feelings, practical reason, social ties, other biological species, games and design of their own environment. In the context of self-management for the patient, this means: drawing up a care plan oneself; the use of client support; teaching health and social skills; contribute to society; taking citizens' initiatives; to represent interests of the patient towards the municipality (criteria by purchasing policy) and institutions (quality policy). As regards the institutions, this means: a coaching attitude of the employees; quality policy; chain approach; tools; deployment of experienced experts in training; clients assessment support and care services; for municipalities: freedom of choice (personal care budget, PGB); filling in 'kitchen table conversations'; role of district teams and visiting nurses; purchasing policy; facilitating citizens' initiatives; involving citizens in policy; implementation UN-Convention. Stimulation of self-management leads to higher quality of life and care. There are many social and political trends in the field of self-management. Many opportunities to enforce this in WMO (Social Support Act) and AWBZ (Law Concerning Reimbursement of Special Health Care Needs)!

SUMMARY

More attention should be on 'learning to live with'. There is little attention for this in the NPRD. For many rare diseases, there is currently no cure available. The decentralization of the AWBZ care touches directly on this. It is therefore necessary to draw up a guide on rare disorders for the care policies of municipalities, with more focus on the person and his/her environment, attention to multi-morbidity, coherence between cure and care and the fact that one never has a condition alone. "My wife and I share a spinal cord injury," said Mr. Dekkers. In the framework of the implementation of the NPRD, the development of quality standards should be adjusted for rare disorders. More emphasis should be placed on generic themes so that the patient organisations involved are challenged to work together.

Comments: there is a need for a guide intended to municipalities on the care policies on rare disorders. Who is going to do this? Courses for municipal employees deal primarily with chronic diseases, not rare disorders or multi morbidity. The municipalities definitely need input in this area. The problems for people with a rare condition are widening: it is also about work, a renewal verification, participation, education.

ADDITIONAL WORKSHOPS

WORKSHOP 2: EUROPEAN COLLABORATION

In this workshop, the following two themes are central:

1. To connect care and research to European Reference Networks (ERNs).

2. Cross-border health care Policy that allows for rare disorders.

INTRODUCTION MR. GEOFFREY CARROL

Mr. Geoffrey Carroll is Medical Director of Welsh Health Specialised Services

Mr. Carrol focuses on the question: How do we design the process in such a way that a practitioner or a person with a complex rare condition can find and obtain the correct diagnosis and care? Half of the people with a rare condition have no diagnosis. The starting point of cross border health care should be that the patient does not travel, but the medical expert or the expertise (virtual). There is an important task at this point for the national reference centre, in consultation with the other European Centres of Reference of an ERN. Even for well-known disorders such as Fabry, the expertise is not in one's own country. Also with many paediatric diseases, cross-border health care will be an issue, and travel has a big impact on the family situation. In any case, it is important that the patients have an independent view on what European health offers for their condition, in so far as it is not in available in their own country.

It is noted that an ERN should give priority to harmonizing guidelines and care standards. Also the EMA (COMP) expects the same quality of care as a basis for all clinical data. However, there is still much to be done in the field of accessibility and harmonisation to make cross-border health care actually work. With such an initiative, it is also important to be able to respond in a flexible way to new developments. As a first step 'best practices' should be shared at a European level. 'Syndromes Without A Name' (SWAN – UK) is known as a best practice to the group of undiagnosed children. It shows that tailor-made care is needed, something that is not taken into account in the healthcare procurement by health insurers in the Netherlands.

The participants also mention Dutch examples: a good example of little *diagnostic delay,* the time to diagnosis is the diagnostic pathway for Lysosomal Storage diseases in The Netherlands.
Mr. Carroll points out in response that primary health care must learn to make the distinction between vague complaints and strange symptoms, and subsequently it needs to be clear on how to refer.

BBMRI (Biobanking and BioMolecular Resources Research Infrastructure) is also mentioned; a network of biobanks within which general conditions and rare disorders can benefit from each other. It is also noted that the publication of a 'case report' in the case of rare diseases has enormous value to get a complete picture of (the diversity) with a rare condition, but it has become very difficult to publish this in respected scientific journals.

INTRODUCTION MS. VALENTINA BOTTARELLI

Ms. Valentina Bottarelli is European Public Affairs Senior Advisor at EURORDIS

Ms. Bottarelli introduced the ERNs in the context of the 'Cross Border Health Care Directive', in particular how these legal and policy tools can answer the question of the individual patient that needs to find the appropriate care pathway, including outside his/her country, what type of reimbursement s/he should expect and how the cross-referral mechanisms do actually work (role of the newly appointed National Contact Point under the Cross Border HC Directive).

The ERNs are going to have a virtual structure that connects care and research in an EU Member State with other Member States and thus, as a ' one-stop-shop ', cross-border care and research collaboration. Experts or laboratories may be part of an ERN; not only centres of expertise. Adopted priority activities of an ERN by EUCERD include:

1. developing and managing inter-operable registries;
2. participating laboratories submit to Quality Assurance and standardization;
3. mechanisms for good information flow of *best practices guidelines for diagnosis and care;*
4. facilitating patient mobility-but firstly data and expertise (telemedicine)-also across borders;
5. developing quality indicators and review procedures;
6. training and education tools;
7. networking not only between existing CEs but also with health and social care providers, relevant research groups and diagnostic laboratories as well as patient organisations;
8. cross border referral mechanisms;
9. use of telemedicine.

To designate the national European Centres of Expertise that are part of an ERN they must have the means to take on their role within an ERN. That is why now the focus should be on implementation at national level, including the provisions of the National Plan.

Outstanding questions are how sufficient funding can be found, how patients really can be involved, how is *comprehensive care* going to be delivered and research actually encouraged. Also, it is crucial that ERNs bring together a 'critical mass' of patients in order to ensure good care and research.

- The vision of EURORDIS is that ERNs should deliver structured healthcare pathways through a high level of integrated expertise to improve diagnosis and care to the best European standards. There should be at least one ERN per cluster of disorders, a cluster that connects to medical specializations and body formats. It is expected that there will be 20 to 30 ERNs. The question is then whether this is not too much global clustering, but on the other hand, 7,000 ERNs is also not an option. There should also be an ERN for the undiagnosed patients with a rare disorder. These principles have been also incorporated into the EUCERD Recommendations on ERNs.

