MINUTES of the Third Meeting of the Rare Diseases Task Force (RDTF)

Luxembourg, 20 June 2005
11.00 to 18.00

Introduction

The first half of the meeting was chaired by John Ryan of the European Commission in the absence of the RDTF leader Ségolène Aymé who joined the meeting at the end of the morning session.

Recall of minutes and main conclusions of the second RDTF meeting held on 14 October 2004

The minutes of the second RDTF meeting held on 14 October 2004 were adopted and will be published on the DG SANCO website [done].

The revised RDTF mandate was also adopted as no further requests for changes had been received.

Membership of the RDTF

It was noted that a certain number of RDTF members had never attended meetings nor replied to e-mails concerning the RDTF. Considering that places on the TF are limited and that enthusiastic potential members would like to participate in future meetings, a proposal was made to remove those that showed no interest in participation from the list of members.

John Ryan noted that the European Cancer Patient Coalition had recently shown interest in participating and other requests had also been received by the secretariat. These requests would be considered by the secretariat once the membership list had been reviewed.

It was agreed that in future, RDTF members representing EU projects on rare diseases should be reimbursed for attendance at the meeting if they had not set aside money for travel to these meetings in their project budgets. All future project contracts should include a budget for representation at RDTF meetings. John Ryan reminded members that EU rules restricted reimbursement to only 25 participants and that these 25 places should be used as intelligently as possible, particularly to allow participants from candidate countries to be reimbursed as private experts.

Three new participants presented themselves:

John Murray, present as an observer, represents the Specialised Healthcare Alliance based in the UK, which promotes the interest of patients suffering from rare or more common diseases with challenging care needs and particularly those who require care from specialised tertiary centres.

Lúcia Do Socorro Costa De Lemos from Portugal, present as an observer, represents the European Federation for Neurofibromatosis, a patients association.

Jean Donadieu, present as an observer, works at the National Institute for Health Surveillance (INVS) in France and is involved in an epidemiological surveillance of rare diseases.

Marianne Jespersen, from Denmark, is a senior medical officer from the Danish National Board of Health, the central administrative health department in Denmark.

RDTF Activity Report

Ségolène Aymé reported that the contract for the scientific secretariat was only signed on 1 June which meant that there had been some difficulties in funding activities. In spite of the delay, some work had already started internally at Orphanet on coding and classification and the newsletter and website have been developed.

One meeting of the working group on standards of healthcare, dealing with European centres of reference, has already taken place. It was expected that the RDTF will receive more and more requests for position papers and recommendations from the Commission as its visibility has increased.

Over the next six months the main tasks will be to plan work programmes for the working groups. Participants were asked to tell the secretariat as soon as possible if they would like to be members of the working groups and to recommend experts from their own countries.

It was agreed that working groups could be opened up to a wider list of experts who could receive documents and make input without necessarily being present at the meetings.

RDTF communication tools

Sally Goodman gave a report on the new RDTF newsletter and website:

i) OrphaNews Europe newsletter
The first issue of the monthly electronic newsletter, OrphaNews Europe, was published on 15 June 2005. Currently 5500 subscribers receive the newsletter. Members were encouraged to send in news for the newsletter and reminded that the newsletter was the main communication tool for the RDTF and the rare diseases community in Europe. The name of the newsletter, OrphaNews Europe, was questioned by a number of participants. It was explained that the newsletter was based on an existing in-house newsletter Orphanews France which was well known and as 40% of the funding came from Orphanet there was justification in retaining the name.

ii) RDTF website
The website www.rdtf.org was also launched on 15 June 2005. Key information on rare diseases in Europe will be made available on the public pages of the website and an inventory of national initiatives in the field of rare diseases and orphan drugs is being compiled and will be accessible on the website. A restricted access section is also available for RDTF members to share information and to comment on draft documents. The website contains a direct link to the newsletter.

John Ryan suggested that national MPs, MEPs and NGOs who would be interested in receiving the newsletter should be targeted in each country. Also regional administrations, science policy offices and e.g. European chief medical officers group. He suggested that NGOs might be approached to translate parts of the newsletter into local languages. It was agreed that where local language versions of documents exist, all language versions should be made available in links from the newsletter and website.

