THE SOCIETY FOR THE STUDY OF INBORN ERRORS OF METABOLISM

SSIEM

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ACTION

European Commission
Health and Consumer Protection Directorate-General
Rare Diseases Consultation
HTC 01/198
11, Rue Eugène Ruppert
L-2557 Luxembourg
Luxembourg

Dear Dr.Montserrat,

Re: Public consultation on rare diseases- inherited metabolic diseases

Background

The Society for the Study of Inborn Errors of Metabolism (SSIEM) was founded in 1963 to "foster the study of inherited metabolic disorders and related topics" and "to promote exchange of ideas between professional workers in different disciplines who are interested in inherited metabolic disease". The Society has more than one thousand members worldwide of who over 700 clinicians, scientists and researchers, geneticists, dietitians and other health service workers are from the 27 EU Member States. These members represent the key experts in the field of IMDs.

The IMDs are a group of over 600 rare disorders and represent approximately 10% of rare or Orphan disorders as defined the EU accompanying consultative document. Although each IMDs is individually rare or very rare they have a collective incidence of at least 1:500 live births. The life expectancy of some RD patients with IMD has improved significantly in recent years with the development and introduction of Orphan drugs, much of the evaluation being carried out in collaboration with SSIEM members. SSIEM members have been at the forefront of IMD research, providing a loose, collaborative network for research and diagnosis both within and across the 27 MS.

The SSIEM Council by making available travel grants to less well-off clinicians and scientists from emerging MS fully supports the EC initiative of equal prevention, diagnosis and treatment for all patients with rare disorders and envisages through its programmes of education and training an improvement in the research and clinical management of IMDs.

The SSIEM Council welcomes the EC initiative on RD and after careful deliberations makes the following responses to the Consultation Document:

1. ***Is the current EU definition of a rare disease satisfactory?***
   Yes. This definition is satisfactory for all known IMDs as none of them has an incidence higher than 5 in 10,000.

2. ***Do you agree that there is a pressing need to improve coding and classification this area?***
   Yes. There is definitely a need to improve coding of inherited metabolic diseases in ICD as the present system does not contain sufficient details for genetic diseases including IMDs. As many of these disorders are monogenic an adaptation of OMIM codes into the ICD may be a suitable way of improving the present status. It is also important that specialists in the field of biochemical genetics would be involved in the revision of ICD.

3. ***Can a European inventory of rare diseases help your national/regional system to better deal with RD?***
   Yes. A European inventory is necessary for planning actions and allocating resources, giving patients equal access across the 27 MS. SSIEM members already operate an informal pan European Reference Network of diagnostic and research laboratories. The Council would welcome EC recognition and support of European Reference Networks particularly for those diagnostic services for very rare IMDs.

4. ***Should the European Reference Networks privilege the transfer of knowledge? The mobility of patients? Both? How?***
   Both modes are needed. The key element of success is the establishment of national/regional centres of reference for various rare diseases which should be the primary entry points for the patients. In the next step networking of these centres of reference will enable the transfer of knowledge among them and harmonization of services in EU. There are already in existence a number of disease related registers for RD, mainly supported by industry and an e-network for healthcare professional in IMD.

5. ***Should on-line and electronic tools be implemented in this area?***
   SSIEM members, through affiliated and associated groups in Europe have been instrumental in developing quality assurance and proficiency testing programmes for European laboratories working in the field of IMDs, as well as developing a network of specialist diagnostic laboratories. We fully support further development in this field.

6. ***What can be done to further improve access to quality testing for RD?***

In the field of biochemical genetics and IMDs three major types of tests are being used:

a. *Population or newborn screening for IMDs.* The situation of newborn screening for IMDs and Congenital hypothyroidism for 2004 was recently reviewed by Dr. Gerard Loeber on behalf of the European Region of the International Society for Newborn Screening (ISNS). The SSIEM Council would welcome a European initiative whereby parents and infants would have equal access to an evidence based pan European screening programme for IMD.

b. *High risk screening for possible IMD following clinical presentation.* Specialized biochemical analyses for metabolites such as amino acids, organic acids, mucopolysaccharides and others with relatively high volume of tests in the order of at least hundreds of each test per million inhabitants per year. These analyses are performed by highly skilled and experienced specialists using expensive instrumentation. Due to the number of tests and 24-hour availability these tests must be accessible regionally or at a national level (as a starting point for discussion a regional centre for biochemical genetics may serve 2-10 million inhabitants). Sustainable accessibility of these tests requires continuous investments into the equipment and specialized continuous training (for some countries even abroad) at national level within a framework set by EU.

c. *Confirmatory testing*, such as enzymatic and molecular genetic testing, including prenatal testing for IMDs, are low volume tests that do not need to be available regionally. Depending on the frequency of the respective disorder such tests must be available at the national or pan-European level. To foster the pan-European access to the confirmatory tests improvement in many legislative and monetary areas are needed as specified in the EU documentation. The reference laboratories identified by EU should be supported centrally in a sustainable manner.