EURORDIS also supports rare diseases ERNs that are multidisciplinary to address multisystem disorders and include social care. Moreover, the involvement of patients should a pre-requisite for the financing of ERNs: patients should have a clearly defined role not only in advisory bodies, but also in the management, and this role should be supported financially;

Pilot projects are being set up by the European Commission and goals are formulated for the short, medium and long term. In 2014-15, a call will be issued for candidates for ERNs. In 2015 the European Commission wants to fund pilot projects from Horizon 2020 to develop a validated model for the organization/coordination of ERNs (incl. accreditation).

Cross border health care (healthcare) is a big issue for patients with rare disorders. It is very questionable whether the European Directive is going to actually make it possible for patients to have adequate freedom of choice. Currently only 12 countries, including The Netherlands, have this European law transposed. It is important that cross-border care is seen as a right, that there are national expert advisory committees for quick decisions on individual applications, that there are lists of conditions/treatments that are eligible and that there are no financial barriers, which, among other things, might occur (for instance, the patient must know whether the cost must be prepaid, whether it is or not -or partly- compensated)

SUMMARY

Europe aims to stimulate the creation of about 30 ERNs, in which guidelines are developed for clinical research and ' social care '. Patient organisations should have an equal position. (Hope is expressed that the NFU will also involve patient organisations in this way with the centres of expertise). At a European level, there is only extra money for ERNs within the framework of further development of overall organization principles, for example in the European programme Horizon 2020. In 2015, there will be a European call for proposals to apply for the creation of an ERN. Funding will be available for the further development of governance principles ' (administration and management) in an ERN. It is also conceivable that being part of an ERN is an advantage when applying for other European or national subsidies.

Remark: this is all very political, but does the system work? The concrete objective of an ERN (diagnostics? care? research?) should be worded much more specifically than is currently the case. The EUCERD recommendations are far too global. In addition, I see the insurability of care as one of the biggest bottlenecks.

Remark: given the expected limited resources, patient organisations should have an important voice in setting the priorities of an ERN in the field of care and research and the balance between the two.

It is important that the NFU, in determining expertise centres, does not act alone but in dialogue with Dutch patients' organisations and the criteria drawn up by the EUCERD. There must be an accreditation system and clear guidelines for entry. They should also address the relationship between commercial influence on the one hand and fragmentation of research, accessibility of health care and public-health objectives on the other. In that context, it is important that the development of ERNs is headed by an independent commission.

With the availability of an orphan drug, the EMA often obliges the company to establish a registry for further data collection, and thus these data are managed by the pharmaceutical company. If there are several pharmaceutical companies involved in the same disorder, the research is often fragmented. That is a serious problem for which a solution must be found. The condition should be the basis for a registry, not the medication. However, records need to be set up much earlier for the natural course of a condition. Such forms of research on rare diseases are indispensable for good care. The administrative management (governance) of registers and biobanks is a matter of concern, as well as a lack of clear objectives: research, substantiation of cost-effectiveness research guidelines, public health, etc. The patients themselves must also have access to the registries in the different networks, i.e. they should also be able to include their own experiences in it, so as to be able to link the medical aspects with the personal experience/ expertise.

DISCUSSION

Question: The NFU is presently looking at Orphanet information to get a picture of the European Reference Networks. Does this mean there cannot be input from others to determine which centre can be a central European reference centre? *Answer:* The question is what influence the NFU can have at a European level. The NFU cannot set up an ERN.

Remark: The NFU-list does not have to be final. Maybe we prefer the list of Orphanet. *Answer*: The NFU has not only drawn up a list, but the boards of Directors have also guaranteed the continuity of the expertise centres that become part of an ERN. In The Netherlands the list therefore has more consequences than that of Orphanet. However both have shortcomings.

Remark: The registration of Centres of Expertise in Orphanet is also not optimal. It includes centres with only part of the required expertise, but these are not Centres of Expertise. *Answer*: There has to be clarity soon about what are real centres of expertise.

Remark: Europe is slow. The Netherlands must wait and see until there is clarity in Europe. On the other hand, sensitive issues such as *public-private partnerships* – important for the ERNs – need to be settled at a European or even international level.

WORKSHOP 5: STRENGTHENING THE PATIENTS' VOICE

In this workshop, the following two themes were addressed: effective advocacy and participation, from the perspective of the patient, in the implementation of the NPRD.

INTRODUCTION MRS CYNTHIA VOGELER

Mrs Cynthia Vogeler is Programme Director at the Patient Federation NPCF (the Dutch Patient Federation)

In 2010, the advice 'Health 2.0' was presented by the Council for Public health and Health Care (RVZ) in which the patient gets a whole new position in health and care. This requires empowerment of patients and patient participation in care, policy and research. The relationship between professionals and patient needs to be more equal, thus making decisions together. The Personal Health Record (PGD) is a means. The unique personal expertise of patients is important to the quality of care, research and policy. This means that studies that are relevant for the patient should be funded and researchers should involve patient experts in their research (other than involving them as respondents only). What participation means: see http://www.nationaalkompas.nl/participatie. For shared decision-making, it is necessary that patients have the resources (tools) to get control. If the patient has a strong role and there is ' shared decision making ', this will lead to a higher patient satisfaction, better physician-patient relationship, a deliberate and also medically wise choice by patients and a better quality of life. Research shows that 70% of patients want to be actively involved in taking important medical decisions. The resources can be found at new e-Health possibilities which give patient a 'toolbox'. Examples of such 'tools' are discussed below.

INFORMATION

Self-management requires knowledge and skills in the medical-technical field. A choice has to be made between treatments, health care providers etc. on the basis of information provided. The chronically ill needs to know what is going on, what the condition entails, what the optimal treatment is and what the consequences are of certain behaviour in the disease process. Customized content and patient versions of the patient care guidelines and standards can facilitate this. However, the patient must also have the skills and techniques to take action himself, such as education in the field of self-control, strengthen self-confidence and (intervention) methodologies for realizing personal goals.

PATIENTPORTALS

There is currently an explosion of patient portals. The problem is the quality of the information. Objective quality information is missing in many cases. ZorgkaartNederland.nl is a kind of ' TripAdvisor ' for care (a website with user-generated content), and is visited 800,000 times monthly. Patients may place reviews and ratings that other patients can use to choose between hospitals and care providers. Often citizens and patients find information from other patients more valuable than information from health care providers or health insurers themselves.

DEVELOPMENT OF TOOLS FOR CHOICE WITH THE PATIENT ORGANISATION

Through 'Zichtbare Zorg' (Visible Care) yearly much quality information is collected about the offered treatment forms, facilities, cooperation and working methods of a particular healthcare provider. With that information, the individual patient is not yet able to do anything: it's a big container with numbers that are not available to the patient. The 'keurzehulp' is a tool to make the information visible and convert into an opinion about the hospital that best suits the preferences of the patient. Other than a quality mark or seal, a 'keuzehulp' is personalized. That means that the best hospital is not the same for everyone. Depending on one's burden of illness, mobility, service expectations and personal situation, the 'keuzehulp' gives advice which hospital is the best adapted to one's individual needs.

