2014 REPORT ON THE STATE OF THE ART OF RARE DISEASE ACTIVITIES IN EUROPE

STATE OF THE ART OF RARE DISEASE ACTIVITIES IN ISRAEL

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The European Union Committee of Experts on Rare Diseases (EUCERD) was established in 2009 and its mandate ended in 2013. It is replaced from 2014 by the Commission Expert Group on Rare Diseases. The EUCERD Joint Action continues to support the activities of the new Expert Group until 2015.

More information on the activities of the former European Union Committee of Experts on Rare Diseases and the EUCERD Joint Action can be found at www.eucerd.eu.

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ACRONYMS

CAT - Committee for Advanced Therapies at EMA
CHMP - Committee for Medicinal Products for Human Use at EMA
COMP - Committee on Orphan Medicinal Products at EMA
DG - Directorate General
DG Enterprise - European Commission Directorate General Enterprise and Industry
DG Research - European Commission Directorate General Research
DG Sanco - European Commission Directorate General Health and Consumers
EC - European Commission
ECRD - European Conference on Rare Diseases
EEA - European Economic Area
EMA - European Medicines Agency
ERN - European reference network
EU - European Union
EUCERD - European Union Committee of Experts on Rare Diseases
EUROCAT - European surveillance of congenital anomalies
EUROPLAN - European Project for Rare Diseases National Plans Development
EURORDIS - European Organisation for Rare Diseases
FDA - US Food and Drug Administration
HLG - High Level Group for Health Services and Medical Care
HTA - Health Technology Assessment
IRDiRC – International Rare Diseases Research Consortium
JA - Joint Action
MA - Market Authorisation
MoH - Ministry of Health
MS - Member State
NBS - New born screening
NCA - National Competent Authorities
NHS - National Health System
PDCO - Paediatric Committee at EMA
RDTF - EC Rare Disease Task Force
WG - Working Group
WHO - World Health Organization
GENERAL INTRODUCTION

This document was produced by the Scientific Secretariat of the European Union Committee of Experts on Rare Diseases (EUCERD), through the EUCERD Joint Action: Working for Rare Diseases (N° 2011 22 01), which covers a three year period (March 2012 – February 2015).

The European Union Committee of Experts on Rare Diseases (EUCERD) was established in 2009 and its mandate ended in 2013. It is replaced from 2014 by the Commission Expert Group on Rare Diseases. The EUCERD Joint Action continues to support the activities of the new Expert Group until 2015.

The present report aims to provide an informative and descriptive overview of rare disease activities at European Union (EU) and Member State (MS) level in the field of rare diseases and orphan medicinal products up to the end of 2013. A range of stakeholders in each Member State/country have been consulted during the elaboration of the report, which has been validated as an accurate representation of activities at national level, to the best of their knowledge, by the Member State/country representatives of the Commission Expert Group on Rare Diseases. The reader, however, should bear in mind that the information provided is not exhaustive and is not an official position of the European Commission, its Agencies or national health authorities.

The report is split into six parts:

Part I: Overview of rare disease activities in Europe
Part II: Key developments in the field of rare diseases in 2013
Part III: European Commission activities in the field of rare diseases
Part IV: European Medicines Agency activities and other European activities in the field of rare diseases
Part V: Activities in EU Member States and other European countries in the field of rare diseases
Part VI: Activities at National level in each EU Member State and other European countries in the field of rare diseases

Parts I – V also include a description of the methodology, sources and validation process of the entire report, and a selected bibliography and list of persons having contributed to the report.

The present document contains the information from Parts II and V of the report concerning Israel. A list of contributors to the report and selected sources are in annex of this document. For more information about the elaboration and validation procedure for the report, please refer to the general introduction of the main report.

Each year, there are around 15 000 downloads of the different sections of the report combined.
RARE DISEASE ACTIVITIES IN ISRAEL

Definition of a rare disease
There are ongoing discussions in the Commission for rare diseases regarding the definition of rare diseases in Israel and the need for a legislation and regulation.

National plan/strategy for rare diseases and related actions
There is currently no national plan for rare diseases in Israel. The costs related to these diseases are included in the national health care budget. There is no funding for action in the field of rare diseases. The Parliament lobby for rare diseases was founded in 2009 and met again in 2013; several laws have been submitted to the parliament but there is no legislation as of yet.

The costs related to rare diseases are included in the national health care budget.

Centres of expertise
There is a Ministry of Health policy to develop centres of expertise for rare diseases. There are several centres in Israel recognised for providing expert services in the field of rare diseases including, the National Multidisciplinary Clinic for Prader Willi Syndrome, and the Hereditary Hemorrhagic Telangiectasia HHT Clinic.