John Ryan for DG SANCO and Catherine Berens for DG Research both agreed to establish links to the newsletter and RDTF website from their respective sites

(http://www.cordis.lu/lifescihealth/major/cardio.htm and http://europa.eu.int/comm/health/ph_threats/non_com/rare_diseases_en.htm)

European Conference on Rare Diseases

Christel Nourissier of EURORDIS gave a short report on the preparations for the European Conference on Rare Diseases which was being held in Luxembourg on the following two days (21/22 June 2005). She thanked members of the RDTF for their help in the preparation of the conference. A webcast of the proceedings of the conference is available on the conference website.

Ségolène Aymé expressed her disappointment that not all members of the RDTF were going to be present at the conference. John Ryan thanked EURORDIS for their work in organising the meeting.

Some key messages from the RDTF to be conveyed to the conference were agreed at the end of the meeting. They were as follows:

- The RDTF is working to deliver new tools for the rare diseases community and to move the rare diseases agenda forward
- The RDTF is working closely in collaboration with partners such as DG Research, DG Enterprise, the EMEA, patients associations and industry
- Rare diseases have cross-links with the whole of healthcare and should not be considered as a separate sub-group.
- European co-ordination is extremely important in the area of rare diseases
- Important to have national and European networks because of the need to access sufficient numbers of patients for research
- Better access to data is needed
- Money for rare diseases is limited at national level and more resources are needed
- Importance of ensuring political support for rare diseases at the national level
- Patients associations play an important role in lobbying and have been leaders in raising awareness in the field

Working Groups

i) Public Health Indicators

Juliette Bloch from the Department of Chronic Diseases at the National Institute for Health Surveillance in France and leader of the Public Health Indicators working group presented the topic to participants. She explained her Institute's own project on epidemiological surveillance of rare diseases which will collect data from existing sources and identify new sources of epidemiological data. Firstly, they will establish a list of indicators that they would like to collect and prioritise the rare diseases, in terms of public health issues, for which they will collect data. This prioritisation will be based on a consensus process using a list of criteria compiled by experts (e.g. prevalence, expensive treatment, early diagnosis…). Once the list of criteria has been established the 500 most frequent rare diseases will be graded according to these criteria so that a list of diseases for priority surveillance can be compiled.

The RDTF working group will be focussed on identifying these public health indicators and making comparisons and sharing experience between countries on epidemiological surveillance of rare diseases using public health indicators. It will establish whether the French results can be applied to other countries or whether each country will need to go through the same process of identifying country-specific indicators because of differences in health systems etc.

Domenica Taruscio from Italy pointed out that similar data has been collected in Italy for the past four years for 547 diseases. She asked whether Italian data could be shared and compared with the French data.

Manuel Posada from Spain pointed out that the list of rare diseases to be monitored would be limited by the differences in the coding and classification systems used - ICD-9 or ICD-10. He also said that it would be difficult to share data between countries without breaking data confidentiality rules.

Anders Fasth agreed that ICD-9 and –10 don't allow for sub-groups of rare diseases and that in Sweden the personal data act would make the exchange of data very difficult.

Edmund Jessop added that international pharmaceutical databases contained much useful data on quality of life concerning very expensive therapies such as enzyme replacement treatments but that, once again, confidentiality rules make it very difficult to share this information beyond national borders.

Eva Steliarova asked whether prevalence criteria would be highest or lowest because this would mean creating groups of rare diseases within rare diseases. Juliette Bloch replied that she thought it would be highest prevalence but that this would only be one criteria among others. Alastair Kent recommended that the group should not attach too much importance to prevalence because of the holes present in much prevalence data.

Cornelia Zeidler pointed out that a clear diagnosis was vital for epidemiological purposes. Juliette Bloch agreed and explained that a precise diagnostic tool was one of the criteria that would be used.

Rumen Stefanov made reference to the dangers of bias if one system of epidemiological surveillance was applied to all countries. He suggested that a methodological guide was produced which could be used in all countries.