E-HEALTH

The mutual exchange of patient experiences is of great value and provides valuable information sources. E-Health is a possibility to do this and the website PatientsLikeMe is a good example. The patient should be director of his own care.

Data from the patient should ' follow ' the patient: information travels virtually with the patient. The patient has self-control in so far as the extent to which the treating physicians can look over their shoulder. E-Health contributes to high-quality affordable, accessible health care and more private management for patients. To embed good e-Health and to avoid fragmentation, framework conditions must be drawn up. The NPCF does that along with ZN (Netherlands Health Insurers and Doctors Federation KNMG. E-Health is the national eHealth Implementation Agenda (NIA) used by NPCF, ZN and KNMG and is published (7 June 2012). The spearheads of the NPCF in National Implementation Agenda are: awareness of the patient, the Digital Care Guide, the digital Care Event and the development of the PGD (personal health record).

PERSONAL HEALTH RECORD

The NPCF wants everyone who wants this to be able to get to a PGD to gather information. Patients should be able, at any time of the day, to get access to their PGD, for example via their smartphone. Patients want understanding of, and commitment to, options and choice-information, processes and appointments (integrated care). They want to have their medical records, co-decision making and an individual care plan, important communications with health care providers, other patients and carers. For the developers, NPCF has formulated a number of requirements that the PGD must meet, both regarding the safety and interchangeability of information. The patient must determine in critical situations who has the so-called 'key' to his/her PGD.

INTRODUCTION MS. JACQUELIEN NOORDHOEK

Ms. Jacquelien Noordhoek is director of the Dutch Cystic Fibrosis Foundation (NCFS). Cystic Fibrosis is an inherited and incurable disorder in which patients die due to problems with lungs and digestive system. The NCFS represents the interests of patients, provides information, is a point of contact for the care, provides contacts, coordinates and funds research. 90% of the patients is member of the NCFS; It employs nine professionals and 100 volunteers with a budget of € 1.5 million per year. The NCFS participates in quality of care, development and implementation directive, registration and benchmarking and has developed a hallmark for CF centres. A CF Centre gets a hallmark if it meets the quality criteria which have been drawn up by the NCFS.

THE DUTCH REGISTRATION OF CF

In The Netherlands, the CF-registration was started in 2006 by the NCFS. There are 125 variables registered: about demographics, diagnosis, treatment, complications and social data. There are annual reports, there are benchmark-meetings and research is done. The coordination of the registration is located at the NCFS who keeps anonymized data files with medical information about people with CF. The purpose is to support scientific research and the care and treatment of people with CF. In the sixth report of the registration (performed in the year 2012) the data from 1,452 of the estimated 1,500 people with CF in The Netherlands are kept. The Registry Steering Committee consists of representatives of all CF centres and the NCFS. The Steering Committee determines the policies of the registration and has clear agreements about recording data, the management and the provision of information. The financing is (still) with the NCFS and amounts to €50,000-70,000 per year.

REPORTS OF THE CF-REGISTRATION

The analyses and coordination of reports are carried out by the NCFS. All treatment centres and various disciplines are involved. Starting in 2008, individual centres are compared, there are public reports (www.cfonderzoek.nl), symposia, conferences and web sessions. An example of what the contribution of registration to the treatment may be, it gives the comparison of the data on the nutritional status of children. In two centres, the BMI (body mass index) of children were found to be lower than in other centres. Through targeted attention to the treatment policy in the area of nutrition the BMI's could statistically improve significantly. Data is compared, not only nationally but also internationally. The registration is still further improved in terms of validity and reliability and guidelines are updated.

The conclusion is that coordination of registration by a professional patient organisation is possible and can be effectively organized; registration has added value and leads to improvement of care!

REVIEW OF CARE – THE NCFS QUALITY HALLMARK

In The Netherlands, there are seven CF-centres for children and adults with CF. In order to monitor the quality of care, the centres are tested every four years from the perspective of the patient. Quality criteria have been drawn up by the NCFS according to 'Kwaliteit In Zicht' (Quality in Sight). The review is based on surveys. All patients or parents of children covered by the CF-Centre receive an online-questionnaire on the care received at the centre. The CF-Centre itself also fills in a questionnaire. A hallmark report about the care in the CF-Centre is then made.

A trained Hallmark Committee (patient, parent, nurse and NCFS) subsequently visits the CF-centres. After the review visit a draft report is made, which is first checked for incorrect facts by the centre. If the CF-Centre fulfils the criteria, it gets an NCFS hallmark. The exact consideration of the Hallmark Committee is not yet public so far. In November 2012, a first pilot visit took place. The structural implementation started in 2013. There are now two CF-centres with the hallmark NCFS, The Hague Hospital and the UMC Utrecht.

The hallmark has been developed to describe the quality of care from the patients' perspective, and aims to improve the quality of care by systematic analysis and improvements. The conclusion is that review by a professional patient organisation can happen in an efficient way, complementary to visitations/accreditation and leads to improvement of care! Participation of patients in improvement of the quality of care is essential, executed simply and asks for a translation to a professional level.

SUMMARY

Question: what to do if a hospital does not want to take part in the review for the quality hallmark? *Answer*: patients will ask questions at their centre of expertise, if they do not wish to work on the certification procedure. It is therefore a motivation for the hospital to meet the criteria of the hallmark.

Question: how to deal with a situation in which more rare disease patient organisations would want to use the hallmark? *Answer*: In this case, cooperation and coordination would be desirable. However: for a patient, the only interest is with the hallmark that is related to his/her illness.

The NPCF has drawn up a statement to encourage the various players in the health care field to get motivated for the PGD. (www.npcf.nl/images/PDF/NPCF_visie_Persoonlijk_Gezondheidsdossier.pdf). Patients' awareness is one of the important priorities, because it is needed before actually start PGD's. The idea is that the patient collects all data in the PGD that is still scattered with different doctors. The patient has a complete overview of his file. The patient is the owner of his PGD. He decides what information he gives to which doctor and care giver. He can also add information which he considers important, such as a diary of his complaints. Based on his PGD, the patient can talk with the GP.

Among the attendees there is the concern that there is too little coordination when registering data. A good example of cooperation is the registration of people who are HIV-positive and the annual publication of the 'HIV-monitor'. Standardization of data is important as it makes exchange possible.

