European Cooperation in Science and Technology
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Secretariat

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COST 4135/10

MEMORANDUM OF UNDERSTANDING

Subject : Memorandum of Understanding for the implementation of a European Concerted Research Action designated as COST Action FA1002: Farm Animal Proteomics

Delegations will find attached the Memorandum of Understanding for COST Action FA1002 as approved by the COST Committee of Senior Officials (CSO) at its 178th meeting on 25 May 2010

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MEMORANDUM OF UNDERSTANDING

For the implementation of a European Concerted Research Action designated as

COST Action FA1002

FARM ANIMAL PROTEOMICS

The Parties 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 4159/10 "Rules and Procedures for Implementing COST Actions", or in any new document amending or replacing it, the contents of which the Parties are fully aware of.

2. The aim of the Action is through the application of proteomic science to resolve problems in farm animal production and post-harvest change.

3. The economic dimension of the activities carried out under the Action has been estimated, on the basis of information available during the planning of the Action, at EUR 112 million in 2010 prices.

4. The Memorandum of Understanding will take effect on being accepted by at least five Parties.

5. The Memorandum of Understanding will remain in force for a period of 4 years, calculated from the date of the first meeting of the Management Committee, unless the duration of the Action is modified according to the provisions of Chapter V of the document referred to in Point 1 above.

A. ABSTRACT AND KEYWORDS

Proteomics offers the ability to define changes in protein expression. This advanced technology has already made a significant impact on biological and biomedical research, where long established collaborative initiatives have stimulated progress. There is an increasing awareness of the potential of proteomic technologies to study production animals but the use of proteomic strategies to investigate animal health and disease has been limited by the lack of international coordination and collaboration. The COST Action will form a network of the leading European scientists who are focused on farm animal proteomics; this network will benefit the European scientific community by providing a conduit for the rapid dissemination of knowledge on the techniques and applications of this rapidly advancing area. It will benefit the European economy by providing advanced analytical tools to enhance animal production, health and welfare, as well as in the assessment of food quality and safety related to the protein in food produced from animal origin. The COST Action aims to establish synergistic interaction across Europe to provide a stimulus for the development of farm animal proteomics.

Keywords: Proteomics, Farm Animal, Animal Health & Welfare, Systems Biology, Food Quality & Safety

B. BACKGROUND

B.1 General background

Farm animal derived products provide the most concentrated and balanced source of protein in human diets. Maintaining animal health during production increases agricultural productivity, enhances food security and leads to the highest quality and safety of food. It is therefore essential to support research aimed at improving the health and welfare of animals farmed for food production and to promote the sustainability of farm animal industries.

Proteins have important roles in controlling many cellular functions and can be used as markers of health and disease status in production animals and to monitor quality traits in meat and food products. Proteomics comprises the large-scale analysis of proteins in biological systems at a specific time and set of conditions. Proteomics can define changes in protein expression and has evolved into a mature science that addresses the technically challenging problems of protein characterisation, protein quantification and the measurement of proteome dynamics. It has benefited from rapid developments in efficient separation technologies, high resolution mass spectrometry and powerful bioinformatic tools in addition to synergistic advances in genomic, transcriptomic and metabolomic disciplines. Proteomics has made a significant impact over the last decade in many areas of life sciences, although studies on farm animals have often had a lower profile in leading scientific journals and at international conferences. In fact, less than 3% of papers with a keyword of 'proteomics' also have keywords of 'cow, pig/swine, sheep, goat, or fish' on the ISI World of Science database over the years 2001-2008. Although a number of these papers have been published by experts within Europe it is noticeable that many papers are being produced by laboratories in North America and Asia, in particular in China. Furthermore, though numerous reviews, books and monographs have been published on proteomics in human physiology and pathology, health and disease there are only a few reviews describing the application of proteomics to farm animals.

Within Europe, some progress has been made in farm animal proteomics (FAP) based on nationally funded research and this will continue However a network across COST countries to establish links between current centres of expertise will be a highly effective mechanism of maximising the overall research output and will create the next generation of global leaders in FAP.

Proteomics is closely linked, but is a distinctly different analytical approach to other developing 'omic' sciences such as genomics, metabolomics and transcriptomics. Each of these 'omics' requires development and training of a different skill set and even though there is valuable interchange between these disciplines it is important that research communities are established in which applications and technical standards can develop. While there have been tremendous strides in the applications of genomics in particular in farm animals, it is necessary that a sufficiently focused COST Action is devoted to proteomics in this area in order to raise European FAP to a similar high level.

The aim of this COST Action is to create a community within Europe, which will bring together scientists whose research is focussed on FAP in order to fully exploit the development of this science for Europe. The COST Action will be fully integrated into animal science and food research in Europe as a high proportion of the members of the Action are either themselves leaders in the field or are early stage researchers based in institutes undertaking animal science and food research at the highest level. The activity of the Action will therefore be readily disseminated to colleagues across the spectrum of disciplines which constitutes the European animal science community. This network will provide a lead in experimental standards for FAP investigations and promote the application of proteomic technologies in production animal research. The formation of a COST Action is the ideal mechanism to coordinate nationally funded researchers in COST countries and will provide a key framework to report experimental advances. It will also facilitate the exchange of information and staff between laboratories and enable early stage European researchers to receive training and develop core skills in this fast developing discipline.

B.2 Current state of knowledge

Farm animal products form the basis of our protein-based food and are crucial to current nutrition in Europe, thus proteomics has a fundamental role to play in farm animal and food research. Nationally funded research in FAP within Europe has been, and is being, undertaken by members of this COST Action. Proteome maps have been established for plasma and tissue in a variety of production animal species such as cattle and swine. Proteomic investigations have also been undertaken to assess meat maturation and to monitor post-catch changes in the protein profile of fish muscle. Proteins in milk have been closely examined by proteomics as it is important to determine changes that occur in its protein composition for assessment of health status, quality and safety of dairy products. Proteomics has also been used to characterise disease states in production animals and to determine the origin and source of feed products. Additionally, proteomic strategies have been employed to measure the dynamics of muscle growth in poultry and advance farm animal reproduction.

