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POLISH ACTIVITY WITHIN ORPHANET EUROPE – STATE OF ART OF DATABASE AND SERVICES

AKTYWNOŚĆ POLSKIEGO ZESPOŁU W EUROPEJSKIM PROJEKCIE ORPHANET – AKTUALNY STAN ORAZ DOSTĘPNE SERWISY

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Abstract

Orphanet is an international project aiming to help in improvement the diagnostic process, care and treatment of patients with rare diseases, and to provide information on development in research and new therapy. Orphanet is currently represented in 38 countries. The infrastructure and coordination activities are jointly funded by Inserm, the French Directorate General for Health, and the European Commission. Moreover, certain services are specially funded by other partners. Orphanet's activities in each country of the network are partially financed by national institutions and(or) specific contracts. In this paper we present the Orphanet portal as well as the Polish national activity within this project.

Key words: Orphanet, Orpha number, rare diseases

Streszczenie

Orphanet jest międzynarodowym projektem mającym na celu ulepszenie procesów diagnostyki, opieki oraz leczenia pacjentów z rzadkimi chorobami, który zapewnia także dostęp do systematycznie aktualizowanych danych o projektach badawczych i wdrażanych terapiach. Projekt ten jest realizowany w 38 krajach, natomiast struktury organizacyjne i koordynujące są opłacane przez francuski INSERM (Narodowy Instytut Zdrowia i Badań Medycznych). Ponadto, wybrane projekty są sponsorowane przez innych partnerów. Aktywność Orphanetu na poziomach krajowych jest opłacana z budżetów narodowych i(lub) oddzielnych umów. W niniejszym artykule zaprezentowany jest portal Orphanetu oraz omówiona aktywność polskiego zespołu działającego w jego strukturach.

Słowa kluczowe: Orphanet, numer Orpha, choroby rzadkie

DEV PERIOD MED. 2015;XIX,4:536-541

INTRODUCTION

A rare disease (RD), also referred to as an orphan disease, is any disease that affects a small percentage of the population. In Europe a disease or disorder is defined as rare when it affects less than 1 in 2000 citizens. Most of them are genetic, and are present throughout a person's entire life, even if symptoms do not immediately appear. While an individual disease might be labeled as "rare", the total number of persons in Europe suffering from

one of the over 6000 different identified rare diseases is estimated at over 30 millions, so rare disease patients comprise 6% to 8% of the EU population [1].

Rare diseases were a priority for action in the Public Health Programme for 2008-2013 years: "Establish and implement plans or strategies for rare diseases at the appropriate level or explore appropriate measures for rare diseases in other public health strategies, in order to aim to ensure that patients with rare diseases have access to high quality care, including diagnostics,

treatments, habilitation for those living with the disease and, if possible, effective orphan drugs...” [2]. Earlier, i.e. a Communication of the European Commission, entitled “Rare Diseases: Europe’s challenge” was adopted on November, 11 2008 [2]. In both these documents, the importance of providing accurate information on RD to all European citizens, and on expert services, is clearly stated: “The establishment of an EU dynamic inventory of rare diseases will contribute to tackle some of the main causes of neglecting the issue of rare diseases including the ignorance of which diseases are rare. The Commission will ensure that this information continues to be available at European level, building in particular on the Orphanet database, supported through Community programmes” [3].

ORPHANET

Mentioned above Orphanet is the reference portal for information on rare diseases and orphan drugs designated for all audiences, i.e. professionals, patients and parents itself and joined in associations. First project was established in 1997 to address problems associated with rare diseases, namely lack of information, scarce

expertise, poor collaboration, difficult recruitment, and isolation of affected patients, families [4]. Its main aim is to help improve the diagnosis, care and treatment of patients with rare diseases. The infrastructure and coordination activities are funded jointly by the French National Institute of Health and Medical Research (INSERM), the French Directorate General for Health, and the European Commission. Moreover, certain services are specifically funded by other partners, i.e. the Caisse nationale de solidarité pour l'autonomie supports the indexing of rare diseases with the International Classification of Functioning, Disability and Health (ICF), the Association Française contre les Myopathies finances Orpha News France and Orpha News Europe, as well as data collection on clinical trials and the Fondation des Entreprises du Médicament finances the collection of data on orphan drugs and clinical trials. Orphanet’s national activities are financed by national institutions and(or) specific contracts (fig. 1).