Remark: the NCFS has a budget of € 1.5 million, while many patient organisations do not have any funds. Ms. Noordhoek answers that collecting this amount is not without effort: 80% of the revenue is generated from own fundraising under the own followers. She advises other patient organisations to start small and reserve ever more hours for fundraising.

Mr. Crasborn (Achmea health insurance) finally advises patients ' organisations to note facts regarding rare diseases very sharply, to state what you want from the health insurers and start the dialogue. Patient organisations should determine what and how they want things done. Mr Crasborn notes that health insurers must cooperate and he's willing to help in this and give his advice.

REPORT OF THE CLOSING SESSION – CONCLUSIONS

Ms. Verbeet is the president of the Patients Federation NPCF and chaired the afternoon session. She explains how she came into contact with the problem of rare diseases in her immediate surroundings. How a diagnosis was late and a family subsequently disjointed. Parents often feel something is going wrong long before doctors do. If that is not taken seriously, it will lead to anger and frustration. Early diagnostics and more scientific research are therefore extremely important. It is important that there is political consciousness for rare diseases, as indicated in the letter from the minister about the NPRD. A lot has to happen: what are we going to do first next Monday?!

SUMMARY OF THE FIRST CONFERENCE DAY

Mr. Oosterwijk, Director of VSOP, notes that the introduction of Ms. Verbeet sums up the core of the previous conference day already, although she was not even present.

VWS - MINISTRY OF HEALTH, WELFARE AND SPORT

After the first patient video, Mr. Fred Krapels announced and explained the contents of the letter from the Minister to the House of Commons. To the surprise of many, the main role seems to be awarded to the NFU with regard to the implementation of the NPRD, in particular in relation to the appointment and role of the centres of expertise. Also it was good to hear that The Netherlands already transposed the cross-border health care directive. In addition, the letter also explained that the Minister adheres to good qualification and hence to better recording of rare disorders.

NFU - DUTCH FEDERATION OF UNIVERSITY MEDICAL CENTRES

The feeling that the NFU is an important stakeholder in this process was also a common reaction, but also, and above all that the NFU needs other parties to overall manage the total care process and promote aspects that are important for the quality of life of children and adults with rare disorders. VWS however, continues to keep a finger on the pulse, but will only intervene if the NFU in very last instance fails to come to an agreement.

EUROPE

Mr. Geoffrey Carroll explained that national expertise centres, ERNs and the Cross Border Healthcare Directive are closely interrelated. Considering the question how simple or complicated it would be to treat a Dutch child with a rare form of cancer in Paris, for example, he indicates that such a simple question ultimately determines whether the system actually works. He stresses that the realization of such linkages can be left to chance and spontaneity, but that clear criteria, control from a directing centre and ongoing monitoring are important. As far as the position of the patient, he stresses the importance of the role in the governance of ERNs and that not always the patient, but primarily the data and the medics themselves should cross borders. That was also the position of EURORDIS, expressed by Ms. Valentina Bottarelli, which gave a further explanation on the role of the ERN and the Cross Border Healthcare Directive. At a European level, further clarification of the ERN is being worked on. It is clear that the development of best practices, interaction with patient organisations, clinical research and attention to social care are important assignments for the ERN, and therefore will have to be a priority for the Dutch expertise centres (adds Mr. Oosterwijk).

COOPERATION IN CARE AND RESEARCH

Ms. Jolanda Huizer reported on the workshop on implementation of the NPRD. She addressed the need which is felt to change the funding system in occupational groups. Because of the divisions in the care, it is now impossible for centres of expertise and treating physicians to ensure adequate provision of care by more institutions working together, integrated care and shared care. Also, in the workshop, the importance of dynamic and modular guidelines and standards of care for rare disorders was stressed. With regard to Centres of Expertise, she indicates the importance of certification, clustering, European assurance, equivalent input of the perspective of the patient and the importance of knowledge sharing towards the overall healthcare field.

Ms. Carla Hollak then emphasized in her presentation that the objectives of the ERN in the field of research, diagnostics, should be much clearer. For example, how can countries learn from each other with regards to a timely diagnosis? She also suggested that cooperation is needed, for example in the field of joint registries with already scarce patients and that in this process a party is needed who can make decisions and can move industry to cooperation and the merging of data. However, no matter how hard we try to regulate, the human factor is often decisive. Still, many alleged specialists are just too set in their own ways to refer to the real expertise centre. Her message was that we should “Allow each other’s his/her experience”.

In addition, several participants emphasized the importance of harmonization of terminology in the field of registries and the importance of the patient’s access to his/her own data and the ability to login and to supplement. It was found that a rare condition only gets interesting if a medication is on the horizon. Ms. Hollak therefore proposed to always bring in pro bono within a Centre a few conditions for which this does not apply.

EARLY DIAGNOSIS

Mr. Gerard Engel briefly explained the role of the FBG (Forum Biotech and Genetics), especially the Rare Diseases Forum, in which currently is explored how earlier diagnostics can be promoted. A lot is to be gained, especially in the cooperation between youth physician, general practitioner and paediatrician. Mr. Gerard Engel stressed once again that rare disorders with 6-8% of the population and 20% of health care costs are not so rare and insignificant. He stressed that diagnostics and then registration of the diagnosis in registries should be inextricably linked.

Mr. Edwin Cuppen addressed this in more detail by illustrating the great opportunities that Whole Genome Sequencing (WGS) offers in shortening the diagnosis process and the many possibilities this offers throughout life. He illustrated that with the analysis of his own DNA, it was confirmed that he, just like everybody else, is a carrier of four recessive inherited rare disorders. Within a few years there will be opportunities where this can be implemented much wider than is currently the case in health care. Both pressure on health insurers as well as more cooperation are considered necessary. Then there was consensus on a joint call to use WGS as a first choice in diagnostics. When it comes to screening, for example neonatal blood spotting, however, there were more restraints regarding the use of these techniques. Also the call for the creation of a national registry of rare or genetic disorders should count on everyone's support.

PATIENT PERSPECTIVE

Ms. Elizabeth Vroom gave an impressive presentation on how a small patient group can be leading and steering in both the field of research and quality of care. Just as Ms Irene Caubo in the video, her urgent message also was: "Dear medical professional: listen to us, parents!”

The overall feeling in the workshop on quality of care and life was that the social aspect and the 'learning to live with' in the NPRD was heavily underexposed. Mr. Jos Dekkers of the Dwarlaesie Organisatie Nederland (DON: Spinal Cord Injury Organization The Netherlands) stressed the importance of the environment of the patient with the line: "my wife and I have my spinal cord injury". An important outcome of this workshop was the call to patient umbrella organisations to develop a guide on joint care policies for rare diseases for the benefit of the tasks of the municipalities within the context framework of the WMO.