Similarly, the quality of meat is dependent on its protein composition which is altered as muscle is allowed to age. Proteomics has been used to monitor this process, in particular the changes that take place in the meat proteome in relation to the speciality dried meats of Southern Europe. Proteomic investigations have also been made of the proteome of muscle and other tissues of caught or farmed fish in relation to health status and the quality of the product for the human food chain. The way in which food is produced, processed and delivered to the consumer is a major concern of the food industry in Europe. Proteomic technologies are increasingly being adopted to monitor food composition, authenticity and safety, for instance by identifying the presence of bovine or porcine blood based binding agents in processed food to enforce accurate food labelling. Similarly, proteomic strategies provide means to define meat and fish quality, detect food allergens and identify markers of spoilage or pathogenic microorganisms in dairy products.
There are currently no other funded EU programmes applying proteomics to animal science, as the application of this technology in farm animal research has not been part of current or previous Framework Programmes.

B.3 Reasons for the Action

This proposal is very timely as more animal, veterinary and food scientists consider using these techniques as their major focus or to complement existing research interests. However, despite the variety of opportunities for FAP, many issues remain that present obstacles to achieving this outcome. The COST Action will address the following issues:

1. Proteomics is a high-cost research, and employs a combination of efficient separation technologies, state-of-the-art mass spectrometry and bioinformatic tools, which are frequently unavailable for farm animal research at a national level.
2. The tissues and processes studied are of specific relevance to farm animal science. For example, investigation of the milk proteome and of post-harvest changes in meat and milk have no counterpart, or only play a minor role, in studies on humans or laboratory animals.

3. The tissues under investigation might have contaminants that are normally not found on more commonly studied specimens (e.g. lipids in milk, fish samples) affecting the quality of the analysis and reproducibility of results.
4. The identification of farm animal proteins has been hampered by lack of sequenced genomes and annotated proteins but with recent publication of genomes for chicken, cattle and swine it is essential that means to exploit this new information for FAP are coordinated across Europe.
5. Post-harvest alterations to proteomes essential to the commercial processing of protein of animal origin (e.g. conversion of milk to cheese) are economically important issues of significant impact to COST countries.
6. Overall in Europe there is a lack of trained personnel with the necessary skill base and there is an uneven distribution of facilities and access to training.
7. Important knowledge on animal protein composition needs to be disseminated to industries dealing with production of farmed animals and of human food based on animals.

B.4 Complementarity with other research programmes

The Human Proteomics Organisation (HUPO) has been successfully promoting the application of proteomics to human health and disease. However, there is no equivalent organisation for FAP. Proteomics offers considerable opportunities to assess animal health during production and to monitor the quality and safety of food of animal origin. Proteomics in these areas will contribute to better and more sustainable animal production systems and will enable Europe to address contemporary agricultural and ecological issues including the criteria of the Millennium Development Goals (MDG) established by the United Nations. The farm animal research community needs to establish networks analogous to the HUPO consortium and this COST Action will initiate this process in Europe by connecting researchers at universities, institutes and industry.

The European Proteomics Association (EuPA) has recently been established linking the national proteomics societies in Europe and developing links with the Federation of European Biochemical Societies (FEBS) and the European Molecular Biology Organisation (EMBO) (http://eupa.isbsib.ch/images/stories/minutes/eupa_gc_20051205.pdf). Several members of this COST Action are active members of the EuPA holding committee appointments. However, this COST Action would be the first time that relevant scientists have grouped together to advance proteomic science and its multiple applications for the progress of farm animal science.
The COST Action closely aligns with the EU policies on Agriculture and Food to achieve the objectives of the European Technology Platform on Global Animal Health in diagnosis of disease by biomarker detection (http://www.ifahsec.org/europe/euplatform/platform.htm) and to the new Animal Health Strategy "Prevention is better than cure" of the Directorate General (DG) Health and Consumers (http://ec.europa.eu/food/animal/diseases/strategy/index_en.htm) by enhancing animal surveillance and disease diagnosis. Further, the COST Action supports the objectives of the European Technology Platform on Food for Life (http://etp.ciaa.eu) by improving food safety and quality assessments and providing crucial knowledge to ensure sustainable food production in Europe.

C. OBJECTIVES AND BENEFITS

C.1 Main/primary objectives

The main objective of the Action is to establish the Europe as the global leader in FAP by creating a dynamic network of researchers who will push forward the boundaries of proteomics in farm animal research and train scientists to apply this advanced technology to the benefit of animal science throughout Europe. This will be achieved through regular Workshops, Conferences, Training Schools and Short-Term Scientific Missions (STSM). Further main objectives are:

1: To instigate the application of proteomic science to resolve problems in farm animal production and post-harvest change by increasing the protein analysis capability of Europe.

2: To train early-stage scientists at Training Schools, by participation in STSM to leading laboratories within the COST countries and by encouragement of new research programmes on FAP within the EU Framework Programmes and in national research programmes.

3: To develop standard protocols for use in FAP to establish the best practice among the FAP community for acquisition, storage and analysis of a particular tissue or fluid irrespective of species leading to more efficient use of scarce and valuable resources.

C.2 Secondary objectives

The secondary objectives of the COST Action are:

1: Promoting the integrated use of proteomic tools in farm animal research reflecting that the technology has widespread applications for instance in animal health and welfare, genetic diversity and breeding and finally post harvest alteration of tissue proteomes.