Registries
Several registries are maintained in Israel including a cystic fibrosis registry, SCNIR registry, trisomy 21 registry and a registry of genetic syndromes causing bone marrow failure. At the moment there is no governmental financing for these registries and no national committee dedicated to the issue of registries nor a rare disease registry.

Teams in Israel contribute to the EUROCARE CF and SCNIR European registries.

Neonatal screening policy
In Israel, all newborns are screened for 9 rare metabolic diseases and 2 endocrine diseases. All activities related to these tests and quality control is carried out under the supervision of the Ministry of Health at at the Sheba-Tel Haschomer governmental medical centre.

Genetic testing
Genetic testing is under the supervision of the Ministry of Health and accreditation is obligatory. There is one private reference laboratory and in many cases the reference laboratories are abroad. There also are Guidelines published by the Medical Genetics Association for prenatal population genetic screening. From the beginning of 2013, the majority of the tests including SMA, Fragile X, Cystic fibrosis are provided for free. While genetic tests should be provided free there are still many challenges; chromosomal microarray are reimbursed for children with mental retardation and malformations and for prenatal testing of fetuses with malformations; mutation analysis and gene sequencing (in part) are reimbursed, although still there are many families who need to pay for genetic tests privately. Genetic testing abroad is possible and testing for any gene is available in private laboratories, but it most cases are not reimbursed and patients pay for these tests privately.

In the Orphanet database, 233 genes are tested in Israel for 258 diseases. Private testing for any known disease-causing gene is available in private labs.

National alliances of patient organisations and patient representation
There is no alliance for rare diseases, although there is a non-rare disease specific patient alliance in Israel who is taking action to promote various themes related to Rare Diseases. There are plans to establish an organisation for rare disease patients.

Sources of information on rare diseases and national help lines
Orphanet activities
The Orphanet Israel country coordinator is currently based at the Sheba Tel Haschomer Medical Centre. Orphanet Israel does not currently receive national or European funding. The representative collects data on rare disease related services (specialised clinics, medical laboratories, ongoing research, registries, clinical trials

1 Information extracted from the Orphanet database (January 2014).
and patient organisations) for entry into the Orphanet database. This activity is not systematic and is based on the free time of the representative. Orphanet has been officially recognised by the Israeli Ministry of Health; there is a need for funding in order to maintain the national website in a systematic matter. The Orphanet team maintains the Orphanet Israel national website\(^1\) in Hebrew.

**Official information centre for rare diseases**
There is no official information centre for rare diseases; there is Health Ministry information website on general issues linked to the health insurance and national insurance.

**Help line**
No specific information reported.

**Other information on rare diseases**
There is some publicly open information on rare diseases in Israel available on the Community Genetics Department at the Ministry of Health Website and at the Israeli site at the Goldenhelix mutation database. Web-based information is available for a limited number of diseases and certain information is maintained using a state budget.

**Guidelines**
No specific information reported.

**Training and education initiatives**
No specific information reported.

**National rare disease events in 2013**
A Rare Disease Day event was organised by the Orphanet coordinator at the Meir medical centre with support from the Clalit health insurance fund. A meeting on RASopathies was organised in June 2013.

**Hosted rare disease events in 2013**
A Cardio-Facio-Cutaneous (CFC) meeting on strategies to study RASopathies and other rare diseases was organised on 24 June 2013 in Haifa.

**Research activities and E-Rare partnership**

**National research activities**
There are fund-raising initiatives by specific patient organisations for various rare diseases such as familial dysautonomia, ALS, etc.

**Participation in European research projects**
Teams in Israel participate/ have participated in 10 rare disease related FP7 projects.

**E-Rare**
Israel is part of the E-Rare consortium, represented by the CSO-MOH (Ministry of Health) and participated in the first two transnational calls in 2007 and 2009 (Israel is represented in three of the selected projects in the first two calls). Israel participated in the third call in the context of E-Rare2 in 2011 and funds Israeli teams participating in 4 of the selected consortia. Israel participated in the 4\(^\text{th}\) Joint Transnational Call in 2012, with teams from Israel participating in 4 out of the 11 projects selected for funding. Israel participated in the 5\(^\text{th}\) Joint Transnational Call in 2013, with teams from Israel participating in 3 out of the 12 projects selected for funding. Israel participated in the 6\(^\text{th}\) joint transnational call in 2014 with teams from Israel participating in 4 projects.

