

PPTA Position Paper
European Commission's Public Consultation on Rare Diseases: Europe's Challenges

The Plasma Protein Therapeutics Association (PPTA) welcomes the initiative from the European Commission to consult stakeholders in the context of its *Public Consultation on Rare Diseases: Europe's Challenges* and looks forward to the Commission's future proposals in this field based on the consultation's responses.

PPTA is the primary advocate for the world's leading producers of plasma protein therapies. The medicines produced by PPTA members are used to treat patients suffering from rare, mostly chronic, life-threatening and/or life-impairing plasma protein disorders and serious medical conditions including bleeding disorders (e.g. Haemophilia), immune system deficiencies (e.g. Primary Immunodeficiencies), auto-immune diseases (e.g. Guillain-Barré Syndrome, Idiopathic Thrombocytopenic Purpura), Alpha-1 Antitrypsin Deficiency, burns and shock.

PPTA would like to bring the attention of the European Commission to the prevalence of some of conditions treated with plasma protein therapies mentioned in the Commission's Consultation Paper. The Commission's paper indeed mentions (Item 1 *The Issue, bulletpoint 4*) that Guillain-Barré Syndrome is among the less than 100 rare diseases that have a prevalence near the threshold of 5 per 10 000 people and that most rare diseases such as haemophilia affect 1 or less in 100 000 people. However the correct prevalence for Guillain-Barré is believed to be ~ 1 to 2 per 100 000 people¹ haemophilia A, the most common form of haemophilia is thought to affect ~ 1 in 10 000 people and haemophilia B ~ 1 in 50 000 people².

PPTA fully agrees with the Commission that Patients with a Rare Disease should have the right to equal prevention, diagnosis and treatment like any other patients. Specifically when looking at plasma protein disorders widely varying treatment levels can be observed throughout the EU depending on which Member State the patients live in. These differences are mainly linked to poor diagnosis rates, lack of awareness and inadequate reimbursement coverage of life-saving plasma protein therapies. PPTA would therefore encourage the Commission to incorporate a provision in its recommendations highlighting the importance of having appropriate treatment levels and equal patient access to these life-saving therapies across all EU Member States.

PPTA is pleased to share its views on behalf of the plasma protein therapeutics industry regarding the following key questions outlined in the Commission's consultation paper:

Question 1: Is the current EU definition of a rare disease satisfactory?

Yes, PPTA believes that the current EU definition of a rare disease as those diseases representing a prevalence of less than 5:10,000 people provides a satisfactory threshold.

It should be highlighted however that the different definitions used by several EU Member States, such as mentioned in the Commission's Consultation Paper, should not exist, and rather be harmonised along the above mentioned EU definition of a rare disease. The implementation of the European Commission's regulation on orphan medicinal products should take this into

¹ GBS/CIDP Foundation International <http://www.gbsfi.com/aboutgbs.htm>

² World Federation of Haemophilia www.wfh.org

account. This is an issue that needs to be addressed as Rare Diseases is a field where effective cooperation at EU level is primordial to share expertise, improve diagnosis rates and treatment levels. PPTA furthermore would encourage the European Commission to strive for a harmonisation of the definitions of rare diseases between the EU, the US and Japan. This makes particularly sense with the currently agreed common EU/US administrative format for an application for the orphan drug status. The process of global harmonisation of the definitions of rare diseases should take the EU definition as parameter basis; this definition captures best changes in population sizes.

Question 2: Do you agree that there is a pressing need to improve coding and classification in this area?

Yes, there is indeed a pressing need to improve codification and classification for rare disorders. The International Statistical Classification of Diseases and Related Health Problems (ICD) of the World Health Organisation fails to capture the variety of sub-classes of certain rare diseases such as immunodeficiencies for example. PPTA supports the European Commission's intent to financially support an improved EU coding and classification system.

Question 3: Can a European inventory of rare diseases help your national/regional system to better deal with RD?

Yes, it can.

Few Member States properly inventorize Rare Diseases. Looking at the EU as a whole only France has implemented a national rare diseases plan and it is where the Orphanet database is coordinated. This is a great initiative that should be further developed. However, experience with patient organisations representing patients with rare, chronic plasma protein disorders show that national registries and inventories are not easy to achieve. The fact that the patient population is small does not help.

