

**Answer to SANCO 2007-07109-00-00-DE Tra-00 (EN)  
From Cystic Fibrosis Europe e.V. to DR SANCO  
Public Consultation regarding a European Action in the Field of Rare Diseases**

Cystic Fibrosis Europe is a federation of national European CF Associations. CFE represents persons with CF and their families in more than 30 member countries<sup>1</sup> in Europe. The website is: <http://www.cfww.org/cfe>

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

Cystic Fibrosis Europe supports the current EU definition of rare diseases as adopted by the Community action programme on rare diseases 1999-2003 and as used by EMEA for the designation of orphan drugs (prevalence less than 2:10 000). In many European member states as for example in Germany or Belgium this definition was accepted by national health care systems. Even relatively frequent "rare diseases" as Cystic Fibrosis (CF) need special national and European Programs to ensure that the needs of these patients regarding care, medical treatment and drugs are adequately observed. A smaller prevalence would risk past, present and future improvements for care and treatment of these diseases. Thus we do apply to the EU to abide by this definition.

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

Cystic Fibrosis is well defined by ICD E 84:- and this code allows sufficient differentiation between CF and other diseases. But this does not generally apply to all rare diseases. Clear and explicit classification and adequate codification, however, are a necessary precondition for being traceable in health information systems. Thus the EU should undertake the necessary efforts for a better codification of rare diseases as described in the current consultation

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

A European inventory of RD as suggested by the current EU consultation and which is being up-dated regularly is necessary to raise the national health authorities' awareness for these diseases and their special needs of medical care, treatment and research. Additionally it would offer patient and support groups a sound fundament on which to build their requests for improvements of care and treatment.

The following passage wants to illustrate the insufficiencies in CF care the patients, their families and care giver struggle with:

According to our, Cystic Fibrosis Europe's, knowledge in all European member states including the new member states there is knowledge about the treatment of CF, at least some individual experts can be found. Furthermore expertise could be disseminated in a relatively uncomplicated way by educational programmes for doctors and non- medical experts and European or worldwide conferences, because there is a good structure for the exchange of expertise in the field of Cystic Fibrosis. **The problem, however, is that not in all countries health authorities perceive the treatment of CF-patients by a team of medical and non-medical CF-specialists as necessary; in several countries health care systems do not provide appropriate access to drugs (with CF, e.g. enzymes or oral antibiotics), experts, specialized clinics and medical devices (with CF: high-performance nebulizers).** In many countries the structural quality

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<sup>1</sup> Albania, Armenia, Austria, Belgium, Bulgaria, Croatia, Czech Republic, Estonia, France, Germany, Georgia, Greece, Hungary, Ireland, Israel, Italy, Latvia, Lithuania, FYR Macedonia, Netherlands, Norway, Poland, Romania, Russia, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Ukraine.

(number of doctors and non-medical experts, medical-technical equipment etc.) of clinics where CF patients are treated does not conform to the European Standard of CF care<sup>2</sup>. For more than 40 years now the CF community, patients, their families, doctors, other caregivers and scientists have been struggling against Cystic Fibrosis. Today scientific and medical knowledge about the biological causes of CF and the way to treat this disastrous disease is far advanced. In 2005 a European Consensus of Standards of CF Care was published in which 36 experts from 18 countries. In countries offering well developed CF care in hospitals which follow these guidelines about 50 % of the CF patients are 18 and older, and the average life expectancy is 40 years and more. In regions where the disease is not yet well known and access to appropriate care is poor, the life expectancy and quality of life are still very low and most patients die in childhood. The lives of CF patients depend on correct treatment according to these standards: International studies showed that CF patients treated in centres which conform to these standards have a better life expectancy, health and quality of life. In some countries the national CF patients' associations try to close these gaps by sponsoring staff members of CF clinics, but this is not a solution: It is the responsibility of the national health care systems to provide appropriate care which is in accordance with guidelines, consensus papers and quality criteria.

A European inventory of RD as suggested by the EU would be a support in this field.

