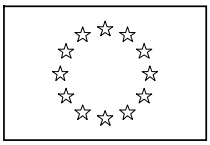

COMMISSION OF THE EUROPEAN COMMUNITIES

Brussels, 12.6.2001
COM(2001) 323 final

COMMUNICATION FROM THE COMMISSION TO THE COUNCIL AND THE EUROPEAN PARLIAMENT

on research activities in Europe related to Transmissible Spongiform Encephalopathies

{SEC (2001) 971 du 12.6.2001}

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1. BACKGROUND

At the invitation of the Research Council of 16 November 2000, the Commission established a group of experts on research on Transmissible Spongiform Encephalopathies (including Bovine Spongiform Encephalopathy, Scrapie and Creutzfeld-Jakob Disease), hereinafter referred to as 'TSE', with the aims:

– to examine the state of TSE research across Member States

– to encourage exchange of scientific information between research teams and

– to identify on-going research activities, which need strengthening, as well as new research activities which need to be launched.

The group of experts on research on TSE, hereinafter referred to as 'TSE expert group', is composed of representatives nominated by Member States and several Associated Countries, some members of the Bovine Spongiform Encephalopathy and Creutzfeld-Jakob Disease ad hoc group of the Scientific Steering Committee of Directorate General Health and Consumer Protection of the Commission, relevant co-ordinators of EU research and technological development projects and the services of the Commission. The TSE expert group met twice, on 15 December 2000 and 16 February 2001.

The TSE expert group has now elaborated an inventory of the research activities carried out in the EU, which contains the information provided by all Member States[1] as well as contributions from Iceland, Norway and Israel. It also includes direct research and technological development actions undertaken by the Joint Research Centre (JRC) and the indirect research and technological development actions funded by the Commission, both in the framework of the European initiative on TSE[2], launched in 1996, and those currently funded in the fifth framework programme of the European Community for research, technological development and demonstration activities (1998 to 2002)[3], hereinafter referred to as the 'fifth framework programme'.

2. MAIN LESSONS FROM THE INVENTORY

The inventory provides a comprehensive and up-to-date description of ongoing research across Europe and demonstrates the complexity of this area, which combines fundamental and applied research in human and animal aspects. It constitutes a very valuable source of information on the research effort from which it is possible to identify strengths and bottlenecks, the areas where more collaboration is required and those gaps where a further effort is needed.

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1 No information from Luxembourg as no research activities on TSE are undertaken in Luxembourg to date.

2 COM(1996)582 final.

3 Decision No 182/1999/EC of the European Parliament and of the Council of 22 December 1998 concerning the fifth framework programme of the European Community for research, technological development and demonstration activities (1998 to 2002). JO L26,1.2.1999, p.1.

The preparation of this inventory by the participating countries has in itself been a useful exercise as it has brought together most of the key TSE research managers and scientists across Europe and facilitated a dialogue and a comparison of the different research efforts across Europe in this field.

The inventory shows, as expected, that the involvement in TSE research and the interaction between different disciplines/teams varies between countries and, in most cases, is directly related to the importance of TSE diseases in these countries. In countries recently affected by the bovine spongiform encephalopathy the involvement is increasing at present and therefore, newcomers are joining this field of research. Finally some countries address specific research activities and their involvement takes place within the framework of EU research and technological development projects, in particular European networks (thematic networks and concerted actions).

The European initiative on TSE, driven by existing scientific excellence, has mobilised a great number of European teams and consolidated very fruitful collaborations both in human and animal TSE. When taken together, the various national TSE programmes, the European research and technological development projects funded under the European initiative on TSE and fifth framework programme, a very considerable and diverse research effort is under way.

The analysis of this inventory, the experience gained from the European initiative on TSE, recommendations on specific subjects in opinions coming from the Scientific Steering Committee of the Health and Consumer Protection Directorate General and discussions carried out by the TSE expert group has facilitated the identification of gaps in knowledge and bottlenecks in different domains and where efforts can be carried out both at national and at EU level. The exercise has also highlighted that in some areas, more co-ordination is needed, while in others a common approach needs to be taken, with some further concentration on a few key issues.