An EU level inventory therefore makes sense. For example, the European Society of Immunodeficiencies (ESID) has put in place an EU wide online registry for Primary Immunodeficiencies, through which centres from all over Europe specialising in PID are collaborating to document their patients into a single database available online. This is a great initiative that could be looked at as a best practice example.

Therefore, an overall initiative on EU level is necessary and a EU funded initiative on a European inventory of rare diseases would be most welcome; it is however essential that such a European inventory would be established on basis of a system of validation of homogenous inventory parameters

Furthermore, an additional challenge in the Rare Disease area lies in the diversified sources for inventorizing these diseases. The two main sources are the European inventory system, OrphaNet, and the US rare disease inventory system NORD. The two systems suffer from a lack of harmonization, they use different synonyms, they inventorize rare diseases in their region on an anecdotal basis without validation of homogenous parameters.

Ideally, there should be a harmonization between the European and US system parameters.

Question 4: Should the European Reference Networks privilege the transfer of knowledge? The mobility of patients? Both? How?

PPTA strongly believes that sharing of information and knowledge in the rare diseases field is crucial to improve awareness on these diseases. Low diagnosis rates and misdiagnosis due to

a lack of education of physicians can have a huge negative impact on patients' health as well as on national health budgets. Patients with certain plasma protein disorders are known to have been treated for their symptoms rather than the cause of their diseases (e.g. Primary Immunodeficiencies). This means that significant healthcare resources are being wasted as proper treatment with plasma protein therapies is not being administered. Transfer of knowledge through an EU network of reference centres would therefore be extremely helpful, for the medical community, and also for industry: limitation in knowledge, e.g. on disease groups per country, is a contributing factor which limits and slows down discovery and research as well as the conduct of clinical trials.

An EU network of reference centres could indeed also have a positive impact on patient mobility. Patients with haemophilia in the newer Member States for example have been known to travel to other Member States when they needed surgery as sufficient coagulation factor VIII was not available to sustain such a procedure in their home country. Other patients such as patients suffering from Guillain-Barré Syndrome are also known to have had to travel abroad to get treatment. Information sharing between different reference centres in the EU would be very valuable and facilitate this process. However, it has to be pointed out that travelling from one Member State to another to get their treatment is not a practical solution in the long-term for patient affected by rare, chronic plasma protein disorders. Several examples and surveys have demonstrated that an investment in appropriate levels of treatment reduces costs which would have been otherwise incurred due to an increased rate of hospitalisations, increased number of missed days of work and increased infection rates. This fact and the need to ensure better access to care for these conditions have been widely recognized and underlined at various EU events. The upcoming Commission Communication should therefore encourage the implementation of appropriate treatment levels of care for rare chronic, congenital life-threatening conditions across the EU and encourage Member States that are lagging behind to follow the example of best practice from Member States with higher levels of treatment.

Question 5: Should on-line and electronic tools be implemented in this area?

PPTA believes that the use of on-line technology would greatly help in the field of Rare Diseases. Such technology could improve the exchange of information between reference centres and the running of EU registries for example. PPTA therefore supports the Commission's forthcoming initiative on Telemedicines in the treatment of rare diseases.

Question 6: What can be done to further improve access to quality testing for RD?

For many plasma protein disorders a simple blood test can result in proper diagnosis. However the lack of awareness of these conditions remains the biggest barrier to proper testing and therefore diagnosis. Better information to physicians and patients is needed to remedy to this situation.

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

PPTA believes that an EU evaluation of population screening is an ambitious undertaking but certainly would be very helpful in providing better and more reliable data in all fields (incidence, treatments, morbidity, onset of disease, social factors etc).

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

Equal access of patients to orphan drugs is one of the most critical issues. It is correct that the healthcare systems are under the responsibility of the EU Member States, and ultimately Member States make decisions that can impact the availability of orphan drugs. But there is a tendency on a national level to shift healthcare funds towards more prevalent diseases. Without general interest and more advocacy, rare diseases may fall between the cracks. Reimbursement patterns and marketing authorisation procedures vary depending on the Member States and can affect patient access to such medicinal products. Without supportive activities on a supra-national level, differences in patient access to orphan drugs will continue to exist from country to country within the EU.