John Ryan asked what EC Public Health sector should be doing in this field, what the group wanted to achieve and for what purpose. The feasibility of collecting data should be taken into account as well as cost. Eurostat have put limits on the number of indicators for which they will collect data. There is a need to make sure that the information will be used by somebody before setting up a system to collect it. On the question of confidentiality, John Ryan explained that the next meeting of the Network of Competent Authorities in July would be discussing the problems of data confidentiality. He concluded that the Working Party on Public Health Indicators is an important one and asked all participants representing countries with a national system in place to send details to the RDTF secretariat for distribution.

ii) Coding and classification

Ségolène Aymé gave a presentation on the proposed work programme for this group. She explained how important it is to have an efficient system for coding and classification of rare diseases in an era where hospitals use computer-based records extensively, researchers use databases and politicians require evidence before they make decisions on public health issues.

The purpose of a coding system is to ensure precise medical diagnosis. A universal system is needed because data is exchanged at an international level. The code should be unambiguous and the system should be flexible enough to be updated regularly.

For rare diseases the current system is very unsatisfactory. For example, in rare diseases only about 300 out of approximately 6000 rare diseases have a code in the ICD-10 system of classification. Many experts have tried to extend the ICD-10 classification for their own purposes but they are not universally accepted and used. The MIM system is not a classification system and not maintained as such. However it is useful for providing unambiguous information about genetic disorders. The MeSH system provides several codes for the same disorder and most rare diseases have no MeSH code.

Currently the Orphanet database of rare diseases is indexing with MIM, ICD-10, by signs and symptoms, and in a future version there will also be an index by the genes involved, by age of onset and by means of transmission. The site will also show the hierarchy of classification that currently exists but will not provide a unique code for rare diseases.

Eva Steliarova-Foucher, from IARC, indicated that WHO is preparing a new edition of the International Classification of Diseases, ICD-11. This is therefore the appropriate time to start focused collaboration. It would be useful to give a mandate to a representative of the future RDTF working group on classification and coding to establish contact with WHO and discuss the possibilities of incorporation of rare disease codes in the ICD-11.

There is a need to actively work on this topic in collaboration with WHO and to collect all the existing codes. An expert group will be set up to work on extensions and to provide a tool for those wishing to code new rare diseases.

The Netherlands has already set up its own classification of rare diseases run by genetic laboratories, based on a combination of the OMIM code and their own code. Those responsible should be invited to be members of the working group.

Dr Aymé expressed her concern that whatever system was proposed by the working group was compatible with what exists already.

Helen Dolk commented that it was important to know who is coding and in what context and highlighted the importance of ensuring that the system is centralised so that some institution has responsibility for maintaining it.

Cornelia Zeidler proposed that initially the working group should identify where there is a need for new codes so that some estimation of the time required to complete the task can be established.

John Ryan reminded participants of the importance of having a mission statement for the working group so that any extra resources required could be taken into account in the next public health work plan.

Ségolène Aymé concluded that the first step was to collect existing expert classifications. This will help to identify the areas where there is no coding and those diseases that are most important in terms of public health can then be prioritised. These existing classifications could be made more accessible by centralising them. She proposed that this was a feasible task within two years. Domenica Taruscio commented that it might be difficult to reach consensus as different experts such as geneticists and clinicians may have different starting points.

Christel Nourissier underlined the importance of coding from the patients' point of view: that when there is a death from a rare disease this knowledge will be used to help the next generation. She regretted that no representative from WHO was present at the meeting. John Ryan explained that the principal point of contact on classification for

death certificates should be Eurostat. He also said that the issue of coding and classification could be raised with WHO representatives at EC level. He added that if international partners such as WHO were to be involved in the working group then it would be very important to ensure that the working group had a mandate and knew what it wanted to achieve before inviting them. It would also be important to see what could be afforded.

A mandate for this working group will be written up by the RDTF secretariat and circulated to members for approval. The first meeting should be called before the end of 2005 and be limited to a maximum of 20 members. Participants may be in common with the public health indicator working group but the work programmes should be kept separate. After discussion it was agreed to hold the public health indicators and coding and classification working groups on two consecutive days in Paris to ensure continuity and reduce travel costs.

iii) Standards of care

Ségolène Aymé reported on the meeting of the expert group dedicated to European Reference Centres held in Paris on 3 June 2005. The recommendations of this meeting fed into a High Level working group on Centres of Reference which held a meeting in Brussels on 16 June. This High Level working group is chaired by the French Ministry of Health. The report of the meeting on 3 June has been distributed to RDTF members and is available on the RDTF website.

