**State of the art for rare disease activities in EU Member States and other European Countries**

**Netherlands Report**

**Definition of a Rare Disease**

The Netherlands has adopted the European Commission definition of a rare disease and the national plan espouses this definition.

**National Plans and Strategies for Rare Disease**

The National Plan for Rare Diseases was approved by the Minister of Health and adopted by The Netherlands in November 2013.

**Content and Funding of the National Plan**

To ensure long term funding and sustainability of the measures detailed within the National Plan a structural budget was allocated. This money will enable the rare disease community to:

- Assess Centres of Expertise
- Issue certificates of approval
- Supply information on Rare Diseases
- Complete or participate in Scientific research (via E-rare)
- Code rare diseases using the example provided by Work Package 5 of RD ACTION, which adopted the DIMDI method.

Plans are being prepared which will ensure the Orphanet function is included within this particular budget.

**Implementation and evaluation of the National Plan**

The Minister of Health established the Coordination Group for Rare Diseases Plan (Afstemmingsoverleg Zeldzame Ziekten), a multi-stakeholder dedicated body, which exists to oversee the drafting and implementation of the National Plan. It is an independent body which advises the Minister on related issues and monitors and coordinates the actions of the National Plan. The coordinating body is independently chaired and is comprised of health care professionals, heath care insurers, patient representatives and clinical geneticists.

See https://www.zonmw.nl/nl/onderzoek-resultaten/kwaliteit-van-zorg/programmas/programma-detail/secretariaat-afstemmingsoverleg-zeldzame-ziekten/

**Major Successes**

The National Plan has warranted many successes, most notably the assessment and endorsement of eligible Centres of Expertise. This task was completed in consultation with both the expertise of patients and the medical community within specified timeframes.

**Organisation of RD Health and Social Cases**

**Centres of Expertise (CEs)**

The Netherlands has an official national policy for the designation of Centres of Expertise which has been fully implemented by decree of the Ministry of Health. The national criteria for designating CEs is fully based on the EUCERD-criteria. These criteria have been operationalized to the Dutch Situation. In some CE's a holistic approach is prevalent, but this has not been established structurally in most CEs.



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**European Reference Networks (ERNs)**

A formal process is in place within the Netherlands to endorse Health Care Providers to participate as members or coordinators of a European Reference Network.

At present a total of 13 HCPs are participating as full members of 24 ERNs and there are 5 HCPs which are coordinating an ERN:

- Rare Craniofacial Anomalies and ENT Disorders (Erasmus University Medical Centre)
- Rare Endocrine Conditions (Leiden University Medical Centre)
- Genetic Tumour Risk Syndromes (Radboud University Medical Centre; Nijmegen)
- Rare Inherited and congenital anomalies (Erasmus University Medical Centre)
- Rare Diseases of the Heart (University of Amsterdam Medical Centre)

**Rare Disease Registration**

In The Netherlands, there are national rare diseases registries however as yet there are no national registration platform or databank for rare disease registration. The overview of all Dutch biobanks includes disease-specific collections. The rare disease registration in the Orphanet database is coordinated and managed by the national Orphanet coordinator and information is shared on the Orphanet portal. The registries which cover a single rare disease are funded by project subsidies, university medical centres and patient organisations.

**Genetic Testing and New-born screening**

In The Netherlands, genetic testing is only completed in DNA diagnostic laboratories within the clinical genetics departments of the eight university medical centres and at the oncologic centres NKI/AvL.

A list of the available tests can be found on the Orphanet website http://www.orpha.net/national/NL-NL/index/homepage/

There is also further information available: http://www.dnadiagnostiek.nl/index.php

Currently, the neonatal screening programme within the Netherlands tests for 17 rare diseases however the programme will extend to 31 diseases in due course. The following diseases are screened for within the programme:

1. Adrenogenitaal syndroom (AGS)

2. Biotinidase deficiëntie (BIO)

3. Congenitale hypothyreoidie (CH)

4. Cystic fibrosis (CF)

5. Galactosemie (GAL)

6. Glutaaracidurie type 1 (GA-1)

7. HMG-CoA-lyase deficiëntie (HMG)

8. Isovaleriaan-acidurie (IVA)

9. Long-chain hydroxyacyl-CoA dehydrogenase deficiëntie (LCHADD)

10. Maple syrup urine disease (MSUD)

11. Medium-chain acyl CoA dehydrogenase deficiëntie (MCADD)

12. 3-Methylcrotonyl-CoA carboxylase deficiëntie (3-MCC)



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13. Multiple CoA carboxylase deficiëntie (MCD)

14. Phenylketonurie (PKU)

15. Sikkelcelziekte (SZ)

16. Tyrosinemie type 1 (TYR-1)

17. Very long-chain acylCoA dehydrogenase deficiëntie (VLCADD)

## Guidelines and Training Activities

### Clinical Practice Guidelines (CPGs)

National Clinical Practice Guidelines for rare disease are produced in The Netherlands and are either evidence or consensus based. The Consensus based CPGs can be found on the websites of several societies of medical specialities for instance:

In addition, patient-initiated CPGs are developed by the National Patient Alliance (VSOP) and published ( www.zorgstandaarden.net/nl/wat-is-een-zeldzame-aandoening/voor-welke-zeldzame-aandoeningen-een-zorgstandaard and www.zichtopzeldzaam.nl/documenten/ ) and subsequently registered in the formal database of the National Health Care Institute (www.zorginzicht.nl/Bibliotheek/Paginas/Raadplegen.aspx?status=IsRegister ). The Netherlands has a national policy for the development of CPGs, the adoption of CPGs and the Implementation of CPGs.