In the evening session on strengthening the patients’ voice, cohesion was sought and found. Ms. Cynthia Vogeler outlined the overarching role of the NPCF. In particular, the advanced plans from the NPCF to realize a personal health file (PGD), was very well received. Then the workshop focused on the role of the NCFS, described by Ms. Jacqueline Noordhoek, in particular in the field of the CF quality mark for centres of expertise. The CF quality mark may or may not be awarded on a professional structured methodology from the perspective of the patient. Also, the benchmarking of quality of care on the basis of the NCFS managed registration in which CF centres and virtually all CF patients participate, is a concrete way to shape 'the voice of the patient'. It was concluded that both a more joint quality mark for Centres of Expertise for rare disorders, as well as the setup of the centres of expertise and registrations, are excellent means to let the voice of the patient not be a vague slogan literally and figuratively, but actually make a contribution to the quality of care and research. Mr. Jeroen Crasborn (Achmea Health Insurance) challenged the patient

organisations to go to the health insurers with a common program of requirements concerning the purchase of care based on criteria in which care standards, centres of expertise and registries are part of the purchase criteria.

FINAL DEBATE IN PLENARY: AND NOW?!

Ms. Verbeet challenged the participants to now 'complete the puzzle'. She suggested that anyone who takes the floor first, first addresses their own responsibility, then appeals to the person who is needed for this.

- *Question*: I am looking for European guidelines for rare disorders? *Answer*: guidelines can be found at the Order of Medical Specialists (OMS). They are also gradually supplemented with guidelines for rare disorders. At the VSOP, there are various standards of care for rare disorders. If there are guidelines elsewhere in Europe, however, an OMS stamp is required.
- *Question*: what is the input of the Kwaliteits Instituut (Quality Institute)? *Answer:* The Quality Institute is compiling a registry of recognized guidelines and standards.
- *Question:* How can cooperation between patient organisations be organised? *Response*: There is too much demand on the voluntary organisations, how can we professionalize? *Answers:* Experiential knowledge must be paid, patients must do less for free. If patients are to come to the table with CvZ, this needs to be rewarded. Advice should be appreciated. From the VSOP, policy officers could be used for these small patient organisations. *Reaction VSOP*: A financing structure is needed that makes that possible. *Reaction NPCF*: there is a global agreement on SKMS-funds[3]. For the first time, there are now NPCF "Quality funds" available that patient organisations can apply for, it is no longer done for free. *Remark:* it is not acceptable that necessary things no longer happen because it is no longer free. *Reaction CvZ*: according to the Quality Institute, guidelines can only be drawn up with participation of patients. Guidelines are developed jointly by health care provider, physician and patient. First guidelines are developed for major illnesses, but there is also attention for disorders with a smaller numbers of patients. Via the VSOP (Ms. Mariette Driessens) priorities and comments can be proposed towards the CVZ (Ms. Linda Saase) are bundled, not by each patient organisation for a rare condition separately.
- *Question*: the OMS does not participate in standards of care for rare disorders if there is no directive for the relevant condition. How is that then? *Answer*: We must not only focus our hope on the SKMS. Making professional medical guidelines is very expensive. They are good for large groups, for generic issues, but for smaller separate disorders it is no solution. Let's focus on quickly setting up centres of expertise together with patient organisations and health insurers. Let them make those guidelines and then implement them through the expertise centre.
- *Question*: it is necessary to make SMART standards. Ms. Wendy Van Zelst-Stams calls to participate in the SMART making of the criteria for centres of expertise. Several attendees promise their cooperation; others find the current criteria actually specific enough.
- *Question* to the NFU: we now have created the Catalogue Rare Diseases of the NFU, based on the inventory provided by the University medical centres. That list is approved by the directors of the UMC's, but patients still have to look at it. There has been consultation with the VSOP about publishing the list. Some things are still missing, this is shown by the comparison with the data of the Orphanet database. The list should therefore be supplemented. Would you consider bringing out the list already and only then look at the perspective of the patient? And what will be the accreditation of centres of expertise? *Answer*: the criteria can be used and there is also the EUCERD input from the perspective of the patient. The NFU-list will be published soon and then via the VSOP the input of the perspective of the patient (review) will be coordinated.
- *Question*: how can it be realised that experts travel or share their knowledge otherwise with the external experts, how is it funded? *Answer*: this requires a storage in in the formal tariff structure. It is possible, there are examples in the fields of CF and HIV/aids.
- *Question*: there are many small patients' organisations, their workload is increasing. The discussion is again about the possibilities to professionalize patient organisations. Is it necessary to cluster associations? Can there be funds available from the health insurance for professionalization and clustering? *Answer*: the insurer prefers independent funding from the Government. Also a request can be made at PGOsupport[2].

[2] PGOsupport is an independent service organization for patient organizations.

- *Question*: what are the possibilities for funding of patient organisations in relation to these tasks? A*nswer*: patient organisations must not become dependent on ' lazy 'subsidies. Come forward with good plans, with good projects, develop own initiatives. Show that you are adding value. Also small patient organisations can have a lot of impact.

PANEL DEBATE

The panel debate was chaired by Ms. Gerdi Verbeet. Panellists: Ms. Martina Cornel (Orphanet), Ms. Melanie Schmidt (NFU), Ms. Linda van Saase (CvZ), Mr. Michel Dutrée (Nefarma), Mr. Jeroen Crasborn (Achmea), Mr. Frits Lekkerkerker (NPRD) and Mr. Cees Smit (VSOP/EGAN).

ROLE OF THE HEALTH INSURANCE COMPANIES

Ms. Verbeet: what can be the role of health insurance companies in improving the quality of care for rare disorders?

Mr. Crasborn: health insurance companies should take the NPRD seriously, be proactive and secure matters.

Mr. Lekkerkerker points out that insurance companies, for example, can be actively supportive in the creation of registries.

Mr. Smit points out that changes in healthcare financing are needed in which the funding of registries can be incorporated. For rare disorders insurance is customized, that doesn't fit well in the current health care system. Setting up a think tank with both the large and small healthcare insurance companies could be a good suggestion

Mr. Crasborn says there is no dynamics without competition. In part insurers could fix prices, but that is not allowed by the NMA (Dutch Health Authority). A joint action to the NMA might be a possibility. ZN (Health Insurance Companies) is the director here and can declare something non-competitive, which for example could result in price agreements on orphan drugs. He advises the patient organisations: "make SMART what you want exactly and submit that proposal to health insurers". He himself commits to making a start with the proposed think tank

ROLE OF POLITICS AND OTHERS

Ms. Verbeet: According to the NPRD different parties have a role in the NPRD, but politics is barely in the picture.