Dr Aymé explained that the situation in Europe regarding centres of reference is extremely diverse with only five countries (UK, Sweden, Denmark, France, Italy) having officially recognised centres of reference and are all very different from one another. Many other countries have expert centres but they are not labelled as such.

In addition, many European networks have been established through EC funding and these are already acting in some cases as reference centres but are not labelled as reference centres.

The RDTF expert group agreed with the High Level working group's definition that the European reference centre should:

- provide outstanding service
- develop guidelines and provide information
- be involved in clinical research and teaching
- and be accessible to patients from other countries

but it recommended that:

- there should be no hierarchical distinction between national and European centres
- that European guidelines for care practice should be validated at European level
- that support should be given to existing centres and existing networks with financial support provided for networking activities and sharing of expertise.

Most existing networks supported by the EC are already doing what is asked by the High Level group of European centres of reference so the expert group recommended that these were supported instead of supporting new centres.

Only European experts should review applications for European centres of reference if there is a review process. Criteria should be established but these should be flexible. ECRs should only be established where there is a real public health need and where diagnosis and treatment cannot be accessed at the national level. The expert group was

critical of the labelling process proposed for ECRs because it was not clear what the label is for. There was also criticism from the expert group over geographical distribution of centres. Only expert ECRs should be labelled rather than ensuring a fair geographical distribution as there should not be an obligation for patients to travel to these centres.

There was also concern about the funding that would be available for these centres as experience has shown that expert centres will have extra work which will need sufficient funding and staff.

The group had questioned whether the ECR label was a label of quality which would incite cross-border referral, whether it was a recognition of expert centres where national bodies would accept to send their patients where necessary or whether the goal was to start organising healthcare at the European level, even though healthcare is supposed to be the prerogative of Member States.

The recommendations made to the High Level group was that cross-border referral should be minimised rather than encouraged as it is preferable that patients are treated close to home in their own language. It should be possible where necessary however. Telemedicine, networking, trans-border training of professionals, production of guidelines, provision of information and research is where the effort and funding should be applied rather than on two or three centres.

The concept of ECRs needs to be clarified as it will induce a lot of confusion and frustration. The concept is not yet clear at the national level therefore it is much too soon to apply this approach at the European level. If the ECRs are established then money needs to be provided and support given for networking.

Mapping existing centres in Europe is vital to establish what the situation is now and what the needs are before because it is too soon to establish new ECRs for 2006. A clear definition of an ECR is necessary before this mapping exercise can take place.

Dr Aymé reported comments from Member State representatives present at the meeting of the High Level working group on reference centres held on 16 June. In general there was no overall consensus on the objectives and definition of ECRs from this High Level Group.

The High Level Group is to provide modified terms of reference for the RDTF expert group [done] and has also modified its own definition of the roles of ECRs:

- To improve local capacities of quality care
- To improve knowledge
- To improve networks between existing centres in Member States

There may be a few situations where it makes sense to give this ECR label to a centre where a treatment can only be provided in one specialised centre and for patients to travel to these centres.

John Ryan explained that networks under the public health programme are financed for a maximum of three years because it is supposed to fund projects which can sustain themselves in the long term.

He explained that in developing the indicator list for public health DG SANCO has negotiated with Eurostat that a legal text be proposed which would oblige Member States to permanently collect statistics on a certain number of indicators. This text will be

proposed by Eurostat by the end of the year. The public health programme on the other hand can be used for developmental work but not for permanent studies.

He also expressed some concern that the High Level group, which was originally set up to deal with issues of patient mobility, was concentrating on issues of care which are not in the competence of the EU and that it is launching debates and new work programmes in areas such as data confidentiality and rare diseases where work is already being financed under the public health programme.

He explained that another High Level group on social protection has also been set up by DG Employment which is dealing with some similar issues. In addition, a parallel group on healthcare has been set up by the Council of Ministers as they do not consider that healthcare is in the competence of the EU. However, he warned that as no budget is attached to any of these High Level groups, any of the activities they suggest would have to be funded out of the Public Health programme.

A number of participants reiterated their concern that labelling centres would be very unhelpful both in terms of patient mobility and financially and that the emphasis should be on raising standards of care everywhere.

