Brussels, 19 January 1998

COST 304/97

DRAFT

Memorandum of Understanding

for the implementation of a European Concerted Research Action designated as COST Action 835

"Agriculturally important toxigenic fungi"

The Signatories to this Memorandum of Understanding, declaring their common intention to participate in the concerted Action referred to above and described in the Technical Annex to the Memorandum, have reached the following understanding:

1. The Action will be carried out in accordance with the provisions of document COST 400/94 "Rules and Procedures for Implementing COST Actions", the contents of which are fully known to the Signatories.

2. The main objective of the Action is to increase the knowledge and to promote biotechnology in the prevention (in the case of toxin accumulation), production and application (in the case of biological control) of agriculturally important toxigenic fungi in a European sustainable agriculture.

3. The overall cost of the activities carried out under the Action has been estimated, on the basis of information available during the planning of the Action, at ECU 12,48 million at 1997 prices.

4. The Memorandum of Understanding will take effect on being signed by at least 5 Signatories.

5. The Memorandum of Understanding will remain in force for a period of 4 years, unless the duration of the Action is modified according to the provisions of Chapter 6 of the document referred to in Point 1 above.

6. A statement concerning ethical, social and economic and ecological problems is attached, to be signed by the future participants.

GENERAL DESCRIPTION OF THE ACTION

COST Action 835

Agriculturally important toxigenic fungi

A. BACKGROUND

1. Current state of the art of research in the field

Amongst plant pathogenic fungi and fungi which colonize agricultural commodities, foods and feeds some ones are capable to produce toxic secondary metabolites (toxins) that induce diseases in human and animal (mycotoxins), insects (entomo-toxins), in plant (phytotoxins) and toward others microorganisms (antibiotics).

Some toxigenic fungi (TF) can parasitize and colonize crops (e.g. wheat, corn, barley) and agricultural commodities. Under environmental conditions favourable to their growth, they can accumulate in infected products significant amount of mycotoxins at every step of the time, i.e. in infected plants starting in the field as well as from the harvesting to the consumption. Such large colonization of TF and consequent accumulation of mycotoxins on agricultural commodities and fodder represent a high risk for animal and human health, causes losses of production for the effects on

animal that ingest them. Moreover, feed contaminated by mycotoxins may not only have a direct adverse effect on the animals that ingest it, but there may also be a carry-over of the toxins, or their metabolites, into milk, eggs, and mea, thus creating a further danger of exposing human beings to mycotoxins. During the last years, many cases of animal and human mycotoxicosis and losses of production due to infertility and growth reduction, have been reported in several European countries. Increasing level and diffusion of fungal toxins in agricultural commodities and the potent toxicity have obliged many European governmental authorities to impose severe limitations on the TF and their mycotoxin occurrence in agricultural commodities. Correct identification and toxicological characterization of pathogens and colonizing fungi of crop plants and food is determinant to assay their toxigenic potential risks and to prevent plant, animal and human diseases.

Reduction of effectiveness of fungicides has been observed in populations of some plant pathogens with increasing frequency. Moreover, reduction of chemicals in agriculture is desirable in order to limit environmental pollution and health hazards. These conditions strongly stimulated research for alternative control strategies in all European countries. Biological control by fungi producing bioactive metabolites (natural insecticides, antibiotics, specific phytotoxins), alone or as a part of integrated control, may play a significant role in the establishment of sustainable and competitive agriculture.

2. Why the cooperation should be carried out within the context of cost

The proposal is multidisciplinary (molecular genetic, mycology, biochemistry, toxicology, plant pathologist, etc...) and has a strong system-oriented component. This is a reason enough to set up a network because cooperation between laboratories is essential to synergy and research efficiency.

Although the interest on toxigenic fungi is strongly increasing in various European laboratories the research effort devoted to toxigenic fungi is smaller than its economic, health and environmental importance deserve.

3. How the action relates to other international scientific programmes

An important aspect of our activity is to improve the promotion of collaboration with other COST Actions dealing with "Early Detection of Plant Pathogens" and "Biological Control of Weeds in Europe".

The collection and the study of agriculturally important European TF will also form the basis for an exchange both of comprehensively characterized fungal strains and of knowledge about their molecular and biochemical characteristics among European research groups as well as other equivalent co-ordinating structures in other countries (e.g. ATCC and FRC in USA; MRC, South Africa; IBO, Argentina).

