12th Workshop
Eurordis Round Table of Companies

"Retooling the European Orphan Drug Regulation and US Orphan Drug Act for Better and Faster Development of Rare Disease Therapies"

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Barcelona, Spain

Concept Paper

In past years, EURORDIS' position, in agreement with all stakeholders, was to prevent any potential Revision of the EU Orphan Drug Regulation until a stronger EU rare disease policy framework was established. This framework is now in place with the European Commission Communication on Rare Diseases, the Council Recommendation for Actions in the field of Rare Diseases, the national plan on rare diseases in every Member states by 2013 and the soon to be created EU Committee of Experts on Rare Diseases.

We know the successes and pitfalls of the EU Regulation on Orphan Medicines and we have regular meetings during which we discuss the limits and potential ways to overcome them. Our colleagues in the USA are also reviewing the orphan drug pathways and other relevant issues on rare disease therapy development.

EURORDIS and NORD are taking joint action to open a discussion on (a) what can be done in the context of the current EU Orphan Medicines Regulation and US Orphan Drug Act to further improve development and access to innovative treatments to patients (b) the need to revise these regulations, and if so, the key points to take a full grasp of the global research & development of

orphan medicines, to address the unmet medical needs of rare disease patients far beyond orphan drugs and to speed up the development and improve access for all patients.

Should the EU Regulation 141/2000 for Orphan Drugs be revised and if so, which particular aspects of this Regulation? This is the main question that the 12th ERTC Workshop will address. It will also be the starting point for investigating if other challenges still remain to be overcome outside the remit of the Orphan Drug Regulation, in order to better foster Orphan Medicinal Products (OMPs) development, as well as other Rare Disease Therapies development in Europe and beyond.

During the morning session of this ERTC workshop, we will trace the history of the last ten years of use of this legislation and try to answer the main question: did the Regulation meet its main purposes? Namely, what are the problems that the COMP is facing to deliver its mission to a full extent (ex: lack of alternates; follow up after designation and loose recommendation on going to Protocol Assistance; Significant Benefit in the new context of effectiveness & relative effectiveness; challenges linked to advances in science)? Did the Regulation really provide sufficient incentives for the pharmaceutical industry to develop medicinal products for rare conditions, as well as stimulate the research, development and placing on the EU market of these medicinal products? The objective is to go beyond the discussions in the context of the 10th Year Anniversary at the European Medicines Agency in May and at the European Parliament in June.

Furthermore, we will discuss two other European Regulations that came into force a few years ago and also have an impact on OMP development: the Regulation for the development of Paediatric medicines and the Regulation for Advanced Therapies. Do these Regulations offer any additional benefit or, do they rather represent additional regulatory burdens for newly developed OMPs? What aspects and measures of these recent pieces of legislation could be used to eventually retool the Orphan Drug Regulation (ex: the Paediatric Investigation Plan in the PDCO; the Paediatric Use Marketing Authorisation for new paediatric therapeutic indication of off-patent drugs in the PDCO; the Research Network in the PDCO; the Certification of data at certain stage of drug development in the CAT; the position of the CAT to Draft Opinion on Marketing Authorisation to the CHMP)?

Due to their longer experience with orphan drugs, our colleagues from the other side of the Atlantic are certainly well-placed to provide us with suggestions for improvement. In particular, under the impetus of NORD in the US, all stakeholders have recently participated in an in-depth analysis of the strengths and weaknesses of the American Orphan Drug Act, as well as other policies and processes that impact orphan drug development in the US. As a result, a list of proposed solutions to address the challenges in the process of orphan drug development has been issued. New

propositions to incentivise rare disease therapy studies for off-patent and off-label use of medicines are being tested. Mr. Peter Saltonstall, Chief Executive Officer of NORD, will present this study which should help us to identify common actions to stimulate orphan drug development to be undertaken at the global level.

Finally, the first part of the 12th ERTC Workshop will offer an opportunity for all interested parties to discuss their experience of ten years of the Orphan Drug Regulation 141/2000 and any aspect of this regulation that should be re-tooled to better serve its scope. As debated by the participants of the EMA meeting for the 10th anniversary of the EU Orphan Regulation, in May 2010, this legislation has been a success, but some actions still remain to be undertaken to ensure arrival at the designation phase of a larger number of candidate medicines for rare diseases and to help them to go from designation to successful marketing authorisation.

During the afternoon session of the 12th ERTC workshop, "food for thought" will be provided to five parallel working groups who will discuss different issues related to increasing the number of potential new orphan drugs entering companies' pipelines. In particular, the five small groups will be asked to discuss:

1. *New medicinal products for rare diseases without an orphan designation on the EU market?*
   The Orphan Designation does not seem to attract all pharmaceutical companies. Even some of the designated drugs have been taken out of the EC Registry at the request of the sponsors. What are the reasons of these choices? Why is the OMP Regulation not attractive enough for some?

2. *Linking significant benefit to effectiveness and relative effectiveness. Which Benefit Management Plan for monitoring the "real life" value of orphan drugs?*
   The implementation of a specific action at the EU level for the central evaluation of the Clinical Added Value of Orphan Drugs at the time of the marketing authorisation is a reality today. The Commission is exploring modalities for putting a new mechanism in place. It will provide the Member States with all possible elements to speed up registration and decision on pricing and reimbursement of Orphan Drugs. As a consequence, most of the newly authorised orphan drugs will very likely be put on the market with the obligation of post-marketing studies to collect information on their real value. What will the impact of such studies be?

3. *Mechanisms to facilitate the development of off-label and off-patent drugs for orphan indications, taking examples of useful incentives from other legislations (e.g. PUMA and certification procedure)*
   As reported by several patient groups, a consistent number of drugs already on the market are prescribed off-label for rare diseases and apparently bring some benefits to the patients. We understand that there is limited or no commercial interest in developing an already authorised drug in a rare population. Nevertheless, patients affected by rare diseases have the right to access drugs that have fully proven their efficacy and thus can be fully reimbursed as medicines

officially authorised for their indication. Some Member States are putting some strategies in place to improve this situation. The group will be asked to discuss any existing initiative or to suggest ways to stimulate the interest of companies in the development of drugs used off-label in rare indications.

4. *How to identify and address the "rare" unmet medical needs? Importance of an early dialogue among all stakeholders to better determine research strategies.*
   The 62 already authorised orphan drugs only cover 57 indications. This means that there are still thousands of rare diseases waiting for a treatment. Of course, it is very difficult to imagine that there will be medicinal products for all rare diseases in a near future, but it is important not to leave rare unmet medical needs unaddressed. Research resources are limited despite the growing investments made by all stakeholders, so how could interested parties work together to optimise the use of their resources and their efforts to address the widest number of rare diseases?

5. *Global orphan drug development and EU-US collaboration: state of the art, limits and how to retool the process.*
   The American experience of orphan drugs covers almost three decades. Our American colleagues are now performing a deep analysis of this long experience and in the coming years will propose new processes to increase the efficiency of the orphan drug development in the US. Our respective experiences in Europe and in the US could be mutually beneficial and provide the basis for an optimal retooling of both regulatory schemes.

The reports from the five parallel groups will enable us to collect ideas and potential solutions and translate these into future actions at the national, European and global level, to address the well-known challenges gradually identified by the different stakeholders during the past decade.