The EU should further set up an inventory of all European organisations, groups, foundations, institutions and services which represent patients with RD or work in this field. This inventory should help patients groups to represent their members' interests on the European level more effectively. If this is not possible the EU should commit their member states to set up such an inventory in the form of an internet portal accessible for anyone who might be interested.

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

The European reference Networks should privilege the transfer of knowledge for the following reasons:

- Patients with RD very often are very ill and not able to travel far distances
- Because of lack of finances these patients and their families often are not able to travel all over Europe. Families also lose income when they have to travel with the patient to get access to appropriate care.
- Language barriers are a severe problem in connection with medical treatment abroad
- Many RD are lifelong chronic diseases which demand frequent and regular expert consultations (with CF: at least once per quarter). Travelling far and cross-boarder distances would be a too heavy burden for these patients and there families.
- RD may develop sudden life threatening crises for the treatment of which an expert has to be available in a distance to allow quick intervention.

There are some very special situations in which a cross- boarder organisation of diagnosis and treatment may be considered as useful, eg:

- For very rare diseases with very small numbers of patients on the national level
- For very specific questions and problems of diagnosis and treatment which can only be provided Europe wide by a very limited number of centers of reference
- In extremely small countries like Luxembourg or Lichtenstein

As a rule competent and appropriate treatment should be offered on a national level.

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<sup>2</sup> Kerem, E., S. Conway, et al. (2005). "Standards of care for patients with cystic fibrosis: a European consensus." *J Cyst Fibros* 4(1): 7-26.

But we do stress the importance of specialized, centralized care in a limited number of CF clinics per country with a sufficient number of patients to ensure the necessary level of expertise, specialized staff and equipment for optimal diagnosis and treatment. To ensure maximum access to optimal care transfer of knowledge between specialists within one country and across borders is extremely important.

Transfer of knowledge should particularly comprise

- development of national/regional centers of reference and the establishment of European Reference Networks. The issue of centers of reference is of the highest importance for patients with a rare disease. This issue was discussed at the European Workshop on Centers of Expertise and Reference Networks for rare Diseases in Prague 12-13 July 2007.
- development of data bases like Orphanet but also databases and registers for single diseases. Databases and registries are very important tools to register the patients' health, to audit the performance at different care centers, to promote best practice, to develop novel therapies and evaluate therapeutic strategies
- development of information networks, especially consensus conferences. To give an example: European Consensus conferences for CF published a standard for the care of CF patients which national patients groups can (and do) use as a reference on which to constitute their demands for better care.<sup>3</sup>

The EU should promote these measures, establish them and if need be finance them when the European level is concerned.

#### **Question 5:**

##### **Should online-and electronic tools be implemented in this area?**

Yes. But electronic services and E-technologies as described in this EU consultation cannot replace direct treatment by competent experts (like physicians, physiotherapists, nurses, nutritionists). They can only support and improve the field in which treatment is situated such as research, exchange of experience and knowledge, establishment of EU accepted standards (see above question 4). The most important task for the EU, however, is to promote patients' access to competent care and treatment of RD Europe wide. To promote E-health in connection with rare diseases is therefore of secondary importance.

#### **Question 6:**

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

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<sup>3</sup> Kerem, E., S. Conway, et al. (2005). "Standards of care for patients with cystic fibrosis: a European consensus." J Cyst Fibros **4**(1): 7-26.

Some more literature representing the "state of the art":

Aris, R. M., P. A. Merkel, et al. (2005). "Guide to bone health and disease in cystic fibrosis." J Clin Endocrinol Metab **90**(3): 1888-96.

Doring, G. and N. Hoiby (2004). "Early intervention and prevention of lung disease in cystic fibrosis: a European consensus." J Cyst Fibros **3**(2): 67-91.

Hoiby, N., B. Frederiksen, et al. (2005). "Eradication of early Pseudomonas aeruginosa infection." J Cyst Fibros **4 Suppl 2**: 49-54.