3. CONCLUSIONS - THE WAY FORWARD

1. A series of emerging priorities have been identified by the TSE expert group which could be addressed by increased co-ordination or concentration of means

– Increased coordination could cover a wide range of initiatives such as:

  – Strengthening on-going activities in Member States

  – Facilitating exchange of information and communication of results

  – Opening of national programmes

  – Expanding research networks to newly associated countries to the fifth framework programme[4].

  – Strengthening training networks

  – Addressing TSE-related social and ethical issues

[4] Bulgaria, Republic of Cyprus, Czech Republic, Estonia, Hungary, Latvia, Lithuania, Malta, Poland, Romania, Slovakia, Slovenia.

Relevant areas for increased coordination include for instance:

- Improved epidemio-surveillance
- Inventory and sharing of animal models and cell lines
- Collection and provision of well-characterised samples
- Quality assurance for the validation of diagnostics tests
- Best practices in abattoir techniques and waste disposal

Much of this co-ordination could be achieved in the context of the new research policy on the European Research Area[5].

- Concentration of means in areas identified on the basis of the urgency of the issue, the fragmentation of current activities, the requirement for critical mass or the need for infrastructure. The TSE expert group has identified the following areas where clear research gaps exist :
  - In vivo test for pre-clinical diagnosis
  - Human TSE and risk assessment
  - Inactivation and prevention
  - Animal TSE and transmission

2. There is a need for the EU to address issues related to the availability of:
   - specific TSE research facilities and sophisticated equipment with the appropriate safety levels;
   - sufficient quantities of well characterised infected and non-infected material notably for the development and validation of diagnostic tests as well as for quality assurance of tests in use;
   - different animal models and cell lines (to be developed but also shared between research teams).

3. Increasing research activities need increasing human resources. Favourable conditions should be available in order to attract the necessary human resources to the field of TSE. In addition, specific training should be organised.

4. Taking into account all the above elements it is clear that a shared effort needs to be done both by Member States and Associated Countries to the fifth framework programme and at EU level. The work carried out by the TSE expert group is a very good example of the need for strengthening research in the context of the European Research Area. Therefore the Commission will

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5 COM(2001)6.

– continue its work with the TSE expert group so as to update the inventory in the light of new developments and the inventory will in the near future be extended to Eastern and Central Europe Countries;

– implement a specific call for proposals launched to remedy the existing research gaps in TSE and

– invite the Member States to examine which further practical steps in the realisation of the European Research Area can help moving forward this important research effort in Europe.

ANNEX I

Analysis of the inventory of TSE research activities in Europe

A Introduction

B General observations

C Observations in the major research areas

A INTRODUCTION

At the invitation of the Research Council of 16 November 2000, the Commission established a group of experts on research on Transmissible Spongiform Encephalopathies (including Bovine Spongiform Encephalopathy, Scrapie and Creutzfeld-Jakob Disease), hereinafter referred to as 'TSE', with the aims:

- to examine the state of TSE research across Member States
- to encourage exchange of scientific information between research teams and
- to identify on-going research activities, which need strengthening, as well as new research activities which need to be launched.

The group of experts on research on TSE, hereinafter referred to as 'TSE expert group', is composed of representatives nominated by Member States and several Associated Countries, some members of the Bovine Spongiform Encephalopathy and Creutzfeld-Jakob Disease ad hoc group of the Scientific Steering Committee of Directorate General Health and Consumer Protection of the Commission, relevant co-ordinators of EU research and technological development projects and the services of the Commission.

The TSE expert group met twice, on 15 December 2000 and 16 February 2001. The first task carried out by the TSE expert group has been to elaborate an inventory of the research activities carried out in the EU. National contact persons were designated to gather the information and channel it to the Commission.

The TSE expert group has now elaborated an inventory of the research activities carried out in the EU, which contains the information provided by all Member States[6] as well as contributions from Iceland, Norway and Israel.

It also includes direct research and technological development actions undertaken by the Joint Research Centre (JRC) and the indirect research and technological development actions funded by the Commission, both in the framework of the European initiative on TSE[7], launched in 1996, and those currently funded in the fifth framework programme of the European Community for research, technological development and demonstration activities (1998 to 2002)[8], hereinafter referred to as the 'fifth framework programme'.

