European Cooperation in the field of Scientific and Technical Research - COST -

Secretariat

Brussels, 29 June 2004

COST 296/04

DRAFT MEMORANDUM OF UNDERSTANDING

Subject : Draft Memorandum of Understanding for the implementation of a European concerted research Action designated as COST 861 “European Network for Pig Genomics”

Attached is the abovementioned Memorandum of Understanding.

DRAFT

MEMORANDUM OF UNDERSTANDING

FOR THE IMPLEMENTATION OF A EUROPEAN CONCERTED RESEARCH ACTION

DESIGNATED AS

COST 861

"EUROPEAN NETWORK FOR PIG GENOMICS"

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 400/01 "Rules and Procedures for Implementing COST Actions", the contents of which the Signatories are fully aware of.

2. The main objective of the Action is to increase the knowledge of the organisation, expression and regulation of the genes involved in pig development, health, reproduction, and product quality.

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 € 13 million in 2003 prices.

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

5. The Memorandum of Understanding will remain in force for a period of 5 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.

COST 861

'EUROPEAN NETWORK FOR PIG GENOMICS'

(PigNet)

A. BACKGROUND

Pork represents about 40% of the world meat production and Europe accounts for about 16% of the world pork production. There is an increasing need to improve overall pig husbandry in terms of health, welfare, sustainability, as well as product quality and safety including traceability. Such improvements require continuous progress in animal science domains such as genetics, physiology, nutrition and pathology. A genomics approach, which is systematic and global, without *a priori* hypothesis, offers an opportunity to meet this requirement by allowing detailed investigation and understanding in these domains. With requirements for access to expensive equipment for high throughput analysis and for investment in sample and data management and analysis, the genomics approach requires investment on a scale that is not achievable by a single organisation. Thus, no research group has all the necessary competences and there is a need for establishing collaborations between the research groups already working in the field. Such integration will give access to genomics and related technologies for European breeders, allowing them to remain competitive at the world level and to determine and develop the most appropriate genetic composition of European pigs for continued success.

1. Pig breeding challenges

Genetic improvement of pigs should meet the requirements of both breeders and consumers. A number of goals can be identified such as improving meat quality and safety, traceability as well as animal health and welfare that can be expressed in terms of breeding objectives: growth and development, infection and immunity, reproduction.

From the consumer's point of view, quality and safety are the main objectives:

- Quality means good nutritional properties and eating quality (taste, flavour, tenderness, colour, drip loss…). For example, increasing intramuscular fat could satisfy consumer demands for some aspects of quality, including taste and tenderness.

- Safety means no contamination with either chemicals (e.g. drug or antibiotics residues) or biologicals, especially zoonotic pathogens. Modification of breeding practices may be required in order to address these concerns. For example, breeding objectives may need to be modified to generate pigs that are productive in animal welfare friendly production systems with minimal chemical intervention. In order to provide consumers with assurances about quality and safety from 'farm to fork' traceability is a key requirement. Molecular (DNA) markers developed within the genome projects provide effective tools for validating traceability schemes.

- Through their purchasing choices consumers can express their views about issues that concern them as citizens, e.g. environmental and animal welfare issues. Recent results from pig genome research projects have provided foundations on which a solution to one welfare problem could be built. The meat from a proportion of male pigs suffers from an unpleasant aroma and taste known as boar taint. In order to reduce the risk of producing tainted meat most male pigs in Europe are castrated. With some further investment in research it should be possible to develop a genetic test to identify pigs with the greatest risk of producing taint meat and thus eliminate the need for castration as the solution.