B. OBJECTIVES OF THE ACTION

This Action will achieve three main objectives:

1. to gather European institutions which intend to cooperate on agriculturally important TF in sustainable and competitive agriculture in Europe: i.e. 1) to harmonize methods; 2) to develop residential and exchange opportunities for students and scientists within network; 3) to establish a regular framework for meetings.

2. to provide the necessary know-how for increasing the competitiveness of European research at a crucial moment for the development of new management techniques in agriculture: i.e. reduce or eliminate the negative consequences of the fungal toxin accumulation (e.g. Fusarium-toxins) in crop- plant, food and feed; knowledge on toxigenicity and mode of action of fungal candidate in biological control, use of specific toxins for selecting resistance in the plant.

3. to promote biotechnology in the prevention (in case of mycotoxins accumulation), production and application (in case of biological control) of agriculturally important TF in sustainable agriculture.

C. SCIENTIFIC CONTENT

The scientific content of this Action consist in the following orientations

1. Biodiversity, phylogeny and taxonomy of toxigenic fungi

Agriculturally important toxigenic fungi will be identified utilising all available techniques, i.e. morphology, chemistry, molecular biology. Intra- and interspecific differences in the toxic secondary metabolites production will be determined among population of toxigenic fungi (chemotaxonomy). Variable rDNA regions will be used for establishing the phylogenetic relatedness among toxigenic fungi. To deposit both toxigenic fungi in European culture collection and their sequences in European gene bank (EMBL).

An expert system for identification of European agriculturally important toxigenic fungi will be developed. Correct identification and toxicological characterization of pathogens and colonizing fungi of crop plants and food is determinant to assay their toxigenic potential risks and to prevent plant, animal and human diseases.

2. Genetics and physiology of toxigenic fungi

Classic and molecular techniques will be used for genetic studies of agriculturally important TF. Studies will be carried out on mating type genes and segregation of the characters among progenies of fertile crosses by strains with opposite mating type and different toxic ability, belonging to species with known teleomorph.

Fundamental knowledge about this will contribute to the control of the pathogen, by providing a system which will allow scientists to detect situations (environmental conditions and cropping systems) in which sexual reproduction is most active.

Characterization of cariotypes of toxigenic fungi for providing further information on genetic variability among toxigenic fungal species. Genes responsible of toxin biosynthesis must be isolated and their products and modes of action characterized. Technique of gene destruction will be adopted to investigate the possible involvement of gene responsible of toxin production in the disease.

The knowledge of the regulating mechanisms of fungi for toxin production, especially in relation to their pathogenicity will allow us to understand the molecular basis of the toxigenicity and to develop new molecular techniques for early detection of toxigenic fungi in agricultural commodities (seeds, crop plant, food, feed etc.)

3. Ecology and pathogenicity of toxigenic fungi

Despite the economic importance of TF there is still a lot to be done to assess their importance as component of ecosystems. Studies will be carried out on fungal ecology: i.e. fungal populations, environmental parameters, possible relation between production of toxins and niches/host/geographical spread.

The biological cycle of fungi and the interaction of the toxins with other organisms need to be better definite. Pathogenicity of toxigenic fungi on their respective hosts, the role of toxins in the pathogenicity and their mechanism of action will be elucidated.

Such knowledge will allow us to predict the toxin formation in field and magazine, to prevent their accumulation in the plant and to improve the efficiency of mycopesticides in field.

4. Chemical and biological characterization of toxic metabolites

Toxins will be extracted, purified and quantified by a range of chemical and bio-chemical techniques.

The biological role of the toxins in eliciting toxic effects needs to be better defined also at the molecular and cellular level.

The active secondary metabolites will be tested in various bioassays for evaluating their potential application in agricultural, industrial, chemical, pharmacological, medical, animal and food and feed sciences.

A particular attention will be given in using specific toxins for selecting plant resistant.

Occurrence of toxins in infected plants, in food and feed.

5. Toxigenic fungi in sustainable agriculture: biopesticides

Biological control, alone or as a part of integrated control, may play a significant role in the establishment of a sustainable and competitive agriculture. In spite of technological interest, the mechanisms of biological control in most cases have not been completely elucidated.

