European Medicines Agency

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RE: COMP Contribution to Public Consultation "Rare Diseases: Europe's Challenges"

The members of the Committee for Orphan Medicinal Products (COMP) congratulate the European Commission for initiating this Public Consultation "Rare Diseases: Europe's Challenges". The COMP members support the Commission in bringing forward a Commission Communication on Rare Diseases and Council Recommendations on Rare Diseases in 2008.

In the remit of the COMP role in advising the Commission on orphan medicines policy, the COMP members are pleased to send their contribution based on their eight years of experience in implementing the EU Regulation on Orphan Medicinal Products (EC) No 141/2000 of 16 December 1999. Beyond designation, protocol assistance, assessment of significant benefit and review of designation criteria at the time of marketing authorisation application for orphan medicinal products, the COMP has a public health experience and perspective to enhance the development of new therapies for rare disease patients. Therefore, the COMP is ready to capitalise on this experience and make it available to European action on rare diseases in the new and broader effort embodied in the future Commission Communication and Council Recommendation.

1. Overall Comments

The European level is the right approach to address the public health challenges of rare diseases.

Policy on rare diseases has a very high community added value which is unique because of the rarity of patient and experts as well as because of the scarcity and fragmentation of knowledge.

Rare diseases are characterized by their low prevalence. Each of the 5,000 to 8,000 rare diseases identified affects a small or very small population, from a handful up to a maximum of 230 000 patients in the European Union based on a prevalence defined of 5/10,000. Expertise is rare. Epidemiology, scientific, medical and social knowledge are scarce, often weak and fragmented. Rare diseases can not attract private investment under normal market conditions. Specific public resources are limited or inexistent for most rare diseases and require common European efforts to increase them together with a common strategy to optimize their use. The vast majority of rare diseases are life threatening or chronically debilitating diseases. Patients' needs are immense. Public health challenges are many.

In the last ten years, the European Union, the Commission and some Member states have progressively developed policies in the area of research, drug development and public health. Rare diseases now require a new step forward in public policies both at European and Member state levels.

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2. Orphan Medicinal Products

The EU Regulation on Orphan Medicinal Products is a great success. As of February 2008, 541 orphan medicinal products have been designated and 45 have been approved with a marketing authorisation. For the next five years, it is anticipated that 10 to 12 new orphan medicinal products will be approved annually.

In 2006, the European Commission, with support of the EMEA through the Committee for Orphan Medicinal Products (COMP) has published a general report on the Orphan Regulation. We are pleased to refer to the final version of this report, which reflects upon the more than 5 years of experience gained as a result of the application of this legislation and provides an account of the public health benefits which have been obtained through orphan legislation.

The overall outcome of the review provided in the report is positive, with the conclusion that the Regulation does not need to be revised. The report contains a number of recommendations to foster EU policy on orphan medicinal products.

In this respect, it is important to underline that the long term sustainability of the Orphan legislation should be supported through appropriate financial resources.

Also, the report highlights the concerns on the availability of orphan drugs. This issue of access to all orphan medicinal products approved for all patients targeted by the therapeutic indication, is a growing concern to COMP. Studies performed by the European Commission (Alcimed study ordered by DG Enterprise) and by Eurordis (Four surveys performed every two years on the availability of orphan medical products in the EU, most recent one being in 2007) indicate that access varies between Member States and within the different regions of Member States, and that Member States shall ensure that a decision on the price which may be charged for the medicinal product concerned is adopted and does not exceed 180 days as laid out in the Council directive 89/105/EEC adopted on the 21 December 1998.

The Communication proposes that "the Commission should present a Report to the Council and Parliament identifying the bottlenecks every two years proposing the necessary legislative changes". This may be a too slow and cumbersome process to address an urgent issue. In addition, such reports would overlap with the regular update of the inventory of incentives measures at national and Commission level, already published by the Commission.

Since the implementation of the Regulation 726/2004 all Orphan Medicinal Products are only authorised at Community level. The COMP is responsible for providing the European Commission with opinion on the designation of Orphan Drugs and for the assessment of the significant benefit of Orphan Medicinal Products before granting marketing authorisation. The COMP contributes to the Protocol Assistance of Orphan Medicinal Products, particularly, on the significant benefit aspects and works closely with the other EMEA Committees, having responsibilities for marketing authorisation (CHMP) and Paediatrics Plans (PDCO).

A first key COMP recommendation for the Communication is to highlight:

(a) the fact that there are specific bottlenecks linked to rarity

(b) that the way forward is to increase collaboration at the European level to do the scientific assessment of the (added) therapeutic value of Orphan Medicinal Products.