The challenge for animal breeders is to produce pigs with the optimal genotype to address these concerns. The breeding goals need to combine aspects of sustainable production (animal welfare, environmental protection), pork quality (animal health, meat quality traits) as described above, as well as efficiency of pork production (growth rate, carcass trait, reproduction). Over the last half-century pig breeders have been remarkably successful at harnessing the power of genetics to improve efficiency of production with increased growth rates, reduced fat levels. Whilst genetic merit for these traits can continue to be optimised through traditional selective breeding to meet the demands of both producers and consumers, the traits of greatest current concern – product quality, animal health and welfare – are less tractable to classical selective breeding. Thus, we need

approaches to disentangle the factors contributing to these difficult traits, at the genetic level but also in terms of interaction with other production factors such as feeding and housing of animals and processing of the carcasses and fabrication of products.

Pig exhibit considerable phenotypic diversity resulting from genetic variability with more than 100 different breeds in the world, plus experimental or commercial genetic crosses. Increased understanding of this genetic diversity on a genome-scale and the identification of quantitative trait loci (QTL) and major genes has the potential to underpin solutions and applications for the issues summarised above.

In addition to its importance in an agricultural context the pig is also a valuable experimental model in the realm of biomedicine. The pig is close to human in terms of physiology (nutritional needs, renal and digestive tract anatomy, etc), biochemistry (drug metabolism, etc), pathology (cardiovascular: hypertension, atherosclerosis: metabolic disease: obesity, insulin resistance; tumour: melanoma, etc) and genome (size, complexity and organisation). Thus, the pig is used as an experimental model for human studies including preclinical testing and it may also be considered as a source of cells or tissues for bioartificial devices or possibly a potential solution for organ and tissue transplantation. Moreover, as many of the traits of interest to the pig industry are also of interest in a human pathology context – adiposity/obesity, food intake/appetite, growth, reproduction – an understanding of the genetic control of these traits in pigs has the potential for spin-offs in medicine.

Besides their biological analysis, these challenges also raise societal questions (*e.g.* breeding practices) as well as ethical questions (*e.g.* tissue transplantation) that should be addressed.

Understanding the mechanisms involved in each trait requires specific analysis and analytical tools to evaluate the various phenotypes and their modification or variation, addressing various levels from the whole animal to organs, tissues, cells, molecules (genes). At the gene level, the analyses and tools to be used are generic and applicable to all traits. In the genomic approach, a large number of genes can be investigated simultaneously, rather than only a few as in classical molecular biology studies, and such analyses have considerable power for integration. A benefit of this integration is the possibility to analyse various level of interactions, between functions such as reproduction and nutrition, or between animal and their environment.

Improved understanding of the pig genome – both structural and functional – will provide the means to dissect the genetic architecture of complex traits such as product quality and animal health and the tools for genetic improvement, for example, through marker assisted selection. There have already been some notable successes in pig genome research that demonstrate this potential.

To take muscle growth as an example, an important contribution has recently been made by an efficient collaboration between several European groups that contribute to PigNet (Van Laere et al. 2003). They detected the causative mutation that underlies a QTL (Quantitative Trait Loci) with a major effect on muscle mass (15-30 % of the variation) and back fat thickness (10-20 % of the variation). There are no associated deleterious effects of the mutation on birth weight, growth or meat quality. The causative mutation is a G to A change in a novel regulatory domain in the IGF2 gene. This SNP (Single Nucleotide Polymorphism) can be tested in the boars from different breeding programmes in order to perform Marker Assisted Selection (MAS) for lean meat (3 – 4 % more meat). This discovery results from both structural data (QTL determination and fine mapping: positional cloning) and functional data (role of IGF2 in muscle growth: candidate gene) illustrating the added value of combining both approaches. However, the effort of fine mapping and positional cloning is still so expensive that industry is not able to carry this out without considerable external help. Moreover, the breeding programmes will also need some adaptation to the specific needs of MAS and implementation of genomics knowledge might also change the indexes used for estimation of breeding value.

Another recent example is the identification of the RN gene involved in meat quality (Milan et al. 2000) that also resulted in selection of animals by typing at the RN locus. Besides these clear-cut examples, still on the genetic side, we have to imagine and practice the use of functional genomics data for breeding improvement, in order to address the environmental components of the phenotypic variability. This is clearly a new research area.

