Niemann-Pick Disease Group (UK). EC Consultation on Rare Diseases.

Reference 1. European Public Consultation, Rare Diseases: Europe's Challenge.
Reference 2. EURORDIS e mail dated 26 Nov 07, providing guidance on the EC paper questions.

The NPDG(UK) is a small rare disease charity representing approximately 100 families in the UK. The disease is acquired through autosomal recessive inheritance, has a highly variable age of onset and progression. It is fatal in all cases with some cases lasting to 30 years. The major challenge is the neurological involvement. Similar numbers are known to be present in many EC countries, the diseases is pan ethnic and disease incidence is increasing, probably in line with greater awareness and improved diagnostic capability.
Attempts to raise the disease problem with the UK health authorities have met with no success although provisions for clinical monitoring are in place. The NPDG(UK) charity provides funding for a Clinical Nurse Specialist who, in turn, provides assistance and advice to affected families throughout the UK. The concept of a national level of partnership between the healthcare providers and the patient representative groups has not been grasped by the Department of Health who appear not to embrace the US/NIH model of establishing an Office for Rare Diseases (RD). This model is being adopted by an increasing number of European Member States (MS). Similarly, the research authorities have failed to recognise the need for a plan to deal with RD, as individually, the numbers involved do not justify the investment. These attitudes have resulted in health inequalities and what in effect, is the abandonment of a significant sector of the population.
The EC Consultation is therefore a major step forward in addressing the overall rare disease management issues and it provides a glimmer of hope for those unfortunate families whose lives have been blighted by chance and, who can get little help from their own healthcare organisations.
It seems that an opportunity for consultation and collaboration within the UK on this EC document has been wasted. My enquiries to date indicate that there has been no contact between the health authorities and the charities in responding to this document. It would have been useful in answering questions about EU, National or Regional level to hear what the view of the authority is and to understand the factors behind any views expressed.
A factor of importance highlighted by addressing this EC Consultation is the range of topics covered. Many of these are outwith the experience and knowledge of small charities such as NPDG(UK). Acquiring this expertise can be challenging and we are grateful to organisations such as Eurordis for providing guidance on the questions raised in the Consultation.

Response to Questions in Ref. 1

The paragraph numbering and headings and bullet points are those given in Ref 1.

4.1 To improve the identification and knowledge of RD.

- **Common definition of RD in the EU.**

Question 1. ***Is the current EU definition of rare disease satisfactory?***

No problem is seen with retention of this although it would be interesting to know if all MS are working towards a harmonisation of the definition. Also it is assumed that no disease group will be disadvantaged if its numbers are borderline in terms of definition of RD.

- **Better codification and classification of RD.**

Question 2. ***Do you agree that there is a pressing need to improve coding and classification in this area?***
I am not aware of issues surrounding this question but I understand that the UK is involved in this exercise which I believe to be one of the management tasks and, therefore important in the understanding of the rare disease overall picture.

- **Establishment of an inventory of RD.**

Question 3. ***Can a European inventory of rare diseases help your national/regional system better deal with RD?***
Without an understanding of the totality of the RD problem in the EU and its MS it is not possible to determine the resources required and how these should be distributed across the EU. The inventory will be an essential tool and will assist the EU and UK management programmes once these are in place.

4.2 To improve prevention, diagnosis and care of patients with RD.

- **Dissemination of appropriate information.**
- **Support to information networks**
- **Development of national/regional centres of reference and establishment of EUreference networks.**

Question 4. ***Should the European Reference Networks privilege the transfer of knowledge? The mobility of patients? Both? How?***
Not sure what this question means but I cannot see why knowledge should not be shared within the EU, and worldwide networks. Similarly if patients can benefit from mobility between MS this must be of value assuming that it is practical and affordable for them to do this. I am unable to say how this may be achieved.
This section heading refers to prevention but I am unable to see how this is reflected in either the section text or the question. I would also be interested to know what is planned for the 'development of measures for patient groups.'

- **Development of e-health in the field of RD.**

Question 5. ***Should on-line electronic tools be implemented in this area?***
It is difficult to envisage an undertaking of this complexity which did not use on-line tools and also records. An example is to record gene defects in families on medical records which could save time in diagnosis and act as a warning to family members in future generations. Yes, there are many problems to resolve regarding implementation. (see next Section)

- **Availability and accessibility of accurate diagnostic tests, including genetic tests.**

Question 6. ***What can be done to further improve access to quality testing for RD?***
I am aware of work concerning harmonisation of quality standards and assessment of access. These activities appear to be progressing satisfactorily in the UK and through Eurogentest. The methods used for deciding which new tests should be introduced

may need to be reviewed to ensure a managed approach rather than a method based on academic interest alone.

- **Evaluation of population screening (including neonatal screening) strategies for RD**

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

This is an important area to address if prevention is to be realised. Post conception testing is fraught with difficult issues and decisions. Cascade screening may not be sufficient by itself to influence the disease frequency but if the partners of known carriers of disease causing mutations can be tested against all known mutations of a particular disease, then this would represent a significant risk reduction measure. A comparison with the OMIM sequence would also contribute to risk reduction. This approach may be considered as targeted screening and would, over time, reduce disease incidence. Long term management action will be essential to achieve this. NIH initiatives to bring down the cost of whole genome screening will influence any considerations over future policy in this area.