As a result of the size and importance of the research effort undertaken in the different countries the degree of detail provided for each country varies. The inventory given in annex 2 provides a comprehensive and up-to-date description of ongoing research across Europe which has been structured as follows:

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6 No information from Luxembourg as no research activities on TSE are undertaken in Luxembourg to date.

7 COM(1996)582 final.

8 Decision No 182/1999/EC of the European Parliament and of the Council of 22 December 1998 concerning the fifth framework programme of the European Community for research, technological development and demonstration activities (1998 to 2002). JO L26,1.2.1999, p.1.

1- Description of the main TSE research activities in each country

2- How these activities fit into the principal areas of the European Action Plan on TSE research :

a) Clinical, epidemiological and social research on human and animal TSEs

b) The infectious agent and its mechanisms of transmission

c) Diagnosis of TSEs

d) Risk assessment

e) Treatment and prevention

3- Principal research teams and their areas of expertise

4- Collaboration with other countries and openness of programmes to collaboration

Pursuing the mandate of the Council, the group has also carried out an analysis of the TSE research activities. A summary of this analysis is presented in this report

B GENERAL OBSERVATIONS

The inventory provides a comprehensive and up-to-date description of ongoing research activities on TSE across Europe. It constitutes a very valuable source of information to identify the existing potential for TSE research and its output and also to promote a better co-ordination in Europe in this field.

The inventory confirms the complexity and multidisciplinarity of TSE research integrating human and animal research and ranging from fundamental research to very specific applied research.

The preparation of this inventory by the participating countries has in itself been a useful exercise as it has brought together most of the key TSE research managers and scientists across Europe and facilitated a dialogue and a comparison of the different research efforts across Europe in this field.

The inventory shows, as expected, that the involvement in TSE research and the interaction between different disciplines/teams varies between countries and, in many cases, is directly related to the importance of TSE diseases in these countries. In this regard, some countries have well established national multidisciplinary programmes for research in TSEs, linking the government and public and private research institutions. Other countries have, since many years, outstanding activities in specific domains. In countries recently affected by BSE the involvement is increasing at present and therefore, newcomers are joining this field of research. Finally some countries address specific research activities and their involvement takes place within the framework of EU projects, in particular European networks.

The European initiative on TSE has, driven by existing scientific excellence, mobilised a great number of European teams and consolidated very fruitful collaborations both in human and animal TSEs. When taken together, the various national TSE programmes, the European

research projects funded under the European initiative on TSE and the framework programme of the European Community for research, technological development and demonstration activities, a very considerable and diverse research effort is under way. This effort will provide answers, not just in TSEs but also in other neuro-degenerative diseases.

The analysis of this inventory, the experience gained from the European initiative on TSE, and discussions carried out by the TSE expert group has facilitated the identification of specific gaps in knowledge and bottlenecks in different domains and where efforts can be carried out both at national and at EU level. The exercise has also identified that in some areas, more co-ordination is needed, whereas in others a common approach needs to be taken, with concentration on a few key issues.

C OBSERVATIONS ON THE MAJOR RESEARCH AREAS:

a) Epidemiological research and surveillance

Human TSE

Epidemiological research and surveillance in human TSEs are co-ordinated at EU level through the network projects (EUROCJD and NEUROCJD), successfully established by the CJD Surveillance Unit and complemented by the neuropathology network (PRIONET) co-ordinated by the Institute of Neurology of University of Vienna. All countries (except LU) participate in these networks coordinated by the UK and AT.

However, in order to achieve a harmonised surveillance within each country and hence achieve harmonisation of national programmes across the EU, there is, in some countries, considerable room for improvement for the provision of the necessary financial, personnel and structural means to perform the tasks required by the networks.

Animal TSE

Epidemiological research in the case of scrapie in sheep has been a major issue in countries most affected by this disease (IS, UK, NO, F and more recently IRL) with the aim to identify risk factors and towards its eradication. In the case of BSE in cattle, the UK is involved in epidemiological research since the beginning of the epidemic. Other countries more recently affected by BSE are now also involved.

At EU level, 2 EU networks on ruminant TSEs, co-ordinated by F and IRL, are in place and are proving to be extremely useful in terms of training, standardisation and harmonisation of techniques and criteria for the identification of suspect cases, and in creating data and biological samples banks.