Lannefors, L., B. M. Button, et al. (2004). "Physiotherapy in infants and young children with cystic fibrosis: current practice and future developments." J R Soc Med **97 Suppl 44**: 8-25.

Saiman, L. and J. Siegel (2004). "Infection control in cystic fibrosis." Clin Microbiol Rev **17**(1): 57-71.

Sinaasappel, M., Stern, M., Littlewood, J., Wolfe, S., Steinkamp, G., Heijerman, H.G.M., Robberecht, E., Döring, G. (2002). "Nutrition in patients with cystic fibrosis: a European consensus." Journal of cystic fibrosis **1**: 51-75.

Yankaskas, J. R., B. C. Marshall, et al. (2004). "Cystic fibrosis adult care: consensus conference report." Chest **125**(1 Suppl): 1S-39S.

In principle every country should provide standard tests to diagnose RD, e.g. with CF: the sweat test or genetic testing for the most frequent mutations. Biological cross boarder tests might be necessary in connection with very rare diseases or when very special questions in connection with diagnosis or treatment are concerned. Particularly with RD very special problems concerning a limited number of patients are to be expected. Therefore, with the exception explained above, we appreciate the activities the EU is planning.

We perceive several problems, though: First national health services and representatives must be persuaded to realize that cross boarder labs are necessary. It is not clear in which way these labs might be financed on a long term basis. According to our experience national and private representatives rather support national services. Thus cross boarder initiatives currently are running out of money after project financing has stopped. Further patients data protection is concerned in connection with cross boarder testing. This matter should be dealt with on the highest priority level.

#### **Question 7:**

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

The EU should promote, initiate and support all measures which provide access to neonatal screening

- If it prevents a future disability of the newborn child like PKU or
- If it improves the course of a rare disease and allows the patient a longer time of relatively good health by helping to start appropriate treatment earlier

#### **Question 8**

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

The description of the problems concerning access to preventive measures, best practices and orphan drugs are correct; we do agree to the EU statements. We want to emphasize, however, that not only orphan drugs which were developed explicitly for RD but **all drugs** which are used to treat any symptom of a RD are of highest importance for the patients. The CFE member organisations report that in many European countries CF patients even may have access to orphan drugs via special programmes but that there is no access to other essential drugs and treatments which are used for treating and preventing certain symptoms like, e.g. with CF, enzymes and oral antibiotics, because the national health care systems do not fund them. Thus patients and their families are constantly financially overburdened or, which is worse, their life expectancy is abbreviated because they are not able to buy the necessary drugs.

We are of the opinion that supportive EU measures might facilitate access to drugs used with the treatment of RD. **All drugs**, not only "orphan" ones, must be regarded. A report as described in the present EU consultation is a suitable measure to enhance transparency, to raise national health care decision-makers' consciousness regarding the necessity to establish access to drugs, to initiate national legislative modifications and provide arguments to support the patients groups positions and requests for better health care with RD. But, to say it again, **all drugs essential to treat a RD must be regarded.**

**CF Europe feels it's very important that access to essential drugs and treatments is endorsed by European measures and guidelines. Our members report the need for European guidelines and stimulation to promote availability of proper care in their countries.**

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

Yes, the EU should start activities in this field, analogue to those proved with orphan drugs. Medical devices but also treatment measures such as physiotherapy, nutritional counselling etc. are of the same importance as Orphan drugs for patients with CF. Special techniques to clean the lungs of the sticky mucus were developed which are very effective and thus fundamental in CF treatment, e.g. Autogenic Drainage.

Physiotherapists have to be trained in applying these techniques before they start treating CF patients. These trainings however in many member states are not financed by the national health care systems, thus the patients groups have to sponsor them. This is not a permanent solution. Thus the EU should turn their attention on this kind of treatment measures also.

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

We agree that all measures and services mentioned in the current EU Public Consultation are necessary and important to enhance the quality of life of patients with RD and their families and care givers. We appreciate that the EU takes caregivers into consideration because they are of high importance for patients with RD.

