Eurordis Position Paper on the WHO Report on Priority Medicines for Europe and the World

Eurordis – the European Organisation for Rare Diseases – is a patient-driven pan-European network of more than 220 rare disease associations from 21 countries (17 of which are EU member states). Thereby, Eurordis reflects the voice of 30 millions patients affected by rare diseases in the enlarged Europe. While welcoming the initiative of writing a Report on priority medicine needs for Europe and the world, we have some serious reservations mainly concerning the following three points, that will be developed below:

1. The inconsistency used throughout the Report when addressing rare diseases;
2. The absurdity of the geographical cut limiting the problematic of rare diseases only to the EU and the US;
3. The absence of a worldwide reflection on Orphan drugs.

To start with, we feel the need to define the following three terms in order to clarify exactly what each notion refers to within the Report:

Rare diseases:

Rare diseases are firstly characterised by their low prevalence (less than 1/2000). They are severe, life-threatening and chronically debilitating. They are heterogeneous. 80% of rare diseases are of genetic origins and 20% are caused by viruses, bacteria and environment causes (chemicals, food, etc). They evolve, with acute and non-acute phases. They are often difficult to diagnose. There is a lack of knowledge, lack of information, lack of training and experience of physicians, lack of centres of care for rare disease. Rare disease patients are isolated. The day-to-day specific technical care changes over time, and is long term. Rare diseases are a major cause of premature death. They affect both children and adults. Three to 4% of children under 18 years old are affected. The figures from the EU and the US show that 35% of children's deaths before one year of age are the consequence of rare diseases. For many diseases described in the past as clinical entities such as mental deficiency, cerebral palsy, autism or psychosis, a genetic origin is now suspected or has already been described. In fact, they happen to be many different rare diseases.

Because the market is so narrow for each disease, the pharmaceutical industry is reticent to invest in research and to develop treatments for rare diseases. There is therefore a need for economic regulation in this field.

Orphan drugs:

Orphan drugs are medicinal products intended for diagnosis, prevention or treatment of life-threatening or very serious diseases or disorders that are rare. These drugs are called "orphan" because the pharmaceutical industry has little interest under normal market conditions in developing and marketing products intended for only a small number of patients suffering from rare conditions. For the drug companies, the cost of bringing a rare disease medicinal product to the market would not be recovered by the expected sales of the product. For this reason, governments and rare disease patient organisations have emphasized the need for economic incentives to encourage drug companies to develop and market medicines for the "orphaned" rare disease patients.

Neglected diseases:

Neglected diseases are common, communicable diseases that mainly affect patients in the poor developing countries. They are therefore neglected by the pharmaceutical industry because the market is usually seen as non-profitable. There is a need for economic regulation and alternative approaches in this field in order to create incentives aimed at stimulating the research and developing treatments to fight neglected diseases.

1. The inconsistency used throughout the Report when addressing the issue of Rare Diseases

We have some perplexity concerning the way rare diseases have been moved around in the Report:

- **In the Executive Summary** (p. xiii), the term “orphan diseases” appear in a title together with neglected diseases, even though in the text of this paragraph nothing at all is said concerning rare diseases;
- **But, in the list of Priority Diseases** (paragraph 6.9, p. 68 – 69), rare diseases are not tackled together with neglected diseases any more.
- **In Chapter 7 « Cross-cutting themes »**, “orphan diseases” are listed within the particular needs of “special groups”, such as the elderly, children and women (paragraph 7.5, p.95). Even though we do not consider “rare diseases” as a special population or an age-related group, if they are placed together with other special groups in this part of the Report, why are they taken away from the paragraph tackling special groups within the Chapter “Conclusions and recommendations”?
- **In fact, in the Chapter « Conclusions and recommendations »**, not only rare diseases do not appear - surprisingly enough - among the conditions requiring priority medicines, but not even do they appear any more together with the “special groups” the elderly, the women and the children. This time it is the neglected diseases that are included within the “special groups” (p.126) and rare diseases have totally disappeared once again.