### Training and Education

Initiatives for education or rare disease related training come from the Centres of Expertise on rare diseases. There is also a website which provides General Practitioners with further information on genetics, advice on the locations of genetic testing and guidance on available courses (https://www.huisartsengenetica.nl/ ). The Genetic Information Centre (Erfocentrum) and the National Patient Alliance (VSOP) provide several training and educational activities

## Information Resources for Rare Diseases

### Orphanet Activities

The Netherlands has a national Orphanet team which is currently hosted within the department of Human Genetics at Leiden University Medical Centre. The Orphanet registry is jointly funded via the EU Joint-Action (RD-ACTION) and partly by the Leiden University Medical Centre. Plans are currently underway to embed the Orphanet function within the structural budget for the national plan. This will allow the team to continue producing, in collaboration with Erfocentrum, information within the Dutch national language.

Orphanet Netherlands collects all information on rare diseases within the Netherlands. This information is obtained via Centres of Expertise, patient organisations, diagnostic tests, laboratories, patient and mutation registries, biobanks, research projects, clinical trials, platforms and the registration of rare disease professionals.

### National Helplines

Through a mixture of public and private funding the Netherlands has a helpline dedicated to rare disease activities available for anyone to use. The helpline is run by Erfocentrum. The helpline does not provide advice for one specific disease but focusses generally on rare and hereditary diseases. Members of the public and healthcare professionals can contact the helpline via an email account.



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**Official Information Centres**

The Netherlands has three official/unofficial information centres for rare disease:

- **Orphanet Nederland:** which receives finance via RD-ACTION and the budget of Leiden University Medical Centre.
- **Erfocentrum:** receives both public and private funding
- **National Patient Alliance VSOP**: public-privately funded via project funding and through its membership

**Rare Disease Research Activities**

**Existence of RD research programmes/projects in your country**

Specific projects relating to rare disease are funded from the general research budget within the Netherlands. A research budget has been allocated to those who participate within E-rare projects as well as projects within the field of priority medicines and translational research. There has been a decision, entrenched in policy, to grant a proportion of the national research budget specifically to rare disease research and a total of €2,000.00 of public funds have been allocated for rare disease research actions/projects per year since the National Plan in The Netherlands began. The National Plan does not specifically mention socio-economic research, however a growing urgency is felt to conduct research into the social implications of living with rare disease. The coordinating body will advise the Minster of Health at the end of 2016 on this matter.

**Participation in E-Rare and International Research Initiatives**

The Netherlands are involved in both E-rare and IRDIRC.

**National Alliance of Patient Organisations and Patient Representation**

The Dutch National Alliance for Rare and Genetic Disorders (VSOP) has achieved many milestones since 2014. The Alliance has:

- Co-executed the assessment of centres of expertise together with NFU (academic medical centres)
- Developed a series of Standards of Care for rare diseases.
- Developed a series of 80 rare disease treatment guidelines for General Practioners (GPs).
- Organised the yearly National Conference on Rare Disorders, the yearly Rare Disease Day and the yearly Date2Innovate (matching patient organisations with research and industry)
- Was active in the field of reproductive health policy and research (preconception care, PGD, prenatal screening / NIPT, neonatal screening)
- Started to support families with a child with an undiagnosed rare disorder
- Was active in the field of patient engagement in research
- Was represented is several governmental and medical committees and institutions
- Launched and maintained several issue-specific websites: zichtopzeldzaam.nl, zeldzameaandoening.nl, zorgstandaarden.net, onderzoekwijzer.nl, ziekteonbekend.nl, checkdecheck.nl, kindenonderzoek.nl, biobanken.org, innovatievoorzeldzaam.nl, ncza.nl, egan.eu, biomedinvo4all.com, preparingforlife.net
- Participated / participates in several major FP7, H2020 and IMI projects

VSOP has a membership of 70 patient organisations for rare diseases. Members and non-members are consulted several times a year on overarching issues concerning national and European rare disease policy, research and care. This includes general assemblies, working groups and consultation meetings. VSOP uses this input in several governmental and national medical and ethical committees dealing with research, healthcare, prevention, reimbursement etc. In addition, all kinds of disease-specific consultations take place by governmental and medical organisations, VSOP and other NGO's.



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**Integration of Rare Diseases to social policies and services**

Specific actions exist in the Netherlands to enable real access for people with rare disease to general social/disability programmes (i.e. training guidelines for social workers etc.) Individual care plans including access to social and support services. There are no specific future plans to support social integration of peoples with rare diseases. However, plans to support rare disease patients will be integrated into existing social measures.

**Orphan Medicinal Products**

Almost all OMPs with a European Union marketing authorisation are available in The Netherlands. This means they are priced and reimbursed or directly provided by the health system of the Netherlands. However some products were not submitted for reimbursement. For all out of hospital medicines information is available on the reimbursement status and price on (www.medicijnkosten.nl/servicepagina/engelse-informatie/objectives).

There are no special approval procedures in place to facilitate access to Orphan Medicinal products for patients within The Netherlands. There are research programmes for Orphan drugs, the Netherlands have incentives to support research into and the development of (designated or potential) OMPs.

**Rare Disease Day**

The Netherlands has organised events on Rare Disease day since 2009. The events are organised by the National Patient Alliance (VSOP) in cooperation with others.

Since the beginning of 2014 a yearly National Congress on Rare Diseases has been organised by VSOP with, in 2016, the NFU (Academic Medical Centres). The 6$^{th}$ European Symposium on Rare Anaemias was also held in Amsterdam in 2015. http://www.rarediseaseday.org/country/nl/netherlands

**Other**

The Netherland has had numerous rare disease related achievements since the beginning of 2014. It has:

- Identified and established a comprehensive network of centres of expertise
- Organised Rare Disease National Policy meetings
- Installed a coordinating body



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