2. Pig genomics

Genome research addresses both the structure of the genome and the function of the genes. The structure of the genome includes both mapping and sequencing. Functional genomics addresses expression of the genes (transcriptome, proteome) and the function of the proteins. Genomics and

so-called post-genomics technologies allow the investigation of the successive levels of expression in the pathway from genotype to phenotype, which are transcription, translation and post-translational modifications. As these powerful tools and technologies are generic, they can be used whatever phenotype is under investigation. We should take advantage of the technical progresses already achieved as well as the large wealth of data accumulated for other species, particularly human and mouse.

1) Structure of the genome

European groups, mainly in the frame of FP4 with the PiGMaP and GenetPig projects have made major contributions to mapping the pig genome. Radiation hybrid panels, which are specific mapping tools, have been developed in Europe and used worldwide, including USA. Around 6,000 markers, including about 3,500 genes have been localised on pig chromosomes using the IMpRH panel. The challenge is now the identification of sequence variations at the single base level, the so-called SNPs (Single Nucleotide Polymorphisms). Such identification requires sequencing of the same segment of DNA in different individuals and comparison of the sequences. These polymorphic markers are used for both identification of the genes responsible for specific traits and genotyping of individuals.

For genome sequencing, the whole genomic sequence and the expressed sequences are complementary approaches that are in progress in pig as in other species.

Expressed sequences are mainly obtained through single pass sequencing of the ends of cDNA, to yield Expressed Sequence Tags (or ESTs). EST sequencing is a high throughput and very efficient strategy for generating information on the coding parts of the genome. For example, in the 26th March 2004 release of dbEST, the specific database for ESTs, there were 5,484,642 human ESTs, 4,088,831 mouse ESTs, but only 272,188 pig ESTs. Further EST sequence data are required to provide comprehensive coverage of the pig transcriptome. A significant jump will be achieved when the Sino-Danish Pig Genome Consortium release their 1,000,000 EST sequences into the public domain.

Completed or draft genome sequences have been completed or are in progress for the human, mouse, rat, dog, bovine and chicken genomes. The efforts of the Sino-Danish Pig Genome Consortium will provide 0.5-1x coverage of the pig genome with a whole genome shotgun strategy. Although 3,000,000 reads (equivalent to about 0.5x) have been generated, 5 to 6x coverage is required to establish a draft sequence of the pig genome. To the best of our knowledge, this is the only pig genome sequencing programme in the world. Complementary data should come from other approaches, which are physical mapping (BAC), BACs ends sequencing and sequencing of a set of BACs with minimal overlap. Several European groups have launched such BAC programmes.

2) Functional genomics

Whilst the number of protein coding genes present in a mammalian genome may be as few as 25-30,000 the transcriptome (the complement of all transcripts) is more complex with more than one transcript for many genes as a result, for example, of alternative splicing. Genomic tools for transcriptome analysis include sequencing and hybridisation strategies. Sequencing strategies are based on either a subset of differentially expressed transcripts (HSS) or design of small tags (10 bases) specific for each transcript (SAGE). The most popular are hybridisation strategies known as "DNA chips"; they are based on macro and micro arrays that allow the expression levels of hundreds or thousands of genes to be assayed simultaneously. Various formats and designs are available in terms of support (nylon, glass), probes (cDNA, oligonucleotides), target labelling (radioactive, fluorescent) and range (pan genomic, specialised). There are also commercial products, but few are dedicated to farm animals; their use in cross-hybridization experiments can be investigated. Macro- or microarray analysis require a high level of skill, and there is a need for standardization of both the tools and the procedures in order to have i) a effective exploitation of these powerful tools by research groups throughout Europe, ii) the possibility to compare data obtained on different platforms. Several European groups have already started to develop such tools.