We find the way of placing rare diseases here and there in the Report, changing continuously the target group to which they are considered to belong inconsistent, confusing and illogic.

In particular, the Report is not consistent when excluding rare diseases from the scope of the Chapter “Conclusions and recommendations” and not including rare diseases in the list of priority diseases.

2. The absurdity of the geographical cut

The geographical cut suggested in the Report is totally artificial. Rare diseases do unfortunately affect any human being, whether living in a rich or a poor country.

When addressing rare diseases, the Report only mentions Europe and the US. By doing so, the Report is building a frontier that doesn’t correspond to the reality. There is no such a frontier. Furthermore, being affected by a rare disease while living in a developing country does make you the poorest of the poor, cumulating health, social and economic vulnerabilities. This is particularly true for inherited diseases, which affect generation after generation, if they are not diagnosed and if genetic counselling is not provided. By instance: Fragile X Syndrome, the most common cause of serious mental deficiency after Down Syndrome, can affect several children in the same families, generation after generation, the condition getting worse and worse. Marfan Syndrome can cause premature death of young adults generation after generation without being diagnosed.

Rare diseases represent a global public health issue and patients living with a rare disease share the same fundamental issues wherever they live: access to diagnosis and information, access to care, social recognition, etc. Furthermore, research is global, drug development and market are global, and this is even truer in the “niche” of drugs for treating rare diseases.

In the executive summary, it is mentioned, “For diseases such as diabetes, cardiovascular disease, depression and cancers, therapeutic advances in Europe will benefit people in countries throughout the world”. We do believe that this is true for all diseases and especially for rare diseases. In addition to that, we shouldn’t forget that some rare diseases can be

extremely useful as models for understanding other much more widespread diseases, as it has been proved concerning cholesterol, malaria, plague, obesity and mental illness.

The usefulness of rare diseases is also mentioned in the background paper used for the Report: “Rare diseases are used and have been used in the past as model systems for new (pharmaceutical) interventions like protein supplementation therapy and gene therapy. Furthermore many orphan medicinal products are innovative biotechnological products that have been the start for several small biotech-companies”.

Patients living with rare diseases do create patients’ groups in different parts of the world, regardless the level of economic development of their country or region (such as FITIMA for neuro-muscular diseases in Burkina Faso). Rare diseases patients’ groups are managing to gather into International Federations, such as by instance the ones for Haemophilia, Cystic Fibrosis and Prader Willi Syndrome.

Internet has already changed the access of patients to information and is proving to be a structuring tool for patients groups worldwide. Ignoring this reality in the Report will increase the health and social fractures regardless of the reality. Information about diseases and best practices for diagnosis and care are now available on Internet throughout the world.

The solidarity of patients affected by rare diseases does not stop at the frontier of the US and the EU, why should the attention of policy-makers do so, as it is suggested in the Report?

3. The absence of a reflection on worldwide access to Orphan Drugs

We do believe that international health authorities, together with patient organisations, should increasingly support orphan drugs development on a global scale and promote orphan drugs regulation worldwide, either at regional and national or at international levels. As stipulated in the background paper, not only the EU and the US, but also Japan, Korea, Singapore, Taiwan, Australia (covering also Papua New Guinea) have developed a policy on orphan drugs. Therefore, when speaking about orphan drugs, the Report should have mentioned more countries than only the EU and the US. We think that WHO should encourage actions aimed at speeding up transfer of designated orphan drugs from the EU or the US to other continents to improve access to patients and availability worldwide.

Drugs needed to cure rare diseases are NOT necessarily all as expensive as it is implied in the Report. Many rare diseases are preventable or treatable at low cost based on existing evidence-based medicines. Much depends on a commercial decision from the industry or on a political decision by the national authorities. For example, Interleukine 2, also used to cure kidney cancer, which is a rare cancer, is one hundred times more expensive in Europe than it is in China. Medicinal products to treat some rare diseases, as by instance the drugs needed against the Mediterranean fever (0,15 € / day) or Wilson disease, are not expensive at all. Prevention of severe hemochromatosis by bloodlettings is one of the cheapest treatments available to international medicine! What is desperately needed in developing countries to treat any kind of diseases, whether rare or common, is the establishment of stronger health structures. The improvement of national health systems is – and must remain – part of any global development policy in the poor countries of the South.