Support activities to be addressed on a EU scale could comprise:

- Raising the awareness of how the EU orphan drugs system is working amongst the payers/sick funds, and other decision makers in the EU Member States;
- Member States reimbursement systems should acknowledge that for certain rare diseases treatment conditions below a certain prevalence, normal Health Technology Assessments are inappropriate, because they delay the process too much, due to the rarity of the disease. The EMEA's COMP, as the expert body for prevalence data review, made up of Member States representatives, should be retained to stipulate whether such (rarity) is the case or not.

The benefit would be that orphan drugs destined for the treatment of such rare prevalence-diseases could then be approved for reimbursement in the Member States after granting of the Marketing Authorisation, upon compliance of the orphan drug with the EU legal requirements either that no other treatment exists or that clinical superiority to another treatment is offered.

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

The development of medical devices and diagnostics for orphan drugs is not within the scope of PPTA.

Question 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 social and educational services to rare disease patients which are proposed in the Commission document should be recommended to be provided at national level because of the national specificities of culture and life style; such proposed services could include: (i) respite care services, for both, patients and care givers, (ii) information services and help lines, (iii) therapeutic programs for children and young adults, (iv) financial and psychological support.

However, the financial support for these activities should come from the European Commission and its Public Health Program and the Disability Action Plan.

Beyond patients, other stakeholders (such as payers, physicians, teachers, etc) should be better educated on rare diseases matters.

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

PPTA believes that the decision on the model of governance and the funding scheme depends on the accessibility of data and the ownership of such registries / databases. For instance, if industry would have an ensured access to these databases-registries, which are to be established on a European rather than on a national level, then an appropriate funding model would consist in a financial co-participation of industry. Provided, of course, that all other involved stakeholders contribute financially too.

Question 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?

PPTA has a long-standing experience in the field of rare diseases, as plasma protein therapies are used to treat patients suffering mostly from rare, chronic, life-threatening and/or life-impairing plasma protein disorders. The expertise of PPTA in patient access related matters would bring valuable help in defining appropriate actions in the field of rare plasma protein disorders in particular. PPTA has recently taken part in an event at the EU Parliament on Plasma Protein Therapies in the Treatment of Rare Diseases and would welcome any other EU platform on this topic.

A continuous information exchange on matters concerning improvement of diagnosis, treatment and access to treatment between the European Commission, patient and physician organisations and the industry would be most appropriate.

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?

Yes, PPTA would welcome such idea of having action plans on a national level.

However, such national action plans should be established with guidance/coordination at EU level. National actions plan should contain not all Rare Diseases, but prioritized areas of Rare Diseases actions in accordance with EU guidance. The action plans should have an approved funding on a national level.

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

PPTA would firstly like to stress that a European Agency on Rare Diseases should not have regulatory matters among its competences, as this would conflict with or duplicate the activities of the EMEA and bring additional administrative and/or financial (supplementary fees) burden for applicants and therefore would be counterproductive.

However, PPTA would see a sense in reflecting on a new European Institution with some oversight/coordination in the EU in the rare diseases field. This coordination could consist, as partly outlined in the EU Commission rare disease consultation explanatory document, in taking care and ensuring the permanence and coherence of relevant strategies at EU level in a couple of areas related to rare diseases. Such areas appropriate for oversight could relate to patient registries, biobanks, information on RD, networks of centres of reference, consensus clinical care recommendations and quality assessment.

Conclusions

PPTA welcomes the Commission's initiative on Rare Diseases and wishes to support the Commission during this process. PPTA would welcome an opportunity to bring its support and further discuss the above mentioned issues in greater detail with decision makers on this important dossier.

PPTA would like to suggest the following potential actions that would help to improve the lives of patients suffering from plasma protein disorders:

- Promoting public/private partnerships in education/awareness programmes in order to better understand symptoms of the above-mentioned conditions and to improve competency of patients and their advocacy groups
- Improving the understanding of symptoms for rare plasma protein deficiency disorders for the medical community in order to improve diagnosis and therefore the level of treatments
- Launch of EU patient registries on plasma protein disorders
- Easy to access centralized information (possibly collected and administered by the European Commission) on reference centres
- Encouraging use of electronic media and interactive technologies to disseminate and share information for patients and physicians on understanding symptoms, best diagnosis, treatment and access to treatment