The proteome is much more complex than the transcriptome, because of sequence variation and alternative splicing as well as of post translational modifications (maturation, phosphorylation, glycosylation, farnesylation, etc). These variations and modifications play crucial roles in the regulation and function of the proteins and can only be observed at the protein level. Proteomics is thus an important complement to transcriptomics. An additional level of complexity relates to protein interactions as nearly all proteins are part of molecular structures or partnerships. For analysis, purification protocols have to take into account the sub-cellular localisation of the proteins and their wide range of concentration (1 to 10^9). These characteristics preclude global analysis of all cellular proteins at one time. In order to characterise structure, function and interaction of proteins and proteomes, it is necessary to integrate a wide range of proteomic technologies including two-dimensional electrophoresis, mass spectrometry as well as classic protein chemistry technologies. Recent developments in proteomics include high throughput tools such as protein arrays and a wide range of specifically modified mass spectrometry approaches.

3) data analysis and integration

Genome research generates huge amounts of data that need to organised, managed and analysed. Current pig genome data management systems are largely concerned with data acquisition, storage and dissemination of data, either sequence data (whole genome, ESTs, SNPs) or expression data (transcriptome and proteome). These data can be generic (whole genome and EST sequences) or specific to individuals (SNPs) or tissues (cells, organs; expression data). For expression analysis, there still is a need for development and standardisation of tools. Bioinformatics, which associates biological and informatics knowledge, thus plays a central role as the challenge is to transform raw data into biological results.

3. National projects and European collaborations

Several European groups are recognised as leading contributors to and internationally competitive in pig genome research (RH panel in France, genome sequencing in Denmark) as compared to our main –US- competitors. As presented above, collaborations between European groups allowed the positional cloning and identification of a major gene, RN, involved in meat quality (Uppsala, Kiel University and INRA groups in Toulouse and Jouy en Josas; Science 2000; patent) and

identification of the IGF2 mutation underlying a muscle mass QTL (Uppsala, Stockholm, Liège, Buggenhout and Roslin; Nature 2003; patent). The European Union can thus play a major role in pig genomics provided that we reinforce our potential by networking national capabilities and coordinating our strategies to take advantage of the large amount of information that is already available and data emerging from current programmes. In this context, the role that PigNet has to play is to establish contacts and collaborations between European groups involved in pig genomics. The PigNet network will reduce the fragmentation of European pig genome research and give Europe an opportunity to keep its leadership in this field. This development of shared goals is of outmost importance in order to promote and effectively exploit challenging projects such as pig genome sequencing. Allowing such networking and coordination, the proposed COST Action would give more insight into pig development, growth, pathology and reproduction.

1) National projects

Some European countries have already made the choice to develop genomic approaches to improve pig breeding and have set up national projects such as “AGENAE” in France, “UK Centre for Functional Genomics (ARK-Genomics)” in Great Britain or the Centre for Animal Genomics in Netherlands. People involved in these national organisations are also involved in the PigNet Action.

More specifically, the Sino-Danish Pig Genome Consortium has produced approximately 3 million genomic shotgun reads and approximately 1 million ESTs. Both collections of sequences will be published and made available before the end of this year. As the Danish scientists involved in this Sino-Danish pig genome consortium are also involved in the PigNet initiative, it will be possible to collaborate on the exploitation of these data within the network through coordinated and joint analysis.