The portal Orphanet offers a range of freely accessible services (www.orpha.net, fig. 2). These are as follows:

- an inventory of rare diseases and a classification of diseases elaborated using existing published expert classifications,



Fig. 1. Orphanet partners (from Activity Report 2014).

Ryc. 1. Partnerzy Orphanetu (na podstawie Activity Report 2014).

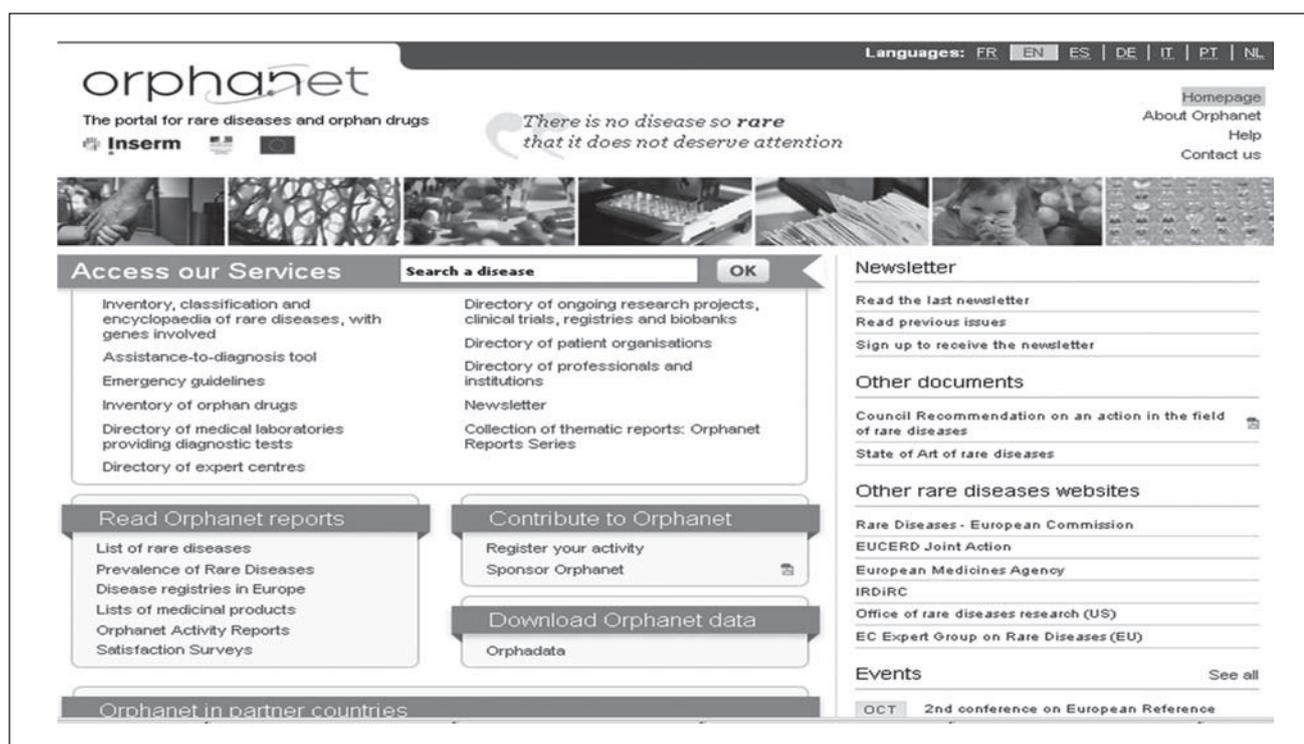


Fig. 2. Orphanet homepage (www.orpha.net).

Ryc. 2. Strona internetowa Orphanet (www.orpha.net).

- an encyclopaedia of rare diseases in English and French, progressively translated into other languages websites (also Polish),
- an inventory of orphan drugs at all stages of development,
- a directory of expert resources, providing information on expert clinics, medical laboratories, ongoing research projects, clinical trials, registries, networks, technological platforms and patient organisations, in the field of rare diseases, in each of the countries in Orphanet's consortium,
- an assistance-to-diagnosis tool allowing users to search by signs and symptoms,
- an encyclopedia of recommendations and guidelines for emergency medical care and anaesthesia,
- a fortnightly newsletter, OrphaNews, which gives an overview of scientific and current political affairs in the field of rare diseases and orphan drugs, in English and French,
- a collection of thematic reports, the Orphanet Reports Series, focusing on overarching themes, directly downloadable from the website [5].