From the floor: who monitors what is happening, if everyone fulfils the attributed tasks? Who looks at whether and when the NFU-list of centres of expertise is published? Politics should have the task of a watchdog.

Mr. Oosterwijk indicates that he has confidence in the NFU for the execution of their role. Upon request he indicates that the VSOP or himself, is willing to play a role in the coordination and monitoring of the implementation, but that there should be consensus and commitment in the field with all concerned parties. Also the contact between the VSOP and VWS is good. The minister of VWS (Health, Welfare and Sports) has not yet announced where the overall directorship will be, other than that of the NFU concerning the centres of expertise.

Ms. van Saase says that that CvZ will organize a consultation with the patient organisations twice per year.

From the floor, Ms. Huizer: The Minister of VWS will inform the House of Commons about the progress. We are talking not only about the NPRD centres of expertise: the letter from the Minister offers other starting points to speak about other business than just expertise centres.

Mr. Oosterwijk: VWS has informed me that the consensus consultation, referred to in the letter from the Minister, will have a real power. It is important to be alert that this actually happens, and is not just talked about.

Ms. Cornel: the Minister should approve the current NFU-list of centres of expertise before the end of the year, so that The Netherlands can participate in the EU Call on the ERNs in 2014. Because there are no “accredited” centres of expertise appointed in The Netherlands, they do not appear in European reviews!

Mr. Lekkerkerker: the list is not yet complete, criticism is still possible, but indeed we have to move on!

Mr. Oosterwijk: In December, the NFU will publish the list on the internet. The list overlaps largely with the list from Orphanet, the VSOP is already involved in the patient consultation on this list.

From the floor: publish the NFU-list provisionally, with a provisional national quality mark. On the one hand, we must not miss the boat in Europe, on the other hand, the NFU-list can still be criticised.

Ms. Schmidt: I will propose to the NFU Board to indeed publish the list in December as a provisional list, in which on the one hand changes are still possible, but on the other hand, could already be approved by the Minister to be recognised at European level proposed by the NFU.

Ms. Knoers: Will the minister of VWS put these and other items on the agenda in Europe?

Dhr. Dutrée: the Dutch Presidency offers possibilities and also the Department of international relations of VWS is important for price formation and research.

ORPHAN DRUGS

Ms. Verbeet: Will orphan drugs for rare disease be too expensive?

The cost factor is in development. The EMA could review and adapt the requirements for medicines intended for small groups of patients. That makes a difference in cost and a medicine can then be on the market faster. Also, with small groups of patients, almost all patients are in a trial. It is important that centres of expertise become part of European networks. Also at a European level, the industry works together with EFPIA (European Federation of Pharmaceutical Industries and Associations).

Question: Is CvZ also active in Europe in regards to pricing and cost effectiveness of orphan drugs?

Answer: not intensively. There are a few pilots on the uniform delivery of data.

PREVIEW

Ms. Verbeet: what are the expectations of each and every one of you for 2015?

Mr. Smit: In the last few years, considerable progress has been made. By 2015, there will be a clear list with centres of expertise where there is a consensus. Hopefully, the impact is that a patient with multiple complaints can be helped in one centre of expertise and no longer has to travel to multiple specialists.

From the floor:

- Care coordinators are important, especially for people with multi morbidity. I hope they will be there in 2014.
- There is now a task for VWS: the Minister can no longer say that work still needs to be done on a NPRD: she now needs to actively implement.

Mr. Lekkerkerker: I look forward to the reaction of the VSOP to the letter from the Minister. I regret that the VSOP is not named in this letter.

CLOSURE

Mrs. Verbeet: this was my first introduction to a field that is very involved in rare disorders. I intend to follow the implementation of the NPRD and see if anyone fails to comply with the commitments and does not live up to the expectations.

Mr. Oosterwijk will contact the Ministry of VWS on the follow-up. He then thanks all participants for their active participation. It was a very successful conference, resulting in concrete agreements. Also, he thanks speakers, chairmen, panel members, and patients who have contributed to the movies. In addition, he congratulates the VSOP-team with the organization of the conference.

APPENDIX I - FINAL LIST OF PARTICIPANTS

Mr. / Ms.	Last name	First name	Organisation	Stakeholder Group
Mr.	Akkermans	Ton	NFVN	Patient representative
Ms.	Ali	Farhana	Eurordis	Patient representative
Ms.	Alvares	Amy	Oscar Nederland	Patient representative
Mr.	Aras	Firat	AbbVie	Industry
Ms.	Beacher	Soroya	Oscar Nederland	Patient representative
Mr.	Beltman	Henk	Programma Aandacht voor Iedereen	Patient representative
Mr.	Benedictus	Jan	NPCF	Patient representative
Mr.	Bertens	Peter	Nefarma	Industry
Mr.	Blom	Ralph	Chiesi Pharmaceuticals B.V.	Industry
Ms.	Boer, de	Liesbeth	Pfizer bv	Industry
Ms.	Booys, de	Marjolein	CVZ/Kwaliteitsinstituut i.o.	Public administration
Mr.	Borkus	René	PG werkt samen	Patient representative
Ms.	Bottarelli	Valentina	Eurordis	Patient representative
Ms.	Bovy - van der Lugt	Nathalie	Radboud UMC	Healthcare Professional
Ms.	Bracke	Sonja	MSSRF	Patient representative
Ms.	Breukelen, van	Silvia	VSOP	Patient representative
Mr.	Brinkmann	Albert	DSD-Nederland	Patient representative
Ms.	Brouns - van Engelen	Marloes	Erfocentrum	Healthcare Professional
Ms.	Buijsman	Anita	patiëntenvertegenwoordiging	Patient representative
Ms.	Carlier	Judith	Orphanet Nederland	Healthcare Professional
Mr.	Carroll	Geoffrey	WHSSC	Healthcare Professional
Ms.	Caubo - Damen	Irene	VSOP	Patient representative
Ms.	Citak	Elmas	Oscar Nederland	Patient representative
Ms.	Claahsen - van der Grinten	Hedi	Radboud UMC	Clinician/GP
Mr.	Coo, de	René	ErasmusMC	Clinician/GP
Ms.	Cornel	Martina	VUmc	Healthcare Professional
Mr.	Cramer	Ton	Stichting Tubereuze Sclerosis Nederland	Patient representative
Mr.	Crasborn	Jeroen	Achmea	Insurer
Mr.	Cuppen	Edwin	UMC Utrecht/Hubrecht Institute	Healthcare Professional
Ms.	Custers	Ilse	AbbVie	Healthcare Professional
Mr.	Dekkers	Jos	Dwarslaesie Organisatie Nederland	Patient representative
Mr.	Dolsma	Klaas	Erfocentrum	Healthcare Professional
Ms.	Driessens	Mariette	VSOP	Patient representative
Mr.	Droog	Herm	Stichting AA&PNH	Patient representative
Ms.	Duin, van	Sylvia	Axon Connect	Industry
Mr.	Dutrée	Michel	Nefarma	Industry
Ms.	Effing - Boele	Marije	VKS	Patient representative
Mr.	Engel	Gerard	FBG	Healthcare Professional
Ms.	Evers	Pauline	NFK	Patient representative
Ms.	Ferrelli	Rita	Europlan	Public administration
Mr.	Fossatelli	Marco	Shire	Industry
Ms.	Gill'ard	Chantal	VSOP	Patient representative
Ms.	Groot, de	Marianne	patiëntenvertegenwoordiging	Patient representative
Mr.	Hagendijk	Rob	UVA	Healthcare Professional
Ms.	Hassels Monning	Cathy	zelfstandige (communicatie patiënten)	Healthcare Professional