Ségolène Aymé concluded that it was too early to launch a call for the labelling process and suggested that the RDTF bring evidence to the High Level group that they should not go forward with the idea. Instead a quality label could be developed for national centres which could then be networked.

The RDTF expert group on centres of reference will meet at the beginning of September and provide a report for the High Level group for their meeting at the end of September. All RDTF members will receive documents for discussion and input.

DG SANCO call for proposals and 2006 work programme

John Ryan confirmed that 60 million euros was available annually for the public health programme until 2008 but future financing depended on discussions in the Council of Ministers. He also explained that in 2005 part of the public health budget had gone to fund the new agency of communicable diseases in Stockholm which does not yet have its own budget line.

John Ryan had to leave the meeting at this point and handed over to Antoni Montserrat from DG SANCO for this agenda item.

Antoni Montserrat explained that information exchange on rare diseases was given priority in this year's work plan. 243 projects had been received in the 15 April public health call of which only four were related to rare diseases. Three of these four projects will be recommended for funding and a final decision would be taken on 6 July. The three projects recommended for funding cover primary immunodeficiencies, myasthenia gravis and networking between patients with rare diseases. Two other projects recommended for funding were linked to rare diseases: one on autism and one on very premature babies.

The number of proposals received in rare diseases was very low and there was a plea for a higher input for the 2006 call. In the 2006 work plan the priorities for rare diseases are likely to remain the same with the possible addition of centres of references. Antoni Montserrat underlined that if the RDTF work groups wanted to do something practical, with funding, then this needed to appear in the 2006 work plan. There had been a suggestion that one inclusion in the work plan could be to use Eurobarometer to ascertain the level of knowledge and the perception of rare diseases in Europe.

A consultation and input on the content of the 2006 work plan by RDTF members would need to take place by September at the latest.

Helen Dolk asked whether it was still the case that projects on specific rare diseases or groups of diseases could not be funded, regardless of sustainability of the project. Antoni Montserrat replied that for cases like Eurocat, funding would not be discontinued but that there would be a reflection on how funding could be transferred in the future. Networks like ENERCA, producing metadata, rather than prevalence data, can be funded, but not indefinitely.

He explained that projects can be submitted in areas that have already been funded as long as new work in the area is proposed. The 2006 work plan will be the last one based on the same model. From 2007, the work plan will be based on the new programme which combines consumer protection and public health.

Genetic testing

Ségolène Aymé explained that the OECD had recently published the results of a survey on genetic testing in member states. DG Research organised two workshops of experts to discuss the implications of the survey's results but these workshops had not resulted in an agenda for European action. It was concluded that quality control in genetic testing was not yet organised at the national level. A network of excellence called Eurogentest, funded by DG Research, was started in January 2005 with the main task of developing quality control in European laboratories.

There is still a need for genetic testing for very rare diseases. Specimens travel frequently around the world because of the lack of expertise. This raises questions on quality control and on data confidentiality.

There is also a question about tests for very rare diseases which are performed by individual researchers, not laboratories. When the researcher's interests change the test may no longer be available if not transferred to a clinical laboratory. A system for this exists in the UK but there is a need to ensure that a system is put in place in Europe to ensure that these tests can be maintained.

DG Research has asked the RDTF to make recommendations in this field and identify areas where there is a need for action. This is very relevant for rare diseases.

The RDTF agreed that this was in their mandate and that they should proceed with making recommendations. Ségolène Aymé offered to write a draft response to DG Research for circulation before September. Domenica Taruscio offered her help in drafting the document.

Data confidentiality

Helen Dolk spoke to two tabled papers and explained that the issue of data confidentiality was a logistical one about obtaining consent. The problem is not specific to rare diseases but whilst major diseases like cancer manage to impose their own rules about registry use, rare diseases are left out. She asked that the RDTF note that rare diseases need specific attention when confidentiality and consent are being addressed. The issue is to be addressed at the Network of Competent Authorities meeting on 16 July.

It was agreed that data confidentiality be assimilated into the RDTF working group on standards of care.

Date of the next meeting

The next meeting will be held before the end of 2005

[Date of next meeting now confirmed as 14 December 2005]