2: Promoting integration of the output of FAP with bioinformatics to develop a systems biology approach for interpretation of experimental and field or environmental studies. A standard approach should be taken to allow the data and interpretations to be compatible within and between nations.

3: Disseminating knowledge on FAP to European industry and to the citizens of Europe in order that the public is kept abreast of technological developments and the benefits accruing from publicly funded science.

C.3 How will the objectives be achieved?

The COST Action will establish a network of European scientists, who are working in FAP and are funded by national research programmes creating a critical mass of researchers in the area. The Action will focus on collaboration, dissemination of current knowledge, mobility of researchers and training. Considerable opportunities will flow from collaborative research in FAP, advancing the scientific and technical capacity of the COST countries. The objectives of the COST Action will be achieved by holding Workshops, Conferences, Training Schools, STSM and a regularly up-dated Website in which the latest findings from the members of the Action will be highlighted.
A Kick-off Meeting will establish the current state of the art of FAP in Europe. This will be the first such gathering in Europe of leading experts in FAP. A Final Conference will allow the full achievements of the COST Action to be disseminated to researchers in Europe providing a springboard to the sustainability of the initiative.

Regular Workshops will be devoted to the scientific focus of Workgroups (WG) and will be especially important for developing and disseminating the research output from the national research programmes of the participants. The Workshops will focus on the distinct but inter-related topics for the three WG of the Action. These are in the following areas:

- Applications of FAP to issues of animal health and welfare,
- Assessment in the safety and quality of food of animal origin,
- Technological advances in proteomic methods with specific challenges for FAP.

It is important that the next generation of scientists in FAP is provided training in proteomics which will allow the proteomes of animal cells, tissues and fluids to be fully exploited by research projects undertaken in the Europe. For this purpose Training Schools will be run by the leading institutes of the Action at which basic and advanced methodologies will be taught. The aim is that this will be undertaken in collaboration with the EuPA education committee.

Short Term Scientific Missions**,** in which Action members will visit partner institutes for knowledge transfer throughout the COST countries, will stimulate interaction between institutes and develop collaborative research. This is important for the development of links between Early Stage Researchers of Europe and for FAP in less developed economies.

An open access Website will be established providing information such as protocols produced for standardisation of the technology for use in FAP, recent research outcomes, Conference and Workshop programmes. A password protected internet discussion forum for Action members to share knowledge on FAP and details of availability of placements for the STSM will also be accessible through this website.

C.4 Benefits of the Action

Benefits to the scientific community

The COST Action will benefit the scientific community by improving knowledge on animal proteomics, allowing the development of standardised proteomic tools and protocols. Information exchange and the mobility of early stage researchers going to Training Schools and STSM will be of great benefit to the scientific community. Collaborations will develop as a result of the Action leading onto future projects on farm animal science in Framework Programme 7 or beyond. The Action will ensure European investment in infrastructure for proteomic research will be more cost effective and will stimulate FAP by increasing applications to national research funds.

Benefits to the society

A major benefit to society from the Action is the potential to improve food safety and quality by establishing consistent protocols for the application of FAP in monitoring animal health and welfare and for monitoring the post-harvest processes of protein rich food. The potential use of deliverables from the COST Action in defining health for the benefit of animal welfare, for example by identification of biomarkers for health or breeding and identification of the status of post-harvest products for quality and safety assessment, will have beneficial impact on society.

Benefits to the consumers and environment

European consumers will have additional benefits to the quality and safety of the protein in the diet from farm to fork. A pre-requisite for safe food from farm animals is to ensure the health and welfare of animals on farm. The Action will develop the relevant technologies to monitor health and welfare of farm animals during production as well as standardised procedures at slaughter and during post-harvest processing. Assessment of post-harvest changes by proteomics has the potential to assess the tenderness of meat during processing and verify the species of meat to avoid adulteration with exogenous protein from non-specified origin. Production animals can be used as sentinels of environmental change and therefore FAP has a role in the early detection of environmental effects on endogenous proteins of animals.

Benefits for employment

Establishing COST countries as global leaders in the application of proteomics to farm animals will stimulate employment in the diagnostic and analytical operations of the animal production and food industries for running the necessary high throughput analytical procedures and also in the commercial production of the instruments, reagents and interrogative software for implementation of FAP for practical application. In addition, the training which will be provided by the Action will produce a cohort of highly employable scientists at the forefront of knowledge with a variety of career opportunities in academia, animal health, pharmaceutical and biotechnology industries in Europe. Companies in these sectors have demonstrated support for the proposal either as members of the group or via letters of support.

Benefits for European research

European research will benefit by agreement on a common approach to dissemination of knowledge on FAP across the COST countries. Europe will be a global leader in the field as no other comparable collaboration has been established as yet in other parts of the world. Research will benefit from the interchange of Early Stage Researchers on STSM and in their participation in Training Schools. Invitation to meetings of the leading specialists from other continents will ensure that FAP science in Europe is competitive globally.

Benefits for reaching the Millennium Developmental Goals (MDG)

The Millennium Development Goals are increase of food availability in order to reduce hunger and to eliminate problems caused by unbalanced diets, which are most frequently devoid of protein. Thus there is a confluence of aims of the MDG and this COST Action. Achieving the objectives of the COST Action on FAP will lead to better means of production and monitoring of the protein quality of food from farm animals and therefore improving the balance of food in the diet.

C.5 Target groups/end users

The immediate target groups and end users will be research institutes and university research groups undertaking studies on farm animal science and on the role and value of protein based food for human consumption. Further end users will be in the animal health, breeding and production industries supplying the human food chain with food of animal origin and those responsible for the safety and quality of such protein containing food.