In this respect the COMP, with reference to its responsibilities under Art 4. of Regulation (EC) n° 141/2000, is at the disposal of the European Commission and considers that its competence and expertise in the field of rare diseases and medicinal products would be a beneficial contribution to any future collaboration at European level on the scientific assessment of the (added) therapeutic value of Orphan Medicinal Products. The COMP considers that a European collaborative scientific assessment of the (added) therapeutic value of Orphan Medicinal Products could lead to a report to be used by National Competent Authorities, in the remits of their responsibilities, when doing the appraisal of Orphan Medicinal Products for pricing and reimbursement. This approach would enhance the

consistency of the scientific evaluation done on solid knowledge base and would support and speed up the decision making process of competent authorities and improve access for patients.

3. Research

Based on COMP members experience in reviewing orphan drug applications, protocol assistance and significant benefit, the COMP suggests strengthening the chapter on rare disease research in the Communication.

Here again the community added value is very high: rare disease is one of these areas where a European research strategy and policy can have a strong, structuring and cost effective impact.
Rare diseases need:

- Common research infrastructures in particular for biological resources, registries, clinical research networks.
- A comprehensive approach to research bridging patients unmet medical needs with science, basic research with clinical research in an unprecedented effort in supporting translational research, academic research with pharmaceutical and biotech company research & development.
- More research on extremely rare diseases, mostly genetic diseases, which attracts less attention from scientists and pharmaceutical industry and which can hardly be addressed at national level in a competitive manner.
- More research on the social aspects of diseases, care management, and measure of quality of life.

A second key COMP recommendation for the Communication is to highlight the need to create an adequate EU mechanism through the Framework Programmes to specifically support the clinical research development of designated orphan medicinal products up to the end of phase II. The COMP should be solicited by DG Research to provide expertise for defining the guidelines of this programme, the research priorities and possibly be appointed as expert to review the applications submitted.

4. Patients empowerment

The EU Regulation on Orphan Medicinal Products and the COMP have pioneered and are still at the forefront in having patient representatives as full part of their policy development and decision making process. This innovative openness to society has been further expanded in new regulatory areas at EMEA level and relevant to rare disease such as protocol assistance, paediatric activities, information to patients with involvement in activities such as review of EPARs, Risk Management Plans and pharmacovigilance.

The COMP applauds to the Commission Communication for recognising the specific role of patient empowerment in the field of rare diseases.

A third key COMP recommendation for the Communication is to go one step further in highlighting the need for the Commission to support adequately the role of rare disease patient organisation and representatives in these medicine regulatory activities.

5. International collaboration

International collaboration is not mentioned in the document. The Communication should have a specific chapter on this. Rare disease and orphan drugs research are international, patients and experts are linked at the international levels, national and regional policies should be put into an international perspective.

6. Answers to questions mostly relevant to COMP experience and activities:

Question 1: Yes the current definition of rare diseases is satisfactory and should not be changed. The same definition needs to be used in all relevant pieces of legislation of the EU such as the Orphan Regulation, the Commission Communication on Rare Diseases and Council recommendations on Rare Diseases as well as in relevant legislations and policies in Member states. This definition has also to be put into international perspective, in particular with the USA.

Question 2: Improvement of coding and classification would be helpful. This future work on coding and classification needs to be inclusive of orphan conditions in the specific context of orphan designation performed by COMP, so to be consistent. Beyond COMP needs, an improved coding and classification will be useful at Member states level for better organisation of healthcare.

Question 4: European Reference Networks are needed for rare diseases. Mobility of expertise and knowledge should be privileged. Mobility of patients is also of utmost importance for second opinion, access to highly technical medical examinations or therapeutic interventions and for access to new treatments.

Question 8: Clearly at the EU scale, in particular for the scientific assessment of the added therapeutic value.

Question 9: An EU regulation on orphan medical devices does not appear necessary from the COMP point of view currently. However the COMP would suggest that the Communication proposes to the Commission to assess the needs in this area and issues from the perspective of the different stakeholders (industry, patients, healthcare professionals, academia, and national competent authorities) and issue a report. With the upcoming new regulatory environment on medical devices increasing the level of evidence to be provided at least in term of security if not of efficacy, this will result in increase costs of development and therefore may increasingly generate a new situation of "orphan" medical devices. This impact needs to be assessed in the coming years.

Question 13: The COMP strongly supports the promotion of national plans or strategies on rare diseases. These plans should include well identified measures with deadlines and budget. These plans should systematically include specific measures to support the development of orphan medicinal products and their improved access to patients. Based on the national experience gained so far, it seems appropriate to elaborate on a general set of recommendations that can be further used by all Member states. For COMP, these national plans should be the cornerstone of the Council Recommendation.

Question 14: The main issue to be addressed is the issue of sustainability of funding for research infrastructures, European Reference Networks and essential ongoing actions currently supported through the EU Public Health Programme in the field of rare diseases. A feasibility study to identify more specifically the key issues and to analyse the different options is a sound and reasonable approach. This study should be performed before the end of 2011 is its outcomes had to be used in shaping the next EU Research Framework Programme and the next Public Health Programme.

Yours sincerely,

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Chairperson of COMP