Standardization of tests and quality assurance programmes including proficiency testing- provided by ERNDIM (http://www.erndim.unibas.ch/)- are important components of providing quality testing for IMDs.

7. ***Do you see a major need in having an EU level assessment of potential population screening for RD?***

Many IMDs fulfil the revised and updated WHO criteria for newborn screening. Recent technological developments have enabled an expansion of newborn screening for up to 30 IMDs (mostly aminoacidopathies and organic acidurias) and further advances may soon lead to implementation of screening for lysosomal storage disorders.

The costs of the expanded newborn screening compared to screening for hyperphenylalaninaemia has increased only marginally and in contrast to the statement in the EC material do not consume major public resources. The introduction of expanded newborn screening within the European MS as lagged well behind such developments in North America and Australasia and the Council would welcome EU initiates to introduce an equitable screening programme across Europe.

8. ***Do you envisage the solution to the orphan drug accessibility problem on a national or on an EU scale?***
Yes, on an EU scale. EU legislation may need to be introduced to compel MS to guarantee equal access to orphan drugs throughout the EU and commercial companies to provide such drugs at comparable cost.

9. ***Should the EU have an orphan regulation on medical devices and diagnostics?***
The patients suffering from IMDs may require special medical devices (such as self-administered bedside metabolite measurements) and orphan regulation may facilitate development of such devices. As far as diagnostics, vast majority of biochemical tests and almost all confirmatory tests for IMDs performed in EU are based on home-made reagents and standards (see also answer to question 6). An orphan regulation may foster the development of new diagnostic kits and result in so much needed standardization of biochemical tests in the field of IMDs. For special confirmatory tests the orphan regulation does not seem to be necessary as the low volume of these tests will barely lead to commercialization.

10. ***What kind of specialized social and educational services for RD patients and their families should be recommended at EU level and at national level?***
The Council would support the development databases, registries, repositories and biobanks to enable pan-European clinical research in the field of rare IMDs. Some registers already exist for certain disorders, funded by commercial companies and these could be used as models for others. All services proposed in the EC material will improve the quality of life of patients suffering from IMDs and their families. It is important to emphasize that substantial proportion of patients with IMDs require special dietary foods (usually expensive low-protein products), repeated emergency hospitalizations and excessive home-care which all pauperise the families with affected members. From this point of view the financial support, respite care centres and therapeutic recreational programmes for children and young adults seem the most needed activities to be supported at the national level within a framework set by the EU.

11. ***What model of governance and of funding scheme would be appropriate for registries, databases and biobanks?***
It seems that databases and patient registries will profit from accumulating vast amount of information, thus a central governance and EC funding is appropriate. There are significant ethical issues in relation to biobanks, compounded if developed on a pan-European basis. Initially these should be maintained at national level with regulation by EU.

12. ***How do you see the role of partners (industry and charities) in an EU action on rare diseases? What model would be the most appropriate?***
The diagnosis and management of RDs such as IMD is a partnership between healthcare professionals, patient advocacy groups and industry. However, ethical guidelines should be implemented to make sure that patients with RD have equal access in all MS.

13. ***Do you agree with the idea of having action plans? If yes should it be at national or regional level in you country?***
The SSIEM Council would encourage all MS to adopt EU acceptable national/regional action plans for RD. Action plans should be at National level; the EU should give careful consideration as to how such plans can be implemented by emerging MS. A thorough analysis of deficits and needs in biochemical genetics should be done for each MS with an involvement of an international panel. Such analysis will logically lead to an action plan as a prerequisite for improving the care of patients with IMDs.

14. ***Do you consider it necessary to establish a new European Agency on RD and to launch a feasibility study in 2009?***
The SSIEM Council would support the idea of creating a European Agency on Rare Diseases and making available an implementation report to the Council and MS but also to pan-European bodies such as the SSIEM whose members manage and advocate on behalf of their patients.

The SSIEM Council hopes that these comments will help in furthering the development in the European Union RD initiative and those of IMD in particular, and can assure the Commission that its members are prepared to collaborate on its implementation.

Yours sincerely

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