Mr.	Hofdijk	Jacob		Healthcare Professional
Ms.	Hollak	Carla	AMC	Healthcare Professional
Ms.	Horemans	Anja	Spierziekten Nederland	Patient representative
Ms.	Huijbregts	Patricia	PGOsupport	Healthcare Professional
Ms.	Huizer	Jolanda	ZonMw	Healthcare Professional
Ms.	Jaarsveld, van	Xana	Longfonds	Patient representative
Mr.	Jong, de	Bert	Genzyme	Industry
Ms.	Kaatee	Marleen	PSC Europe i.o.	Patient representative
Mr.	Kadiks	Hans	Nina Foundation	Patient representative
Ms.	Kaptein	Leonie	Erasmus MC	Healthcare Professional
Ms.	Karsenberg	Kim	VSOP	Patient representative
Mr.	Kattekamp	Ber	Interstitiële Cystitis Patiëntenver.	Patient representative
Mr.	Kimpen	Jan	UMC Utrecht	Healthcare Professional
Ms.	Kleinegris	Carmen	NET-groep	Patient representative
Ms.	Knecht, de - van Eekelen	Annemarie		
Ms.	Knoers	Nine	VKGN & UMCU	Academic / Researcher
Mr.	Koenen	Paul	Novartis Pharma	Industry
Mr.	Kranen, van	Henk	RIVM	Public administration
Mr.	Krapels	Fred	Ministerie VWS	Public administration
Ms.	Kruijshaar	Michelle	Erasmus MC	Healthcare Professional
Ms.	Landa	Diana	Bijniervereniging NVACP	Patient representative
Ms.	Lanphen	Joke	FBG	Healthcare Professional
Ms.	Lanser	Anke	Spierziekten Nederland	Patient representative
Mr.	Lekkerkerker	Frits	Klankbordgroep za	Public administration
Mr.	Leufkens	Bert	CBG	Public administration
Ms.	Leyten	Claire	Prosensa	Industry
Mr.	Lincke	Carsten	NVK	Healthcare Professional
Mr.	Linde, van der	Michael	NVHP	Patient representative
Ms.	Link	Angèl	College voor Zorgverzekeringen	Public administration
Ms.	Linthorst	Gisela	Genzyme	Industry
Mr.	Loenhout, van	Jos	GSK Nederland BV	Industry
Ms.	Mark, van der	Hendrien	Pfizer BV	Industry
Ms.	Marks - de Korver	Muriël	Bijniervereniging NVACP	Patient representative
Ms.	Martens	Maria	VSOP	Healthcare Professional
Ms.	Meijden, van der	Margaret	BPRA	Consultancy
Mr.	Meuleman	Tom	BioMarin Europe	Industry
Ms.	Meutgeert	Hanka	VKS	Patient representative
Ms.	Musters	Anne	AMC	Academic / Researcher
Ms.	Nieuwenhoven	Anja	Nierpatienten Vereniging Nederland	Patient representative
Mr.	Nieveen	Jos	AbbVie B.V.	Industry
Mr.	Nijhoff	Gerrit	SCCH	Patient representative
Ms.	Nijnuis	Marianne	VSOP	Patient representative
Ms.	Noordhoek	Jacquelien	NCFS	Patient representative
Mr.	Nugteren	Rutger	RIVM	Public administration
Mr.	Ommen, van	Gert-Jan	LUMC	Academic / Researcher
Mr.	Oosterwijk	Cor	VSOP	Patient representative
Ms.	Overveld, van	Petra	LUMC/Orphanet	Healthcare Professional
Mr.	Ploegmakers	Hans	STSN	Patient representative
Ms.	Plug	Iris	Erasmus MC	Clinician/GP