D. SCIENTIFIC PROGRAMME

D.1 Scientific focus

The focus of the Action will be on the application of FAP to farm animal research and will be integrated across investigations into the health and welfare of farm animals during production and for assessment of protein alterations taking place post-harvest in food derived from farm animals in order to attain and maintain high levels of food quality and food safety in Europe. These will be supported with an additional focus on technological advances of common interest to both application areas.

The focus of WG1 will be on research relevant to animal health covering biomarkers of infectious, parasitic and metabolic diseases, and genetic phenotype detection for breeding toward production goals as well as for resistance to disease. It will be expectable to interact with and be fully integrated with investigations into other aspects of farm animal science such as reproduction, microbiology, parasitology, virology, immunology and nutrition.

The focus of WG2 will be on the fundamental and translational research fields in which proteomics can be applied to areas of food quality and food safety. The WG will develop proteomic protocols for characterization of raw materials and food products of animal origin, for example characterizing the process whereby milk is converted to cheese and to allow post-harvest product analysis for example to prevent adulteration with protein from exogenous species.

The focus of WG3 will be on the technical aspects of animal proteomics, from sample collection/preparation (including possible pre-treatment or pre-fractionation) to protein separation, identification, and quantification in production animal body fluids and tissues. It will compile knowledge from the COST Action members to develop generally applicable protocols for different types of specimens, offer technical support to the other WGs and highlight technological advances within the field of FAP.
The work plans of these WGs will be flexible to allow for inclusion of unanticipated developments in proteomic technology or unforeseen applications to farm animal research.

D.2 Scientific work plan methods and means

Working Group 1: Proteomics and Animal Health

WG1 will cover major aspects of animal health related issues from a proteomics perspective. Understanding the mechanisms by which animals respond to diseases and parasites and in some cases are able to resist or tolerate such processes is of central importance to the development of novel means of pathogen control.
Due to the major technological advances of the recent years proteomics has become an essential methodology in many fields of health related research with a broad range of applications from physiology to oncology and has become integral to human health studies for 10-15 years. In farm animal health research proteomics is still of limited but growing use. WG1 will lead application to animal health studies by developing the use of FAP for the major production animals: cattle, swine, chicken and farmed fish.
In the study of diseases or the effects of infections and the analysis of responses to biotic stress factors, the identification of involved metabolic pathways can be deduced from the function of the affected proteins. In molecular quantitative genetics, proteomics can be used to map translated genes and loci controlling their expression, which can be used to identify proteins accounting for the variation of complex phenotypic traits. Linking gene expression to cell metabolism on one hand and to genetic maps on the other, proteomics is therefore a central tool for functional genomics.

Domestic animal proteomics should, as a consequence, culminate in knowledge and tools or assays that can be practically applied in diverse research fields with direct impact on animal disease in its various components. Proteomics is therefore essential to the development of sustainable and rational animal production systems in an internationally competitive agricultural context, aiming to minimize health issues and risks with potential trans-boundary repercussions.
The following tasks have been identified for WG1.

Task 1 Proteomics of infectious diseases in farm animals

In this task WG1 will liaise between groups using FAP for investigation of infectious diseases which are a major concern of farm animal research and will be a key focus of the WG. Many pathophysiological processes are involved in different phases of animal-pathogen interactions in the major domestic species and the investigation of these will be enhanced by FAP.
The members of WG1 will aim to understand biochemical consequences at cellular and tissue level of events induced by infections, as well as the immune responses mounted by farm animals and their consequences on animal products, specifically meat, milk and eggs and some derivatives.
The attention will be focussed on the whole range of infectious agents, using an integrative approach with different disciplines including bacteriology, virology, parasitology or mycology. In this background, parasitic disease vector proteomes in their varied forms, particularly insects and ticks, will be also determined.
Due the complexity and the extreme variety (and variability) of these biological specimens, the work on characterization of proteomes of specific body fluids with potential importance to transmission or diagnosis of disease such as blood/serum, semen, urine, saliva, milk, etc, will be coordinated in joint workshops with WG 3.
The understanding of processes listed above together with mechanisms involved in tolerance to agents of disease or the consequences of infection would open interesting perspectives for animal scientists towards a sustainable low veterinary input in animal production (e.g. limitation of the use of antibiotics), infectious disease control and limitation of their nefarious consequences.

Task 2 Proteomics in animal production

Task 2 will coordinate advances in the use of FAP in the investigation of efficient production of livestock developing, validating and standardising proteomic approaches which will be fully integrated with other animal sciences, including reproduction, nutrition, husbandry and breeding in order to ensure food security in Europe.

Animal production systems have a tendency to develop certain characteristic pathologies related to metabolic and/or environmental conditions such as atrophies or fragilities induced by specific nutritional stresses and deficiencies (e.g. hypocalcaemia in high-production dairy cows) or as a result of selection by breeding (muscle hypertrophy in ruminants or turkeys). This aspect is of particular relevance in high intensive production systems namely poultry, dairy, pork and aquaculture sectors. Proteome studies at this level are still extremely limited. However, this is a very sensitive issue due to its obvious implications on animal health and welfare and the limitations imposed by legislation in the European Union regarding production, handling, transport and processing of farm animals. FAP will for instance contribute to the definition of markers of stress, for optimal growth rates and for phenotyping of desirable/undesirable traits.

The importance and commonality across Europe of the issues of WG1 indicate that proteomic scientists working in farm animal related topics would benefit immensely from interacting in a functional network such as the one arising from the approval of this COST Action.