Studies are needed for enabling the improvement of the biocontrol activity by means of genetical engineering and for evaluation of potential toxicological risks related to the delivery of promising microrganims in environment for biocontrol purposes. Investigation on development of production of biopesticides should be pursued with the aim of making use of them for the improvement of biological control.

D. TIMETABLE

The time required to pursue the scientific projects will be four years. The evaluation of the progress of the Action will be by annual meetings on specific subjects in the following sequence:

1998: Molecular and biochemical techniques for characterizing the biodiversity in agriculturally important toxigenic fungi.
(1st meeting)

1999: Advances in studies on European toxigenic fungi and their secondary metabolites: pathological and toxicological aspects (1st meeting)

2000: Molecular and biochemical techniques for characterizing the biodiversity in agriculturally important toxigenic fungi.
(2nd meeting)

2001: Advances in studies on European toxigenic fungi and their secondary metabolites: pathological and toxicological aspects (2nd meeting)

A final meeting will be held in 2001 to evaluate the achievement of the Action.

International experts from outside Europe will be asked to participate and provide a critical analysis on the achievements.

E. ORGANIZATION AND MANAGEMENT

The action will be divided into the following 5 working groups:

1. Biodiversity, phylogeny and taxonomy of toxigenic fungi.
2. Genetics and physiology of toxigenic fungi.
3. Ecology and pathogenicity of toxigenic fungi.
4. Chemical and biological characterization of toxic metabolites.
5. Toxigenic fungi in sustainable agriculture: biopesticides

Coordinators of these working groups will be designated by the Management Committee. These working groups will meet regularly to coordinate and promote research activities.

Annual evaluation meetings (see Timetable) will be held:

- to review the results achieved and will include non-European-Experts and Officials from the EC Commission;
- to promote cooperation within participating institutes,
- to harmonize methods and finalize publications;
- critically to evaluate progress achieved in practical applications.

Special emphasis will be placed on agriculturally important toxigenic fungi in Eastern Europe Countries through organizing working meetings on the development of experimental approaches and methodology. Research activities on toxigenic fungi from the different European regions will thus be integrated within a pan-European Action.

The Management Committee will meet at least twice a year, if possible in conjunction with the annual meeting.

Joint working groups will be promoted between this Action on toxigenic fungi and other relevant COST Actions (i.e. 817, 823). The Management Committee of these Actions will establish the rules of such cooperation.

The final evaluation of the Action is specified under "4. TIMETABLE".

The preliminary potential participants in this COST Action are: Denmark, Germany, Greece, Finland, Hungary, the Netherlands, Poland, Slovak Republic, Spain, Sweden.

F. ECONOMIC DIMENSION OF THE ACTION

The economic dimension of the Action is estimated on the basis of current activities of the interested groups. The estimation includes manpower, national and international research grants already available or expected to be available in the near future for the work planned.

Scientists	22 persons x	ECU 60,000	ECU 1,320,000
Technicians	16 persons x	ECU 40,000	ECU 640,000
PhD Students	16 persons x	ECU 25,000	ECU 400,000
Total Personnel per year			ECU 2,360,000

Total Personnel in 4 years	4 x		ECU 9,440,000
TOTAL Investment	4 years		ECU 1,280,000
Total Running COST	4 years		ECU 1,520,000
Coordination Cost (COST)	4 years		ECU 240,000
TOTAL economic dimension	4 years		ECU 12,480,000

For all Participants

Ethical, social, economic and ecological statement:

In implementing the proposal research I shall adhere most strictly to all national and international ethical and safety provisions applicable in the country(ies) where the research is carried out.

I shall conform in particular to the relevant safety regulations concerning the deliberate release into the environment of genetically modified organisms.

I shall also conform to the ethical guarantees included in the 4th Framework Programme ([1]).

Date: Name of the responsible scientist

Signature:

([1]) "whenever possible, experimentation and testing on animals should be replaced by in vitro or other methods. No research modifying, or seeking to modify, the genetic constitution of human beings by alteration of germ cells or of any stage of embryo development which may make these alteration hereditary, nor research seeking to replace a nucleus of a cell of an embryo with a nucleus of a cell of any person, embryo or subsequent development of an embryo, known as cloning, will be carried out under this framework programme."

Decision No 1110/94/EC of the European Parliament and of the Council of 26 April 1994 concerning the fourth framework programme - Annex 3 - First Activity - Section 4. Life Sciences (OJ L 126, 18.5.1994)