Data about these contents show how rich source of knowledge the portal is. We can find here, among others, information about (data from October 2015): 5833 diseases and 6636 expert centres, 573 articles in French of which 113 are for the general public and 34 emergency guidelines for professionals, and 728 articles in English

of which 9 are emergency guidelines. The Orphanet encyclopedia contains more than 13000 summaries on rare diseases in 6 languages (French, English, German, Spanish, Portuguese, Italian). Moreover, 3280 medical laboratories dedicated to a specific diagnosis are mentioned, and about 20 000 professionals are referenced in the database. Daily the Orphanet website is visited by more than 40 000 visitors.

How to register your activity in Orphanet?

Orphanet online registration service (<https://www.orpha.net/professor/htdocs/>) allows healthcare professionals and patient organisations to register and update their activity dedicated to rare diseases as an expert centre, medical laboratory, patient organisation, clinical trial, research project, patient registry or biobank. After creating an account every professional can access personal workspace with 4 sections: update my activities, update my personal profile, register new activity or access my forms. To register a new activity please choose the type of activity: expert centre, medical laboratory (diagnostic tests and quality assurance, patient organisation, research project, patient registry or clinical trial and then complete the appropriate registration form). Registration forms contain information about contact details, rare diseases concerned and professionals involved in the activity. To evaluate the appropriateness of registering an expert centre that is not officially-designated by Ministry of

Health, professionals should fill in the Orphanet Quality Criteria questionnaire (adapted from The European Union Committee of Experts on Rare Diseases (EUCERD) recommendations on quality criteria for expert centres for rare diseases).

Medical laboratories should provide a list of diagnostic tests for rare disease. There are specific inclusion criteria depending on the type of test:

- Molecular genetics: All constitutional genetic testing analyses are collected, even for non-rare diseases and pharmacogenetics.
- Constitutional cytogenetics: molecular cytogenetic analyses like FISH or MLPA or array CGH are registered in Orphanet only if they are designed for specific microdeletion/microduplication syndromes.
- Tests for chromosome number anomalies and ring chromosomes done by FISH (e.g. Trisomy 11) are not registered in Orphanet, as their detection does not require a specific expertise in molecular cytogenetics.

Medical laboratories accredited and(or) certified (EQA schemes) should attach a corresponding document. Do not forget to click on 'SUBMIT' to validate and send the information to Orphanet, if the form isn't ready please click on 'SAVE' and you can go back to the form at any time. Submitted data are then validated and quality controlled by both national and coordinating team and then published online.

Registered data can be updated at any time. When clicking on section 'update my activities' the name(s) of the already registered resources appear. You access all the information available on the expert resource and you can modify it by clicking on the button '+' next to each section.

The section 'Access my forms' gives access to ongoing forms: these are the forms which you are modifying and you have saved because not ready to be submitted, forms submitted to Orphanet: forms already submitted but not yet treated by the Orphanet team and forms treated by Orphanet: in this section you can find the treated forms and the date of treatment.

Concerning the Orphanet Report Series, in May 2015 the List of rare diseases and synonyms was published (http://www.orpha.net/orphacom/cahiers/docs/GB/List_of_rare_diseases_in_alphabetical_order.pdf). As mentioned in this document "Rare diseases registered in Orphanet are defined according to two scopes:

- every entity is defined by its clinical homogeneity, regardless of its etiology or the number of causing genes identified,
- the rarity is defined according to the European legislation defining a prevalence threshold of not more than 5 affected persons per 10 000 (Regulation (EC) N°141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products, http://ec.europa.eu/health/files/eudralex/vol-1/reg_2000_141/reg_2000_141_en.pdf).

Registered rare diseases have been described in the international scientific literature (peer-reviewed articles) with at least two cases confirming that the clinical signs are not associated fortuitously. However, some diseases are registered although only one case has been reported

in order to reproduce the comprehensiveness of a specific classification (notably within the classification of inborn errors of metabolism).

Rare diseases are registered with a preferred name and as many synonyms as necessary. A unique identifier, the ORPHA number, is randomly attributed by the database to each disease. This number is never re-used, so it is stable in time [6].