Objectives of WG1

- To coordinate the application of proteomics to farm animal science,
- To integrate proteomics with farm animal investigations in physiology, biochemistry, genomics, microbiology, virology, mycology, parasitology and immunology in health issues in farm animals,
- To exchange experience in experimental design and data analysis in specific and aimed joint workshops with WG2 and WG3 to take advantage of the respective achievement and avoid duplication of efforts,
- To establish an efficient network of scientists working in the field of proteomics applied to health and production of farm animals,

- To communicate and disseminate knowledge of proteomic applications in health related issues in farm animals especially to early stage researchers, in an international forum,
- To establish beneficial interaction between proteomic research with commercial partners in the animal health industry,
- To exploit the techniques already available in basic science-oriented proteomics to develop more specific tools for applications in animal health.

Working Group 2: Proteomics of food of animal origin

WG2 will focus on the application of proteomics to food of animal origin and the transformations that take place during processing. This occurs for instance as muscle turns to meat or milk turns to cheese. In this context FAP is important for the characterization of protein/enzymes involved in metabolic pathways or structural proteins influencing product quality.
Despite the fact that proteomics has had a major importance in the study of human medicine over the last decade in relation to animal and food sciences its input, with few exceptions, has been extremely limited, mainly due to the lack of access of animal and food scientists to proteomics and mass spectrometry methodologies and equipment. Research on this subject is of extreme importance to all involved in downstream processes from production (particularly food industry), its regulators, and ultimately the consumer. It is therefore of utmost importance, particularly in the context of animal science applied to food technology, to enhance access of animal scientists to these methodologies and equipment and to promote the exchange of experiences between them.
In this WG particular relevance will be given to muscle tissues from all domestic species, with particular emphasis on cattle, swine, poultry and farmed fish. Dairy products will also be of major concern of researchers involved. Despite the major focus on these specific areas, all aspects of animal science and food of animal origin will also be considered. In all the above-mentioned contexts, particular attention will be devoted to regional traditional products and production systems. The heightened importance of food security, quality, traceability and safety means that this WG is an essential and integrated part of the whole COST Action.

The scientific activities of WG2 are divided in the following tasks:

Task 1 Proteome analysis of food of animal origin at harvest

Variation in product quality is related to variations in raw material composition at harvest which can have a significant effect on maintaining high quality products during storage and distribution. Knowledge of the factors affecting raw material qualities and the optimisation of their utilisation are increasingly important to ensure a sustainable production of meat, milk and other products of animal origin. The WG will focus on coordinating investigation into monitoring the changes that take place on harvest of food of animal origin. It will also provide the basis for more cost-effective and competitive production and added value to the producers and will potentially have beneficial effects on the environment by maximising the efficient use of resources.

Task 2 Proteome changes in food of animal origin during processing

Different processing conditions, e.g. during long-term ripening of dry-cured hams and cheese, affect the end-product properties, with special reference to those related to quality. Changes in protein degradation are one of the most important factors that affect such quality and a better understanding of such processes by FAP will contribute to better production systems and less product heterogeneity. This aspect will be of particular relevance to specific European traditional and local products with a market differentiation (local cured ham or cheeses for instance).
This task will also aim to contribute to the use of proteomics in food safety issues, namely at the level of the contamination of animal products with microorganisms or toxins (in coordination with WG1). The detection of illicit growth promoters such as steroids or antibiotics in the fattening of animals which may alter muscle and liver proteomes, will also be very important. Finally, particular attention will be given to the changes in the proteome of food of animal origin as a consequence of the development of value-added functional foods.

Objectives of WG2

- To establish the role(s) of proteomics to provide the most specific and sensitive means of monitoring protein in food of animal origin,
- To integrate proteomics with investigations on food composition, quality, preservation, safety, traceability, adulteration and processing technology,
- To generate and communicate fundamental knowledge on proteins in food and their relation to food composition,
- To establish beneficial communication between proteomics scientists researching on post-harvest alteration in protein towards the identification of common needs and opportunities for future collaborations,
- To establish an efficient network of scientists working in the field of proteomics applied to post-harvest analysis of food from animals allowing coordination for efficient use of resources,
- To exchange experience in experimental protocols, design and data analysis with WG1 and WG3 to avoiding duplication of efforts,
- To establish a beneficial interaction between proteomic research with commercial partners in the food and food processing industries and with public regulators and food safety agencies within the European Union, to the benefit of competitive European agriculture and food sectors, and ultimately the European consumer.

Working Group 3: Advancing Methodology for Farm Animal Proteomics

Proteomic approaches require a combination of efficient and stringent separation technologies, high-resolution mass spectrometry and powerful bioinformatic tools to characterise a broad range of proteins in body fluids and tissues of farm animals. Technical aspects of FAP covered by this WG will deal with the relevant tissues and body fluids of the major farm species included in this Action (cattle, swine, chicken and farmed fish). The scientific outcomes of WG3 will be especially valuable for application in farm animal research in WG1 and WG2 providing direction on state-of-the-art proteomic technologies. There will be constant interaction with WG1 and WG2 to ensure close coordination of the focus of the Action and effective dissemination of knowledge.

Task 1: Sample Handling

This task will establish standard protocols for handling samples used in FAP experiments (e.g. blood, muscle, milk) as sample collection, storage and extraction are known as critical steps for protein analysis. Standardised protocols for these pre-analytical factors will be established by the Action in order to achieve a consistent quality of samples and produce valid and reproducible data sets. Animal body fluids and tissues are of highly complex protein composition, containing proteins that may differ considerably in solubility, physicochemical properties and abundance; in addition, they may contain large amounts of components that strongly interfere with protein separation e.g. lipids. Common preparation and extraction procedures need to be developed for a given sample type.