Therefore, in the case of ruminant TSEs, there is as well room for improvement through mobilisation of more countries not yet involved. At national level, efforts should be made to transfer knowledge to the laboratories newly involved in surveillance and diagnosis.

b) The infectious agent, mechanisms of transmission and pathogenesis

This is a very broad area of research involving many disciplines. There is clear leadership of some countries with the UK involved in all fronts and a strong commitment of D, F and I in some of the areas. IS and NO have leading roles in research on scrapie.

Further collaboration should be encouraged:

- in the physico-chemical studies of the normal and abnormal forms of the prion protein by centralising the utilisation of the high cost instruments under the safety conditions required.

- by establishing networks for research tools in this area: transgenic animal models, analogous models, cell lines, reagents, tissues.

c) Diagnosis of TSEs

Major efforts are undertaken in this area both with respect to human and animal TSEs and progress has been achieved. However, definitive diagnosis can only been confirmed at the post-mortem stage. The development of specific, sensitive, pre-clinical and in vivo tests continues therefore to be the major challenge in TSE research. Research undertaken in the UK, D, F, NL is strongly committed to different approaches to diagnosis. Other MS are carrying out various research activities (IRL, B, I, E, S).

There is also considerable collaboration in the framework of EU projects. Diagnosis is of great interest for industry as shown by the creation in recent years of start up companies dedicated exclusively to the diagnosis of TSE.

Further collaboration should be encouraged in order to address specific problems and ease bottlenecks encountered in this area, such as:

- establishment of a methodology, so as to examine, in a systematic way, the claims for new diagnostic tests

- assessment and validation of emerging diagnostic tests and reagents

- maintenance of a bank of tissues and body fluids from animals with known TSE incubation or clinical status

- increase and networking of animal facilities needed for infectivity bioassays.

- discussion of specific problems in the daily application of the diagnostic tests such as the state of the sample, the tissue to be used for confirmatory testing etc…

d) Transmission studies and risk assessment

A considerable effort has been undertaken in the UK towards different aspects of transmission and in performing risk assessment such as the determination of the effective oral exposure in cattle, tissues carrying infectivity, BSE in sheep, lateral and vertical transmission, TSEs in other food animals (pigs and poultry) etc…

Other countries are currently also involved in transmission studies in the framework of EU projects: BSE in sheep (NL), transmission of BSE to pigs, transmission of scrapie and BSE to fish (I,F,E), environmental vectors of transmission (F, IS)

Transmission studies are of long duration and very costly but are essential for risk assessment. Further involvement of countries in this area should be encouraged. In addition, the networking of the titration assays and experimental infections would avoid duplication of funding.

e) Therapeutic research

Therapeutic research is identified as a priority for human TSE in the national programmes in some MS (UK, D, F, NO). In addition, there are consolidated collaborations through EU projects.

This area is underpinned by intensive fundamental research on the molecular and cellular pathogenesis of the disease in order to identify therapeutic targets. Other activities involve studies on specific compounds with anti-prion activity and vaccination strategies.

Further collaboration should be encouraged:

- in the development of cellular and animal models for rapid in vitro and in vivo screening and evaluation of new molecules or approaches in TSE therapeutics
- with related fields (neurodegenerative diseases, amyloidosis)
- in setting up networks for clinical trials
- in further cellular and pathogenesis studies

f) Inactivation procedures and decontamination, prevention

Decontamination and inactivation procedures are major areas of research in the UK. Other important activities are undertaken in some MS, most of them in the framework of EU projects, and are related to decontamination of blood, the rendering process and gelatine production, disposal/utilisation options for meat and bone meals (MBM) and tallow.

Research on inactivation of contaminated materials should be encouraged due to the number and the variety of issues involved such as decontamination of surgical materials; disposal of carcasses and abattoir wastes and MBM; food, pharmaceutical and cosmetic industrial processes; survival and degradation of prions; persistence in and decontamination of the environment (soils, farms, abattoirs, hospitals); potential persistence in wild life.

g) Other areas

In view of the experience gained since 1996, the group of experts has also advocated the need to address two important topics in a coordinated way at European level:

- social and ethical issues related to TSE

- dissemination of TSE research results between scientists, research managers, decision makers and the general public.