According to Polish law, and the last Minister of Health's ordinance (dated 18/12/2014), giving the ORPHANET disease number is required for proper rare disease classification and has to be given together with the International Statistical Classification of Diseases and Related Health Problems-10th (ICD-10) number [7].

Orphanet's structure

Orphanet is led by a consortium of around 40 countries, coordinated by the French INSERM team. The French coordinating team is responsible for the infrastructure of Orphanet, management tools, quality control, rare disease inventory, classifications and production of the encyclopedia. National teams are responsible for the collection of information on expert centres, medical laboratories, ongoing research and patient organizations in their country. All Orphanet teams work according to the Orphanet Standard Operating Procedures. At national levels, the National Advisory Board is composed by members nominated by the appropriate legitimate institutions which are defined at country level. The board members contribute with their expertise to Orphanet at country level.

The beneficiary of EU Joint Action for Rare Disease Project since 2011 is the Children's Memorial Health Institute, with Prof. Małgorzata Krajewska-Walasek as the Coordinator and Prof. Krystyna Chrzanowska as the Project Manager, M.D. Ph.D, and Aleksandra Jezela-Stanek and DVM Dorota Karczmarewicz as Information Scientists. During that time a Polish-language home page of Orphanet was developed – <http://www.orpha.net/national/PL-PL>. Moreover, we have translated over 475 summaries on RD, several emergencies guidelines as well as thousands of diseases names with synonyms with Orphanet numbers (above 22 000). All these data are available on www.orpha.net, after searching for a specific disease.

On 17 September 2015 in Luxembourg, under the auspices of John Ryan, Acting Director of the Health Division and Food Security (DG Health), Jacques Remacle, Head of Health CHAFEA unit (Consumers, Health, Agriculture and Food Executive Agency) and Patrice Dosquet, representing the French Ministry of Health, the new Joint Action, called RD-ACTION, consisting of the member states of the European Union for rare diseases, was launched. Following the two previous Joint Actions – mentioned above Orphanet Joint Action and EUCERD - RD-ACTION represents renewed support of the European Commission (EC) to rare diseases, through its Directorate General for Health (DG SANTE). RD-ACTION has three main objectives:

- to contribute to the implementation, by member states, the recommendations of the EC Panel in relation to policies on these diseases,



Fig. 3. Main page of Orphanet newsletter, OrphaNews (from www.orpha.net).

Ryc. 3. Strona główna informatora Orphanet, OrphaNews (ze strony www.orpha.net).

- support the development of Orphanet and make it sustainable, and finally
- help Member States to introduce the ORPHA code in their health systems to make rare diseases visible.

With a global budget of €8,344,079, this work will last three years (until June 2018), following the logic of coherence and continuity vis-à-vis the previous actions, but aims to go further in terms of concrete implementation and consolidation policies.

SUMMARY

Orphanet's activity details as well as news concerning rare diseases are freely accessible and published as OrphaNews, the Newsletter of the Rare Diseases Community (the last one for example is at: <http://www.orpha.net/actor/EuropaNews/2015/151010.html#53947>, fig. 3). Moreover, Orphanet's activity report is produced annually and is published online on the Orphanet website. Thus we encourage you to read either of these documents, to be updated with information on rare diseases, as well as actively use Orphanet in your everyday practice reading summaries of rare diseases, using information about diagnostic laboratories or references to the numbers of diseases (ORPHA number) and related medical databases.

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PROGRAMME OF EUROPEAN UNION



Co-funded by
the Health Programme
of the European Union

This publication is part of the project / joint action '677024 / RD-ACTION' which has received funding from the European Union's Health Programme (2014-2020). The content of the publication represents the views of the author only and is his/her sole responsibility; it can not be considered to reflect the views of the European Commission and/or the Consumers, Health, Agriculture and Food Executive Agency or any other body of the European Union. The European Commission and the Agency do not accept any responsibility for use that may be made of the information it contains.

Author's contributions/Wkład Autorów

According to the order of the Authorship/Według kolejności

Conflicts of interest/Konflikt interesu

The Authors declare no conflict of interest.

Autorzy pracy nie zgłaszają konfliktu interesów.

Received/Nadesłano: 27.10.2015 r.

Accepted/Zaakceptowano: 24.11.2015 r.

Published online/Dostępne online

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