Task 2: Separation and Identification Technology for Farm Animal Proteomics

The extensive dynamic range of protein concentrations in the body fluids and tissues of farm animals presents problems for analysis. In these samples there is typically overrepresentation of a few proteins (there are 6-10 orders of magnitude in concentration between highest and lowest abundant reported protein). To reduce the complexity and allow study of proteins of lower abundance, different depletion strategies or pre-fractionation methods will be compared and best practice recommended for different sample types. Emphasis will be put on evaluation and implementation of new techniques.

A variety of instrument platforms are presently used for mass spectrometric protein identification by the Action members, ranging to those for analysis of intact proteins, for peptide mass fingerprinting (PMF) or for *de novo* sequencing strategies. Action members will share methodology to accurately determine the identity of animal proteins, including also liquid chromatography tandem mass spectrometry, ‘shotgun proteomics’ and multidimensional protein separation / identification technologies. Implementation of the use of new knowledge on farm animal genomes to FAP will be a critical function of this COST Action.

Task 3: Protein Quantification and Bioinformatics

For comparative proteomic studies it is imperative that the concentration of individual proteins can be defined on a global scale. Application of new gel-based methods such as difference gel electrophoresis (DIGE) helps minimizing variation between samples, allowing relative levels of proteins (e.g. comparison of differing cellular states) to be quantified with greater precision. There are also recent advances in mass spectrometric-based approaches to develop label-free strategies for the absolute quantification of proteins. Best options for FAP will be reviewed and disseminated to the members of the Action.

Application of bioinformatics will include evaluation and review of the databases used in the identification of proteins for FAP and the value of cross-species matching in animal proteomics investigations. The focus will be on experimental schemes both of species whose genomes are sequenced or very well described (chicken, swine or cattle) or other less-studied species (farmed fish). The evaluation and interpretation of the quantitative proteomic data using bioinformatic schema analysis will also be under constant review. This task will include standardisation of methods to deal with biological variability and the multiple testing problems where large numbers of variables (i.e. proteins/peptides) give rise to high numbers of potentially false positives; it will also help to determine the best means to calculate false discovery rates in FAP.

Task 4: Advanced Proteomics: Post-Translational Modifications (PTM) and Protein Complexes

Post-translational modifications (PTMs) such as phosphorylation, glycosylation and ubiquitination, can regulate protein functions, determining their activity state, cellular location and dynamic interactions with other proteins. The analytical methodologies used to characterize PTMs of relevance to FAP will be reviewed and optimal protocols developed. Most physiological processes are carried out by the interaction of several proteins in the form of protein complexes. These interactions can not be studied by classical proteomics methods, but need other approaches, e.g. affinity methods or non-denaturing/non-reducing separation systems. Task 4 will identify whether these methods need modification for species-specific applications.

Objectives of WG3:

- To collaborate and coordinate with the other two WGs providing them with essential methodology and aiming to contribute to the standardisation and general use of proteomic tools in the widest context of animal sciences,
- To develop efficient and reliable protocols for extraction, separation and detection of proteins from a wide variety of tissues, organs, fluids and post-harvest products of farm animal origin,
- To refine strategies for protein identification in species whose genomes were not extensively sequenced or studied,
- To develop the technology to rapidly characterise PTMs and isoforms in samples relevant to farm animal science,
- To establish optimal methods for investigation of protein-protein interaction and of protein complexes in relevant samples,
- To evaluate pre-fractionation methods for the use in FAP for easier analysis of proteins of lower abundance,
- To establish databases: collect and distribute useful information on a) commercial antibodies, b) consumables (e.g. for sample pre-fractionation), c) animal protein/proteomics literature,
- To establish a forum/platform for troubleshooting and rapid exchange of technical know-how among different members.

E. ORGANISATION

E.1 Coordination and organisation

Coordination of the COST Action will be undertaken by a Management Committee (MC) which will be presided over by a Chair and Vice-Chair. To implement the programme of the Action, three Working Groups (WGs) will be established; WG1: Proteomics and Animal Health; WG2: Proteomics of Food of Animal Origin; WG3: Advancing Methodology for Farm Animal Proteomics The responsibilities of the MC will be to:

- Appoint at the first meeting the Chair, Vice-Chair(s) and WG Coordinators;
- Coordinate and plan the MC meetings, WG Workshops, Conferences, Training Schools and STSM;
- Review and assess the activities of the Action (Workshops, STSM, publications, Training Schools, etc.);
- Receive and review the reports made by the WGs to ensure their respective objectives are met;
- Ensure that collaboration and exchange of knowledge between the WGs is maintained;
- Promote, approve and review STSM according to the recommendations of an established ad-hoc committee;
- Establish and monitor training schools in FAP;
- Establish and update a FAP website for communication between partners and for dissemination of knowledge on FAP to the external community;
- Stimulate the creation of Europe wide collaborative research projects related to FAP;
- Prepare annual reports;
- Coordinate Intellectual Property matters in relation to exploitation and dissemination of project results;
- Maintain contacts and run common workshops on areas of synergistic overlap with concurrent COST Actions and other research bodies such as European Science Foundation, EUREKA or the EU Framework Programmes.

After formation at the Kick-Off Meeting the MC will meet twice in the first year in order to ensure the successful start of the Action and once a year thereafter. With the large size of the Action it is considered that more frequent meetings in years 2-4 would dissipate resources which could be used for training and for STSM and would not allow sufficient time between meetings to yield additional achievements for reporting at each meeting. Effective communication will be maintained between meetings among the MC and WG members by use of modern electronic communication.
The MC meetings will be linked to WG workshops in order to ensure efficient coordination of the activities and discussion about the objectives and critical points of the programme.