- **Primary preventive measures when possible**
- **Best practices on RD care**
- **Equal access to orphan drugs.**

Question 8. ***Do you envisage the solution to the orphan drugs accessibility problem on a national or an EU scale?***

It would seem logical to deal with this problem at the highest level possible. After all, the drug companies are international. Perhaps this is not possible at present so the next level is the EU. This would also appear to make sense from a numbers point of view. Whereas the numbers of patients with a specific rare disease may be small in any one MS, they become more viable when considered in the EU as a whole.
The first bullet point is about prevention but this is not reflected in the question. This aspect should be explored for applicability and practicality across the range of RD. The technology is available to introduce risk reduction measures to known disease gene carriers and their partners.

- **Orphan medical devices and diagnostics.**

Question 9. ***Should the EU have an orphan regulation on medical devices and diagnostics?***

This area is where rare disease questions merge with the issues raised under specialised healthcare services. If problems are being experienced the one solution might be regulation. A considered view supported by evidence is required.

- **Health technology assessment of orphan drugs**
- **Coordinated compassionate use programme**
- **Specialised social services**

Question 10. ***What kind of specialised social services and educational services for RD patients and their families should be recommended at EU level?***

A survey of families would provide evidence for this question. My own experience shows that dealing with financial support for care services, social activities for affected teenagers/young people, transition between child and adult status, distances for consultation, timely action by social services are all among the many problems

faced by families. Most of these are obtained at local level and can in general, only be accessed at local level.

4.3 To accelerate research and developments in the field of RD and OD

- **Supporting databases, registries, repositories and biobanks.**

Question 11. ***What model of governance and of funding scheme would be appropriate for registries, databases and biobanks?***

Not sure what models exist and can be adapted but patients, their families and their representative groups should be involved in formulation of requirements and decision making. I do not understand the consequence of funding schemes but such tool are needed over many decades if they are to be of value. This is especially so for prevention programmes.

- **Biomarkers**
- **Data protection**
- **Networks of research for RD**
- **Coordination between MS funding agencies**
- **Intensifying research**

Question 12. ***How do you see the role of partners (industry and charities) in an EU action on RD? What model would be most appropriate?***

This may depend on the range and type of actions conceived. Perhaps drug companies may not have a major interest in prevention where no drug product is to be developed although this may depend on how drug product is defined. More information is needed on this topic.

4.4 To empower patients with RD at individual and collective level

- **Common approach to the empowerment of patient organisations**

Noted that no question has been posed under this heading.

Medical work has at its end point, members of the population. RD is no different. It is essential to involve charities/patient organisations in any process of programme formulation, progress monitoring and assessment of outcomes. It is recognised that this is not a simple task especially where individual representation is needed. A further problem relates to the diversity of charities, their different and parochial interests and the need to develop an attitude of cooperation/mutual assistance.

4.5 To coordinate policies and initiatives at MS level and EU level.

- **Adoption of national/regional plans for RD.**

Question 13. ***Do you agree with the idea of having action plans? If yes should it be at national or regional level in your country?***

The alternative to not having an action plan is to have no plan at all. In the UK it would appear that this is the current position for RD. Those affected find this unacceptable.

My view is that regional plans for RD would be a disaster due to the RD numbers issue, diversity of regional authorities and the need for central, coordinated funding. Not only do the small numbers work against regional plans but each region would produce its own plan or perhaps no plan at all. The UK already experiences what is known as 'post code prescribing' and RD would suffer from this also. Perhaps there are other arguments to support regional plans but I am not aware of them.

- **Development of health indicators in the field of RD**
- **Organisation of European Conferences on RD**
- **Creation of the EU Advisory Committee on RD**
- **RD in the EU budget**
- **Establishment of a Community Agency for RD**

Question 14 ***Do you consider it necessary to establish a new European Agency on RD and to launch a feasibility study in 2009?***

It is essential that a new or existing agency adopt the role of champion for rare diseases. This would provide the organisation and management need to acquire and distribute resources, provide an infrastructure to steer research and other programmes and deal with ethics and social issues. It should also provide for a direct point of contact on specific RD to families and charities.

The danger is too much bureaucracy could divert funding into administration leaving the front line, ie patients, out in the cold – where they are at present.

- Regular report on the situation of RD in the EU.

Noted that no question has been posed under this heading.

The proposal for a three yearly Implementation report on RD is a reasonable interval for major reporting. The patient groups would need something on a more frequent basis in order that they can stay in touch with the many areas of subject matter. Such reports need not be lengthy but would provide reassurance. Visibility needs to be a main feature of the RD programme.

Other Points

Ref 2 suggested that there should be a question on **Priorities for Research.** If this means prioritising one RD against another then this would work against the smaller minorities. However some way grouping diseases such that commonality of research action would produce wide benefits will need to be considered: eg groups such as lysosomal storage diseases may benefit from a particular research approach. Also gene therapy if progressed may solve many RD problems. The area is complex and would require in depth study.

Ref 2 also notes that there is no question on **empowerment and support of Patient Organisations.** This is another complex area but it is clear that this is important in any plan for RD. Many of the groups are small and vulnerable due to lack of resources – people and funding, but to date have been the only lifeline for information, care support and emotional assistance. An understanding of what POs are in existence and their continuing viability should be high on the work programme.