Furthermore, there is no reason for all biotechnology products to be that more expensive than chemical medicinal products. It shouldn’t be out of price to produce in very high quantity medicines issued from living tissues such as plants, animals, bacteria and yeast. Also diagnostic tests are not all necessarily very expensive. On the long term (5, 10, 15 years), prices should decrease as a result of a technological learning curve and an obvious link between volumes of sales and prices when reaching out more patients progressively worldwide. As stated in the background paper on rare diseases, “orphan drugs in developing countries should get special attention, as distribution of safe and efficacious drugs in these countries is a problem”.

As citizens of the world, as well as patients living with rare diseases, we cannot accept that the right to health depends on where you live and which kind of disease affects you.

We do believe that it is a dangerous mistake to limit the reflection on orphan drugs only to certain regions of the world. We have to think global. We have to escape the equation ”rare diseases only refers to very expensive orphan drugs and therefore, we raise the problem of rare diseases only in the rich countries of the EU and in the US”. If we do not come out of this circle, we will continue to build and reinforce the creation of a health for the rich and a health for the poor, based on geographical and political frontiers regardless of their social, economic and cultural environment and individual abilities, ignoring that poor families are struggling to access existing treatments in rich countries, as well as rich families in poor countries.

In conclusion

1. The place of rare diseases along the Report, the artificial way to limit the problematic of rare diseases only to rich countries, the absence of any kind of reflection worldwide on drugs treating rare diseases, do leave patients affected by rare diseases out of the scope of the WHO Report on priority medicine needs in Europe and the world. We consider this as a dangerous mistake that will lead to further inequalities and reinforce the existing uneven health “lottery”.

2. Furthermore, we would like to underline that the Report is in flagrant opposition with the background paper that was supposed to serve as the basis for elaborating the Report. We do not understand why the general stance finally adopted by the Report on the issue of rare diseases is in contradiction with the perspective present in the background paper. This latter underlines the existence of a pharmaceutical gap on rare diseases and also the attention that is required in developing countries for rare diseases (contradicting the geographical cut of the Report). The background paper concludes (p. 7.5-20): “*In conclusion, the disease burden for patients with a rare disease will in general not change in future unless the attention of policy makers for these diseases will increase both in developed and in developing countries. More fundamental research is needed to develop a treatment, the interest of physician, researcher and industry has to be encouraged and measures has to be taken to improve the availability of (pharmaceutical) care*”.

3. Finally, we are disappointed with the use made of stakeholders’ comments. The Final Report is fundamentally the same as the Draft Report presented before receiving comments by relevant stakeholders (with the notable exception of paragraph 6.17 added in the final Report concerning smoking cessation, including therapies and programmes). By instance, one contribution mentions that “*For the more than 5 billion people living in lower-resource countries, medical genetic services have been incorrectly considered to be too high-tech, expensive and not a priority. The myth exists that the health services of these countries need to focus mainly on infectious diseases and malnutrition. Little recognition is given to the fact that for 63% of the world’s nations (…) congenital disorders are a major contributor to infant and childhood mortality and morbidity*”. Another contribution “*would welcome the inclusion of rare disorders in the scope of the revised WHO report. Also, it is important to see the link between rare and common disease therapies through the research since research into rare diseases often leads to improved knowledge and treatments for common diseases*”. And IAPO’s comments (which also includes Eurordis’ point of view): “*IAPO therefore supports the statement in this report that research must be encouraged into conditions which, for whatever reason, are not focused on by pharmaceutical companies*”.

   The final version of the Report does not reflect these contributions. This is not the way patients’ organisations do view public consultations or wish to be involved, as their views seem not to matter in the end.