The COST Action aims to include experts representing the range of knowledge that currently exists in Europe. The experts include a) those who are world leading authorities on general aspects of proteomics, b) those whose main focus is in animal sciences but who have used advanced proteomic methods in their research and who are therefore aware of the particular problems in FAP, and c) those who desire to use proteomics in their animal science research but who have so far been deterred by lack of resource, expertise or access to proteomic facilities. In combination, the members have the necessary expertise and motivation to achieve the aims of the Action and will use their ability for the benefit of FAP to European research. Furthermore, members of this Action are or have been Management Committee members in other COST Actions and/or have experience in management of EU projects. This experience will be at the disposal of the Action and will be essential for its successful management.

In addition to the Working Groups (see E.2 below) the Action will undertake the following initiatives:

Short-Term Scientific Missions will be established in which researchers will be able to travel and visit other institutes in the Action with the objective of exchanging knowledge and expertise in FAP and with the further aim of developing collaborations between partners. An ad-hoc committee will be formed with a coordinator and one representative of each Working Group (WG) to evaluate proposals of these missions and to review their outcome. The mobility and training of early stage researchers with a balance of genders will be particularly encouraged, with an emphasis on less developed COST countries.

Training Schools will be organised by the COST Action on an annual basis. The Training School will provide a high-level course in the theoretical and practical aspects of proteomics, including sample preparation, separation strategy, mass spectrometric analysis and bioinformatics and will have a particular emphasis on application to samples encountered in FAP. With the great expertise in FAP available through the members of the COST Action this training initiative will be of great value in development of the next generation of research leaders in this field. The participation of early stage researchers (PhD students and Post Docs) will be particularly encouraged. Gender balance will be a major aim of the school which will not be restricted to the COST Action members but will be available to farm animal scientists in Europe. The training course will be organised by members of the Action in collaboration with the MC and will liaise with educational and training events being organised by the EuPA with which there are already close links.

E.2 Working Groups

The WGs will be managed by WG coordinators and WG committees who will undertake to meet the objectives of the WGs by:

- Participating in appropriate sessions of the MC;
- Reporting progress of the WG to the COST Action Chair and MC;
- Planning and coordinating the scientific meetings and other activities of their WG;
- Encouraging WG members to prepare common publications including reviews and educational material;
- Establishing joint research programmes within and between WGs.

Meetings of the WGs will take place twice in the first year to establish the framework for actions being taken and thereafter once per year to allow additional activity to be reported on each occasion. The workshops will be hosted by different Action partners in different countries and will have an agenda designed to encourage interchange of ideas and expertise, develop collaborative research and to address problems of concern to the WG. A general meeting with the MC will coincide with the specific meeting of WG1 in the first year (month 3), with the second workshop in the first year of WG2 (month 11), with the workshop of WG3 in the second year, with the meeting of WG1 in the third year, and with WG2 in the fourth year. This will allow for extensive interchange between all members of this COST Action and ensure a high level of attendance and integration within the Action.

E.3 Liaison and interaction with other research programmes

The COST Action will establish efficient interaction with already existing COST Actions in this domain to bring benefits to all parties. These include FA0603 | Plant Proteomics in Europe (EUPP); FA0805 | Goat-parasite interactions: from knowledge to control (CAPARA); FA0601 | Fish Reproduction and Fisheries; 861 | European Network for Pig Genomics; BM0702 | Urine and Kidney Proteomics. There will be scope to expand the network and establish new collaborations across many disciplines in order to address key challenges within the field of proteomics. When possible, WG meetings will be organised to coincide with meetings of other COST Actions with similar or complementary interests.

E.4 Gender balance and involvement of early-stage researchers

This COST Action will respect an appropriate gender balance in all its activities and the Management Committee will place this as a standard item on all its MC agendas. The Action will also be committed to considerably involve Early Stage Researchers (ESRs). This item will also be placed as a standard item on all MC agendas. The WGs will also assure that such a general rule will be applied in all activity planning and implementation.
It is worth emphasizing that ESRs of both genders from several countries have already played a major role in the conception and delineation of the objectives of this Action. It is therefore expected that ESRs of both genders will also play leading roles in the Management of the Action. As described above, gender balance will be observed in the Workshops, Teaching Activities and STSM where also ESRs are expected to form the overwhelming majority of participants.

F. TIMETABLE

- The duration of this proposed COST Action is 4 years.
- A Kick-off Meeting will initiate the Action when the Chair, Vice-Chair and WG coordinators will be selected and responsibilities such as Training coordinator and STSM coordinator assigned.
- Two plenary MC Meetings will be held in year 1 (months 3 and 11) and thereafter will be held once per year (months 23, 35 and 47) with Annual Reports submitted in months 12, 24, 36 and 48 and will be linked to WG workshops.
- Each WG will hold 2 workshops in year 1 (months 3 and 11) and thereafter one per year (months 23, 35 and 47). The three WG workshops will overlap allowing Action members to attend a mix of events.
- An EuFAP homepage will be created on the web soon after the kick-off meeting and will be updated regularly (at least 4 times per year).
- Training Schools combining the expertise of the three WGs will be organised every year.
- Short-Term Scientific Missions can be requested after the first WG meeting.

- Inter-COST Meetings will be with other ongoing COST Actions allowing for the cross-fertilisation of outputs and ideas.
- A Final Conference will be held at the end of the Action where all the partners involved will present their results. It will be arranged to maximise the dissemination of the accumulated knowledge of the Action.

Table 1. Timetable

	Year 1				**Year 2**				**Year 3**				**Year 4**			
Coordination	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**
Kick-off meeting	**x**															
Homepage	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**
Reporting				**x**				**x**				**x**				**x**
MC meeting	**x**			**x**				**x**				**x**				**x**
WG1 meeting	**x**			**x**				**x**				**x**				**x**
WG2 meeting	**x**			**x**				**x**				**x**				**x**
WG3 meeting	**x**			**x**				**x**				**x**				**x**
Inter-Cost*																
Training Schools			**x**				**x**				**x**				**x**	
STSM		**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**	**x**
Final Conference																**x**

- MC meeting: Management Committee meeting
- WG meeting: Working Group meeting/workshop
- STSM: Short-Term Scientific Missions to be initiated after the first MC and WG meetings
- *Inter-Cost: Timing of the Inter-COST Workshops will be defined in agreement with the Management Committee of that specific Action.