We do agree with the EU analysis concerning the role of health technology assessment of orphan drugs and support the idea that the EU should support research regarding the development of assessment methods which do justice to the particular importance this issue bears for patients with RD. We agree that a coordinated approach to this issue by member states is necessary.

As suggested the issue of compassionate use should be coordinated between Member States. The EU should support activities in this matter.

All specialised social services mentioned in this publication are of major importance for patients with RD, their families and caregivers. We appreciate that the consultation refers to the wellbeing of caregivers also, because sufficient care is so important for many patients with RD and their families. However, these services are part of the national health care and social systems, depend on national refunding schemes and thus differ widely between member states. Perhaps there is a possibility for the EU to coordinate the development of recommendations concerning which services should be provided in all member states. In this case the benchmark must be the highest level of social services offered; an adaptation towards the lowest level must be avoided.

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

We agree with what the EU in their consultation remarks on the issue of supporting databases, registries, repositories and biobanks. Depending on their functions databases should be organised and managed either on the European or on the national level.

Samples could be shelved peripherally or locally, according to

- the issues concerned,
- to problems
- type of samples (sputum, genetic material, tissue) or
- methodology.

Databases could be organised either referring to single diseases, or comprise several diseases, e.g. if certain diseases have similar symptoms (like e.g. Cystic Fibrosis, Alpha1-Antitrypsin-deficiency syndrome, Kartagener syndrome). Because of the low frequency of the diseases it is very important to have databases including the data of all European

patients to enable scientific analyses and conclusions which can largely contribute to improved life expectancy and quality of life of patients.

Studies based on the American CF registries have made important progress possible and limited the need of clinical trials, thus saving money, time and patient burden. Because of lack of funding the European CF registry is far behind of the American registry, resulting in slower progress of the knowledge and treatment developments in Europe. Although the need for a European registry was known since long and the willingness to collaborate was present in all most countries, the realisation of a European registry was only made possible thanks to the funding through EurocareCF. This proves the importance of EU support and we hope this will be sufficient to ensure the continuity once this project is finished.

Principally the question of ownership has to be answered because this is **the** qualification for certain models of funding, e.g. charging fees for making the samples available. **The participation of patients must be assured institutionally.** This is of special importance for biobanks and repositories which are owned by patients groups. The pharmaceutical industry in general is interested in having access to this kind of banks. Thus patients groups have to take care that they are not fleeced. The EU should support the building and exploitation of such registries, biobanks and depositories even fund them, at least initially, if necessary.

#### **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?**

We agree that the EU support new techniques for bio marker discovery, studies and activities bringing potential biomarkers to their validation and clinical use. Final goal of these activities must be the systematic development of new therapies. Partnership between academia and pharmaceutical companies should be enhanced and supported. We doubt, however, if it is possible to develop and use one and the same biomarker for very different diseases. As effective as this may be for financial reasons it must nevertheless be guaranteed that medical requirements of every single rare disease are given appropriate attention.

Data protection is an issue of high importance for patient organisations; the regulations described in the consultation must be observed.

We principally agree with the EU analysis concerning the three hurdles of the development of specific therapies for RD faces. There are many problems on the track from idea to bed-side. Support of the EU is necessary with many steps, eg.

- the first academic proof of an idea
- finding biotech- enterprises, including small-scale companies, willing to further develop or put into practice certain methods or to do research on active chemical compounds e.g. by doing preclinical studies or toxicological tests
- finding pharmaceutical companies willing to finance multicentric Europe-wide studies to further develop certain methods or test potential substances.

This process can be advanced by developing networks. Networks of research already exist on the national and the EU level, e.g. in the field of Cystic Fibrosis: European CF Clinical Trial Network. The creation and support of these coordinated networks should remain a priority in future DG RD programmes.