2) Complementarities with European projects

a) Other COST Actions

The present proposal will complement other COST Actions that have objectives that are close to our proposal such as COST Action 846 (measuring and monitoring farm animal welfare) and 925 (importance of prenatal events for postnatal muscle growth in relation to the quality of muscle based foods). Contacts have been established with chairmen of both Actions who agreed that communication between their Action and PigNet would be a good thing, and the discussion is open. Moreover, a member of the COST Action 925 MC is also involved in PigNet. We also have contact with a COST Action using similar tools (WG1 of the Action 853, Agricultural Bio-Markers for Array Technology).

b) Other European projects

PigNet will also complement FP5 projects such as PorDictor (New predictors for Pork quality derived from gene expression profiles of skeletal muscle during prenatal development) that is in its last year. PigNet will also complement and interact with EADGENE (European Animal Disease Genomics Network of Excellence for Animal Health and Food Safety). The EADGENE project shares the genomic approach with PigNet but it addresses several species, not only pig, and is focused on host-pathogen interaction. However, even if host-pathogen interactions play a major role in infection and immunity, this is only part of the main interests of the PigNet partners, other major ones being related to meat quality (growth and muscle development) and reproduction. Moreover, EADGENE regroups 13 national research institutes or faculties *versus* 34 for PigNet; among these 13 participants, 10 have expressed their interest in this COST Action proposal, and 7 people represent their institution in both projects.

Clearly, there will be a direct communication between EADGENE and PigNet. We will take advantage of it and develop working contacts with this network; as a first approach, a presentation and a discussion is planed for the next EADGENE meeting in May. To avoid duplication of effort, some tasks will be done in close collaboration (*e.g.* WG 1 in part D).

B. OBJECTIVES AND BENEFITS

The main objective of the Action is to increase our knowledge of the organisation, expression and regulation of the genes involved in pig development, health, reproduction, and product quality. This knowledge in physiology, nutrition, pathology and genetics of the pig will serve as a basis for the development of sustainable pig production as well as for the use of pigs as a model or resource in human health.

Figure 1 illustrates the flow from the original questions to the implementation of new knowledge generated through genomics studies.

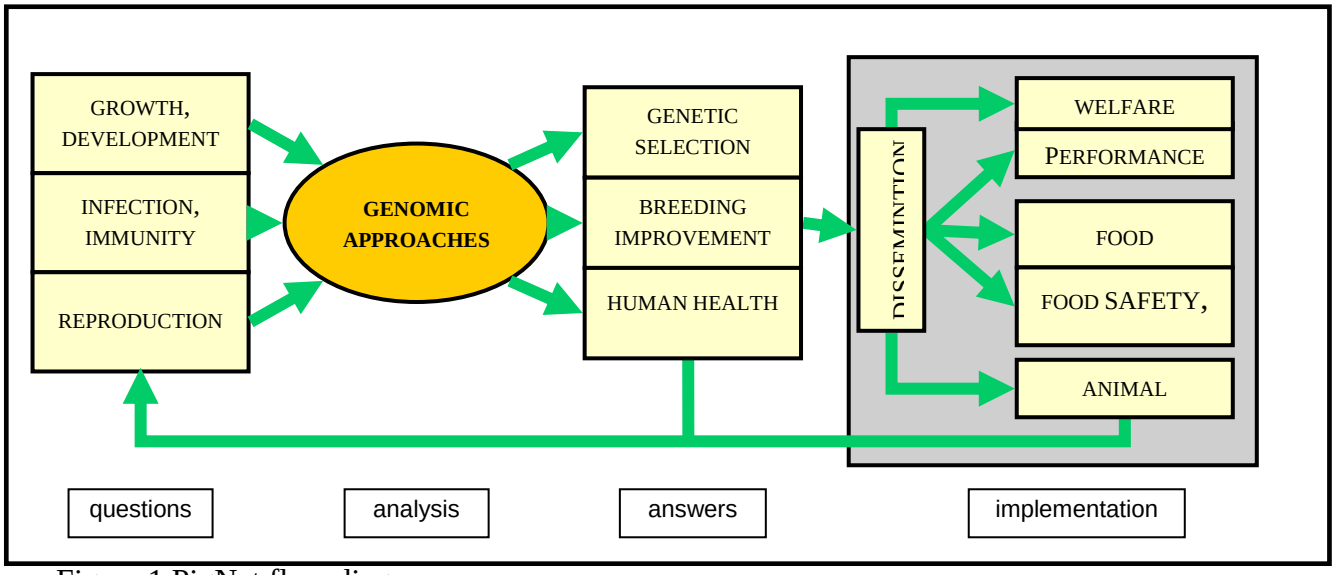


Figure 1 PigNet flow diagram

This main objective encompasses the following goals:

(i) analysis of the structure of the pig genome by mapping (physical, large fragments) and sequencing (genome, ESTs, SNP polymorphism);

(ii) analysis of the expression of the genes under various experimental or breeding conditions in order to find the most relevant genes involved in functions of interest (growth, reproduction, response to pathogens and to xenobiotics);

(iii) dissemination of these knowledge and know-how (students, researchers, pig industry), dialogue with society.

The benefits will include an overall improvement in breeding and genetic merit of European pigs in terms of health, welfare, sustainability, as well as product quality and safety including traceability. This will meet both consumers' expectations and breeders' requirements.

This overall improvement will result from specific benefits:

(i) The new knowledge will be used in the identification and mapping of genes that control quality traits; this will lead to the design of new predictive tools and one main implementation of genomics in pig genetics will be the use of genetic markers in selection (Marker Assisted Selection). Better understanding of biology as a result of functional genomics research will potentially lead to new breeding goals and practices that are more environmentally friendly, and to the production of safer pigs.

(ii) The network will ensure dissemination of these results to European breeding companies, mainly SMEs unable to undertake this genomic effort on their own. Some companies have already expressed their interest in this COST Action. The network will also include training programmes for young researchers to ensure dissemination of achieved knowledge and know-how within the network. Finally, the network will promote a continuous dialogue with society while developing sustainable future breeding and reproduction strategies.

(iii) These challenging objectives require a wide range of expertise and tools that more or less exist in several European countries. The organised network will associate a wide body of researchers including physiologists, biochemists, molecular biologists and geneticists. The benefits of sharing of equipment, data and knowledge will be to improve and accelerate genomic research and reduce costs.

Finally, COST seems to offer the best framework to secure these benefits as we need, above all, to develop communication and interaction between European research groups. Allowing integration of individual and national projects and activities, the proposed COST Action will result in the synergy necessary to achieve genomics projects that are "naturally" ambitious. This synergy will increase the research potential and will contribute greatly to European integration.

C. SCIENTIFIC PROGRAMME

In order to increase our knowledge of the pig genome with the aim of improving pig breeding and it's the effective use of pigs as an animal model and resource in human health studies, several complementary approaches should be taken and should be co-ordinated. The corresponding objectives are described below.

1. STRUCTURE OF THE GENOME: MAPPING AND SEQUENCING

Genome mapping studies provide fundamental knowledge and descriptions of the pig genome. However, to date most pig genome mapping studies have been conducted with the purpose of mapping and identifying genes of agronomical interest and subsequently to characterize genetic variability at the molecular level. Such mapping studies allow identification of genes or genomic regions involved in zootechnical traits such as growth, meat quality, fertility, disease resistance in a strategy called positional cloning. The goal is to establish linkage between molecular, polymorphic markers with the phenotype of interest by analysing their transmission to offspring. A successful illustration of this approach is provided by the identification of the major gene RN involved in pork quality (Milan et al, Science 2000). However, the transition from the initial localisation to a chromosomal region of perhaps 20 centiMorgans (20 cM) or more to the identification of the causal gene and genetic variation is time consuming and requires the development of high resolution physical maps of each region of interest.. The efficiency of this transition would be enormously improved by access to detailed genome-wide physical maps. International projects to develop such genome-wide (BAC contig) physical maps of the pig genome are in progress, including research groups in France and the U.K. that are members of PigNet. Of course, the ultimate whole genome physical map is the sequence itself.