G. ECONOMIC DIMENSION

The following COST countries have actively participated in the preparation of the Action or otherwise indicated their interest: Austria, Belgium, Bulgaria, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Israel, Italy, Luxembourg, Netherlands, Norway, Poland, Portugal, Slovakia, Slovenia, Spain, Sweden, Switzerland, Turkey, United Kingdom. On the basis of national estimates, the economic dimension of the activities to be carried out under the Action has been estimated at 112 Million € for the total duration of the Action. This estimate is valid under the assumption that all the countries mentioned above but no other countries will participate in the Action. Any departure from this will change the total cost accordingly.

H. DISSEMINATION PLAN

H.1 Who?

The findings and results of the COST Action will be disseminated to the varied target groups including other researchers in the field; other research frameworks; research and agricultural institutes and universities; animal health, food and biotechnology (proteomic) industry; European level policy makers in the DG for Agriculture & Rural Development, DG for Research and DG for Health and Consumers of the European Commission; Government policy makers in Departments of Agriculture and Departments of Industry or Commerce; Region and City planners and policy makers; and not least the general public.

H.2 What?

The results of the COST Action will be disseminated to the target groups by:

- Press releases
- Public access website
- Internet discussion forum (password protected)
- Research publications
- Non-technical publications

- Workshops and conferences of the Action
- Conferences of associated learned societies
- Short-Term Scientific Missions
- Teaching activities

H.3 How?

Press releases

The activity of the COST Action will be drawn to the attention of the scientific community, governments, policy makers and the citizens of Europe by production of a press release at the commencement of the Action at the Kick-off Meeting and at the Final Conference. These will be released in all the countries taking part in the Action.

Public Access Website

A public access Website will be established in order to provide a portal to the mass of information generated by the Action for access by the international scientific community. The Website will also facilitate communication between the partners and WGs of this project. This Website will be established and maintained by one designated partner in this Action to be agreed at the Kick-off Meeting. The Website will contain general information about COST and this COST Action on FAP and its WGs (e.g. workshops, meetings); publications; contact details of Action members; details of courses including on-line content and other teaching material; calls for STSM; reports of workshops and meetings; links to other COST Actions and proteomic websites; job and fellowship availability.

Internet Discussion Forum

In association with the website a password protected discussion forum will be established for communication of information within the members of the Action. This will be extremely valuable for the circulation of technical details to enable comparable proteomic investigations to be undertaken by Action members.

Research Publications

1. The scientific results of the project will be published in refereed scientific journals where intellectual property is not jeopardised and with co-publications being encouraged.
2. Review articles, book chapters and trade journal articles will also be encouraged in order to disseminate results to a broader, less specialized public.
3. Standard Protocols and Technical guidelines will be produced to stimulate a generic approach to FAP allowing greater compatibility of research in the area.
4. It is anticipated that at least one scientific book giving overviews of the most important results of the Action will be generated during the Action with the MC taking the lead in this initiative.

Non-technical publications

The COST Action activities will be highlighted in non-technical and trade journals such as those that circulate in the agricultural, veterinary and biotechnology space to provide information to farmers, veterinarians and related professions.

Workshops and conferences of the Action

The Action will run open sessions at Kick-off Meeting and Final Conference and the WG workshops to inform interested scientists, regulatory bodies and policy makers about the results of the project and about new technologies developed throughout the project. These sessions will provide theoretical as well as practical opportunities and will be organised in different geographic regions to allow participants from across Europe to gain access to the leading European expertise in FAP. Efforts will be made to have the proceedings of the conferences published in special issues of proteomics and/or farm animal related international peer-reviewed journals. Members of the Action are either on editorial boards of such journals or have contact with the editorial boards.

Conferences of associated learned societies

The COST Action will send delegates to international and national conferences on proteomics and on farm animal science, such as the European Federation of Animal Sciences, European Society of Veterinary Clinical Pathology and the European Proteomic Association, in order to disseminate the knowledge and data resulting from the COST Action activities. Action members attending such conferences will promote the novel technology and know-how generated by the Action and will make efforts to organise satellite symposia to such conferences. This will promote the increase in the knowledge base in COST countries achieved by the activity of the COST Action and will further lead to increased international collaboration in which the Europe can be the driving force.

Short-Term Scientific Missions

Short-Term Scientific Missions will allow dissemination of accumulated knowledge of FAP to early-stage as well as senior scientists acquiring knowledge of proteomics for the first time. Thus the STSM will facilitate technology and knowledge transfer within the Action by stimulating the shared use of proteomic equipment and farm animal research facilities, thus increasing the opportunity for synergy between expert and early-stage researchers in both areas.

Teaching activities

The COST Action will generate substantial knowledge and material which can be used for teaching activities in Universities at undergraduate and post-graduate level. ESRs and bio-engineers in COST countries will have the opportunity during their educational experiences to become fully acquainted with the state-of-the-art technology for the application of proteomics to farm animal science. It is expected that the dissemination of the results of this Action will result in changes in the practice of proteomic research in Europe. It is important to note that the dissemination plan will be updated during the course of the Action taking into account the progress of the Action as well as the results of its evaluation. The research published in the field during the final years of this COST Action and application of guidelines produced in this research will allow evaluation and determination of how successful this Action will have been in realizing dissemination of the results in the field.