Ms.	Poelgeest, van	Mary Lynne	ICP	Patient representative
Ms.	Posthuma	Anja	HME-MO Vereniging Nederland	Patient representative
Ms.	Prantl	Karen	NVN	Patient representative
Mr.	Pruijs	Hans	VOI	Patient representative
Ms.	Rademaker	Karin	UMC Utrecht	Academic / Researcher
Ms.	Ravenswaaij, van - Arts	Conny	UMC Groningen	Clinician/GP
Mr.	Reuser	Bernard	VSOP	Healthcare Professional
Ms.	Roelofs	Ilze	VSOP	Healthcare Professional
Mr.	Roseboom	Henk	Belangenver. Longfibrosepatienten	Patient representative
Ms.	Royen, van - Kerkhof	Annet	Wilhelmina Kinderziekenhuis UMCU	Clinician / GP
Ms.	Saase, van	Linda	CVZ	Public administration
Mr.	Salemink	Gerrit	ZN	Insurer
Ms.	Sar, van der	Heleen	Baxter B.V.	Industry
Ms.	Schmidt	Melanie	NFU	Healthcare Professional
Ms.	Schouwenburg, van - Joosten	Biene	SCCH	Patient representative
Ms.	Segers	Marèl	VSOP	Healthcare Professional
Ms.	Siderius	Liesbeth	SSSSH	Patient representative
Mr.	Smit, de	Denhard	MediClara	Healthcare Professional
Mr.	Smit	Cees	VSOP/EGAN	Healthcare Professional
Ms.	Snijder	Irene	FOP stichting Nederland	Patient representative
Ms.	Snijder	Vera	Rubinstein-Taybi Stichting	Patient representative
Ms.	Sparnaay	Marjolein	NVHP	Patient representative
Ms.	Speijer	Anne	VSOP	Healthcare Professional
Ms.	Steen, van der	Leny	Stichting PHA Nederland	Patient representative
Ms.	Stiene	Andrea	Contactgroep AA&PNH	Patient representative
Ms.	Stoel, van der	Annie	Stichting PHA Nederland	Patient representative
Mr.	Stoep, van der	Bart	Galactosemie Vereniging Nederland	Patient representative
Ms.	Stoyanova - Beninska	Violeta	CBG	Public administration
Mr.	Toenders	Wil	Toendersdegroot consultancy	Patient representative
Ms.	Vajda	Ildikó	VSOP	Patient representative
Ms.	Valk, van der	Tessa	VSOP	Patient representative
Ms.	Veen, van der	Ytje	VSOP	Patient representative
Ms.	Veldhuizen, van	Thea	VSOP	Patient representative
Ms.	Verbeet	Gerdi	NPCF	Patient representative
Ms.	Verkamman	Annemiek	HollandBIO	Industry
Mr.	Vink	Paul	SCCH	Patient representative
Ms.	Visser, de	Marianne	Forum Biotechnologie en Genetica	Healthcare Professional
Ms.	Vogeler	Cynthia	NPCF	Patient representative
Ms.	Vries, de	Anneke	Stichting Noonan Syndroom	Patient representative
Ms.	Vroom	Elizabeth	Duchenne Parent Project	Patient representative
Mr.	Vugt, van	Joris	Pfizer bv	Industry
Ms.	Waddell	Paula	VSOP	Patient representative
Mr.	Wagemaker	Gerard	Ned. Ver. Gen- en Celtherapie	Healthcare Professional
Ms.	Weely, van	Sonja	ZonMw	Healthcare Professional
Mr.	Weijma	Hans	NVN	Patient representative
Ms.	Weinreich	Stephanie	VU Medisch Centrum	Healthcare Professional
Mr.	Westen	Marcel	Synageva BioPharma	Industry
Ms.	Westerlaken, van der	Mignon	Genzyme	Industry
Ms.	Wever	Kim	VSOP	Patient representative

Mr.	Wiers	Pieter	patiëntenvertegenwoordiging	Patient representative
Ms.	Wind	Wilna	NPCF	Healthcare Professional
Mr.	Zeijden, van der	Albert	International Health Forum Gastein	Patient representative
Ms.	Zelst, van - Stams	Wendy	UMC St Radboud	Academic / Researcher

APPENDIX II – FINAL PROGRAMME OF THE NATIONAL CONFERENCE

DAY 1 - 14 NOVEMBER 2013

	Morning chairs: Ms. Martens (VSOP) and Mr. Lekkerkerker (NPRD, ZonMw)		
8.30	Registration		
9.30	Welcome and opening by the chairs		
9.35	**The voice of the patient (video 1)**		
9.40	**Mr. Krapels (Ministry of Health Welfare and Sports)**		
10.10	**Mr. Carroll (Medical Director WHSSC, UK)**		
10.40	Break		
11.00	**Morning workshops**		
WS 1 – Implementation National Plan			**WS 2 - European cooperation (in English)**
Chairs: Ms. De Visser (FBG), Ms. Monissen (De Friesland) **Speakers: Ms. Huizer (NPRD, ZonMw), Dr Salemink (ZN)**			Chairs: Mr. Van Ommen (LUMC), Mr. Oosterwijk (VSOP) **Speakers: Mr. Carroll (WHSSC), Ms. Bottarelli (Eurordis)**
12.30	Lunch break		
	Afternoon chairs: Mr. Dolsma (Erfocentre) and Ms. Van Breukelen (VSOP)		
13.15	**The voice of the patient (video 2)**		
13.20	**Ms. Hollak (AMC)**		
13.50	**Ms. Vroom (Duchenne Parent Project)**		
14.15	**Afternoon workshops**		
WS 3 – Research and diagnostics			**WS 4 – Quality of health care and life**
Chairs: Mr. Wagemaker (Erasmus MC), Mr. Engel (FBG)			Chairs: Ms. Vroom (Duchenne Parent Project), Mr. Dekkers (DON)
Speakers Mr. Cuppen (UMC Utrecht), Mr. Engel (FBG)			**Chairs: Mr. Beltman (Attention for Everyone), Ms. De Booys (Quality Institute)**
15.45	Intermission		
16.00	**Plenary reporting WS 1 – Implementation National Plan**		
16.15	**Plenary reporting WS 2 – European collaboration**		
16.30	**Plenary Reporting WS 3 – Research and diagnostics**		

16.45	**Plenary Reporting WS 4 – Quality of health care and life**
17.00	Closure and drinks
17.45	Diner buffet

19.00 - 20.30	**WS 5 – Strengthening the patients' voice**
Chairs: Ms. De Knecht - van Eekelen and Mr. Crasborn (Achmea)	
Speakers Ms. Noordhoek (NCFS) en Ms. Vogeler (NPCF)	

DAY 2 - 15 NOVEMBER 2013

	Morning chairs: Mr. Leufkens (CBG) and Ms. Lanphen (FBG)		
8.30	Reception and registration		
9.15	Welcome and opening by the chairs		
9.20	**The Voice of the Patient (video 3)**		
9.25	**Mr. Kimpen (NFU)**		
9.50	**Mr. Crasborn (Achmea)**		
10.15	**Mr. De Jong (BioFarmind / Genzyme)**		
10.40	Break		
11.00	**Morning workshops**		
WS 6 - Realisation of Centres of Expertise			**WS 7 – Access to orphan drugs and health care**
Chairs:	Ms. Stoyanova - Beninska (CBG) Ms. Knoers (VKGN)		Chairs: Ms. Rademaker (WKZ) Mr. Van der Zeijden (IAPO)
Speakers	**Ms. Van Zelst-Stams (RadboudUMC)** **Ms. Meutgeert (VKS)**		**Speakers: Mr. Toenders (ToendersdeGroot BV)** **Ms. Evers (NFK)**

12.30	Lunch break
	Afternoon chairs: Ms. Verbeet (NPCF) and Mr. Oosterwijk (VSOP)
13.15	**Recapitulation Day 1**
13.30	**Plenary reporting WS 6: Realisation of Centres of Expertise**
13.45	**Plenary reporting WS 7: Access to orphan drugs and health care**
14.00	**Plenary closing debate: And now?!**
15.00	**Panel debate**
15.45	**Conclusions, closure**
16.00	Bites and drinks