Molecular markers, by revealing polymorphism at the DNA level, are playing an increasing role in animal genetics studies. Most widely used are microsatellites, which are based on tandem arrays of simple di- or tri- nucleotides repeats, the variation of the number of repeats being the source of the polymorphism. Microsatellites are often considered the markers of choice for linkage analysis as a result of their easy use by simple PCR, followed by a denaturing gel electrophoresis for allele size determination, and the high degree of information provided by the large number of alleles per locus.

An additional source of polymorphism is the variation of single bases, or Single Nucleotide Polymorphisms (SNPs). This class of polymorphism is gaining in popularity mainly because SNPs are more frequent, they will be more often close to the site responsible for the phenotypic variation and some of them actually will be responsible for this variation.

In order to fill the gaps in the description of the pig genome (*i.e.* structural genomics) three developments are required – detailed physical (BAC contig) maps, draft genome sequence and panels of SNPs.

1) *Physical (BAC contig) maps*. Three groups (INRA, Jouy-en-Josas; INRA Toulouse and Roslin Institute) that are members of the proposed PigNet network together with The Welcome Trust Sanger Institute and the University of Illinois are making major contributions to the development of genome-wide physical (BAC contig) maps of the pig genome. Fingerprints for ca. 300,000 BAC clones, plus about 450,000 BAC end sequences together with radiation hybrid mapping data will be used to establish BAC contigs anchored to the RH and genetic maps of the pig genome by the end of 2004. The maps will be published and made freely available to the PigNet collaborators. By sharing information on BAC clones and genes of interest the PigNet collaborators will provide a rich source of annotation for the physical maps.
2) *Draft genome sequence*. Raw genome sequence data equivalent to 5-6x coverage of the pig genome (~ 15 x 10^9 bp of primary DNA sequence data) will be required to establish a draft sequence of the pig genome. The sequence data generated by the Sino-Danish Pig Genome Consortium will provide about 0.5 – 1x genome coverage. The Sino-Danish data are derived solely from whole genome shotgun sequencing, in which the ends of clones from independent libraries containing fragments of different length, namely 3 kb, 10 kb and 50 kb are sequenced. An effective and efficient strategy for developing a draft genome sequence combines 4-5x coverage from whole genome shotgun libraries with 1-2x coverage from sample sequencing of BAC clones representing a minimum tiling path through the genome – a so-called BAC skim. The physical (BAC contig) maps described above will allow the identification of a minimum tiling path. A critical task for the PigNet collaborators is to promote international efforts to secure funding to complete a draft sequence of the pig genome.

3) *Single Nucleotide Polymorphisms (SNPs).* SNP identification proceeds through various approaches, all based on sequencing of various individuals, either directly or through mining of existing data. It is necessary to differentiate true polymorphism from sequencing errors. Several groups have already developed projects for identifying SNPs. By combining our resources, sequences and chromatograms, we will increase our potential to get a common, large, efficient database, and achieve complete genome coverage at lower costs.

2 FUNCTIONAL GENOMICS: SEQUENCING AND EXPRESSION

Functional genomics is concerned with understanding a phenotype or trait of interest by identifying the genes that are involved in that phenotype, by correlating the activity of these genes, and by determining their role in the precise context of the phenotype under analysis and in relation to whole body homeostasis. The targets of functional genomics are the organs (tissues, cells) in which the physiological mechanisms that shape the phenotype take place; for some phenotypes there will be multiple organs or cell types involved. For example, for reproduction, the target is clearly the gonads, but also involves the hypothalamo-pituitary axis. Moreover, the gonad itself is complex and composed of different tissues or cell types that may merit specific, separate analysis. Thus, for a functional genomics analysis, physiological knowledge of the function is a prerequisite. This analysis will, in turn, enrich the knowledge of this function.