**IRDiRC**
The CSO-MOH as member of the E-Rare Group of Funders joined the IRDiRC in 2012.

**Orphan medicinal products**

\(^1\) [http://www.orpha.net/national/IL-HE/index/%D7%93%D7%A3-%D7%94%D7%91%D7%99%D7%AA-%D7%A9%D7%9C-%D7%90%D7%A8%D7%A4%D7%98-%D7%99%D7%A9%D7%A8%D7%90%D7%9C/](http://www.orpha.net/national/IL-HE/index/%D7%93%D7%A3-%D7%94%D7%91%D7%99%D7%AA-%D7%A9%D7%9C-%D7%90%D7%A8%D7%A4%D7%98-%D7%99%D7%A9%D7%A8%D7%90%D7%9C/)
Currently in Israel there is no agreed definition of an Orphan disease or drug. In addition, there is no special legislation regulating the development registration and payment for orphan medicinal product therapies. Thus these products and patients find themselves competing with general diseases, to their disadvantage.

**Orphan medicinal product committee**
There is currently no such committee. Attempts to reform the law and regulations have thus far not succeeded, but a draft law is currently going through the Parliament.

**Orphan medicinal product incentives**
No specific information reported.

**Orphan medicinal product market availability situation**
All new drugs (including orphan medicinal products) must be registered with the Ministry of Health. The pharmaceutical division has regulations regarding the registration of new drugs, similar to those of the EMA and FDA. There are 63 drugs for rare diseases available in Israel, including: Rilutek, Flolan, Novoseven, Replagal, Lyozyme, Elaprase, Incredlex, Soliris, Firazyr, Kuvan, Carbaglu, Orfadin, Naglazyme, Elelyso.

**Orphan medicinal product pricing policy**
No specific information reported.

**Orphan medicinal product reimbursement policy**
Hospitals and health insurance companies pay for the drugs which are registered in the national ‘health basket’. Since 1995 the year of the national health insurance law the committee in charge of the ‘health basket’ meets once a year in order to decide which drugs and technologies will financed by the government. The committee is composed of representatives of all the relevant stakeholders and interested parties. Since budgets are limited, this process of selection is always controversial. More products are proposed than are accepted and the process is complex and competitive. Nevertheless, some orphan medicinal products have been accepted in recent years (e.g. myozyme, elaprase, naglazyme, fabrazyme, replagal, Kuvan, carglumic acid, nitisinone and miglustat for Gaucher disease, cystagon, berinert).

**Other initiatives to improve access to orphan medicinal products**
A "compassionate" procedure ("Form 29g") exists by which life-saving products may be given to individual patients on the responsibility of the treating physician, even if the drug is not registered, or is off-label, or is not included in the basket. However, obtaining such products and paying for them may be challenging.

**Other therapies for rare diseases**
No specific information reported.

**Orphan devices**
A draft law on this subject has been proposed.

**Specialised social services**
No specific information reported.
DEVELOPMENT OF RARE DISEASE ACTIVITIES IN 2013 IN ISRAEL

**National plan/strategy for rare diseases and related actions**
The Parliament lobby for rare diseases was founded in 2009 and met again in 2013; several laws have been submitted to the parliament but there is no legislation as of yet.

**Centres of expertise**
There is a Ministry of Health policy to develop centres of expertise for rare diseases.

**Genetic testing**
Genetic testing is under the supervision of the Ministry of Health and accreditation is obligatory. There is one private reference laboratory and in many cases the reference laboratories are abroad. There also are Guidelines published by the Medical Genetics Association for prenatal population genetic screening. From the beginning of 2013, the majority of the tests including SMA, Fragile X, Cystic fibrosis are provided for free. While genetic tests should be provided free there are still many challenges; chromosomal microarray are reimbursed for children with mental retardation and malformations and for prenatal testing of fetuses with malformations; mutation analysis and gene sequencing (in part) are reimbursed, although still there are many families who need to pay for genetic tests privately. Genetic testing abroad is possible and testing for any gene is available in private laboratories, but it most cases are not reimbursed and patients pay for these tests privately.

**National alliances of patient organisations and patient representation**
There are plans to establish an organisation for rare disease patients.

**National rare disease events in 2013**
A Rare Disease Day event was organised by the Orphanet coordinator at the Meir medical centre with support from the Clalit health insurance fund. A meeting on RASopathies was organised in June 2013.

**Hosted rare disease events in 2013**
A Cardio-Facio-Cutaneous (CFC) meeting on strategies to study RASopathies and other rare diseases was organised on 24 June 2013 in Haifa.

**E-Rare**
Israel participated in the 5th Joint Transnational Call in 2013, with teams from Israel participating in 3 out of the 12 projects selected for funding. Israel participated in the 6th joint transnational call in 2014 with teams from Israel participating in 4 projects.
LIST OF CONTRIBUTIONS

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3 The contributors and validators of the report have contributed information which is accurate to the best of their knowledge. However, readers should take note that the contents of this report are illustrative and not exhaustive.

4 All websites and documents were last accessed in May 2014.