Different approaches to issues of research should be coordinated by a managing institution such as the mentioned forum; this forum could work as described. It is to be asked, however, how such a forum could be organised in order to be efficient without causing overflowing bureaucracy. Certainly national and Europe wide patient groups

active in the field of RD research must have an essential part in such a forum. Their role could be for example

- Finding partners for cooperation
- Supporting the building of networks between working groups and scientific teams
- Supporting transfer (idea to preclinical studies) and translation (preclinical studies to multicentric and Europe-wide studies)

This institution (the said forum) would give a broad view over the different approaches to issues of research, and ensure that ideas reach the patient in the form of specific therapies or drugs. Thus it would configure and accompany the therapy developing process from the first idea to the final results, including those phases when there still is no interest on the part of the pharmaceutical industry.

Social research in RD should target the development of specific social or pedagogic services and support for patients and their families. Based on the analysis of national social and educational services designed to compensate or ease disadvantages caused by disabilities and chronic diseases Europe wide models should be developed to meet the burden of living with a RD. Thus access to social and educational services throughout Europe should be enhanced. This should lead to a harmonization of living conditions for patients with RD. The most accomplished services must form the benchmark. Adjustment to the lowest level of services must not occur.

#### **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 EU should continue supporting activities enhancing the empowerment of patients and patients' organisations as described in the consultation. However, we are opposed to the EU approach explained to board members of Cystic Fibrosis Europe (CFE) during a consultation in 2005. The CFE representatives were informed that the EU would exclusively fund those networks and their activities involving greater numbers of RDs, not networks in favour of a single disease (see also explanation in Question 14). Only a policy of supporting both, "general" networks and networks specialising on a single RD may satisfy the particular needs of patients and their families.

We support the suggestion to establish action plans on the national level of member states. Member states should decide if they need regional action plans also. These action plans should take all aspects of RD into consideration: that is research, therapy, care and medical treatment, psychosocial services, access to therapeutic measures, to medical devices and drugs. These action plans should on the one hand address aspects affecting **all rare diseases**, on the other hand consider particularities of single rare diseases. National patient organisations must be involved in developing these action plans on a par. The EU could support activities to establish national action plans by

- Inviting member states to start activities
- coordinating these activities
- coordinate the development of European wide guidelines for the elaboration of action plans for RD
- strongly recommending member states to adopt these guidelines

Consequently we support the EU approach in this issue as presented in the current public consultation.

#### **Question 14:**

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

We appreciate the EU suggestions of question 14. A European Agency on RD might be helpful for all issues connected with RD. However, at the moment there are many open questions. An adequate representation and involvement of patient organisations must be guaranteed; there must be ways for European and national patient associations to

participate on equal levels in decision making boards and committees. If need be patient groups representing a single disease or very rare diseases may conjoin nationally to be represented as a group within the agency.

We also like to stress, that although major European campaigns and action plans are needed in order to make substantial changes in the lives of people with a RD, relatively small scale actions and projects done by the stakeholders: patients, families and patients associations, for instance can be as (and sometimes more) effective than large scale official programmes. Patients' association can use their own resources and rely on capable, experienced people who are very willing to work towards progress without needing major budgets. Cystic Fibrosis Europe organized its first Central & Eastern European CF Network Building Conference in 2006 in Warsaw, Poland. The primary aim of this conference was to reinforce patient associations, define the needs in the region and develop strategies to improve the care and quality of life. Representatives, mostly CF parents and young CF adults, from 14 European countries came together to learn from each others' experiences and from the expertise present in countries where CF care is more developed. The conference was an inspiration for many participants, as one of the representatives concluded: "We will go home with the idea that we can do more and better". Since then, several of the associations who took part in this meeting have made enormous progress; they obtained better access to care in their country and developed strong associations who can really help patients and families to improve their life. Many claim they obtained this progress thanks to what they learnt and experienced at this network building conference. But when looking for support with official and private funding agencies we were always told this project was not big enough. An EU official told us to come back if we 'added a few zeros behind our budget'... Fortunately we were able to fund this project with donations from a couple of western European CF associations, but few associations have the money available to sponsor international meetings. The EU should stimulate this type of small scale, low budget but effective actions and projects of groups of committed stakeholders.



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