For a particular phenotype or trait, the genomics analysis encompasses i) identification of the expressed genes, ii) analysis of their expression and regulation, iii) description of their role in the trait iv) integration of these genes (proteins) into regulatory networks. Understanding the role of the different players acting in the complex networks will increase our understanding of the physiology and biology of the traits being studied. This will also allow the identification of interactions between traits and thus will take into consideration whole body homeostasis. This will ensure more balanced production / animal husbandry and thus healthier breeding in the future.

The biological questions that are addressed are related to the domains of growth and development, infection and immunity, and reproduction. Whatever the question is, there still is a need for reference data as well as, upstream, for reliable methods and an important part of the Action will be devoted to meet these needs. Then, specific programmes will be developed, according to the fields of interest of the participants.

The functional genomics will be approached through the following main focuses.

(1) Transcriptome:

a) Identification of expressed genes always proceeds through sequencing of cDNA obtained from a specific organ (tissue, cell) and new sequences (EST) from pig specific libraries are to be released in the public domain by different groups. Clustering of the EST on the basis of their sequence identities gives rise to collections of clusters, each containing sequences that represent a unique gene (UniGene from NCBI, Gene Index from TIGR). In the last releases, there are 20,426 pig UniGene clusters including 5,553 singleton (Build #23 February 2004), and 63,620 pig (TCs) clusters including 38,800 singleton ESTs+ETs in the TIGR Gene Index (release 8.0, January 2004). As indicated by the discrepancy in these results, both clustering methods do not lead to the same results. A collaborative, careful evaluation is needed in order to build the most representative "UniGene" collection. Establishing such a collection is a prerequisite to the design of "whole genome" arrays.

b) Expression analysis or expression profiling is mainly done by hybridisation to cDNA arrays. Such arrays are generally based on limited collections of genes frequently designed for the analysis of specific functions or tissues (immune response, muscle …). Another approach is to use a "UniGene" set of non-redundant cDNA that represents "whole genome" expression array. Such an approach adds a specific value as the use of the same collection of cDNAs (or oligonucleotides, see below) will generate a large amount of data on each gene represented in the set. In addition, these "whole genome" arrays may be useful to define the specific set of genes of interest to be analysed further in specific projects. Definition of the sets and production of arrays are clearly activities that should be co-ordinated.

c) Expression analysis using arrays requires a high level of skill as the technique(s) are not yet standardised. Development, standardisation and quality control of array experiments, including sampling process and design of the experiments, is of outmost importance and should be co-ordinated. Among potential developments is the use of long oligonucleotides (50 to 70 mers) instead of cDNA for spotting. Establishing such a collection of oligonucleotides is a challenge

and will be more efficiently done at the European level as there is a need for bioinformatics (oligonucleotides design), synthesis and spotting of oligonucleotides, array distribution. Such a long oligonucleotides collection has just been made available by a private company and a careful evaluation of this alternative will be done in a limited number of laboratories for the benefit of the whole community. Although not specific to pigs, these developments will take place in the objectives of PigNet.

(2) Proteome:

Proteomics applied to animal production is in its infancy. More than a million proteins are thought to exist in humans and other mammalian species including pigs so that identification and characterisation of new proteins is a huge task requiring sophisticated equipment (two-dimensional gel electrophoresis -2DE, mass spectrometry) and a high degree of skill and expertise. Some high resolution 2 DE protein maps for muscle tissues and meat fluids have already been established in order to characterise molecular markers that relate to meat quality. There is a need to establish and integrate such maps of other tissues such as liver, intestine, and serum, and from a large variety of physiologic and pathologic conditions. These maps will be used to evaluate the modifications of the protein repertoire in relation to those conditions. Such evaluation will allow developing markers for the corresponding physiopathological or experimental situations and genes that influence certain traits or diseases can be recognised. It will also be of interest to identify protein modifications that relate to technological processing in the food industry.

The network should co-ordinate projects and should promote interfacing of the proteomics centres available among the potential partners, as well as promote new projects. An important role of the network should also be to facilitate integration of proteome studies in ongoing functional genomics studies.

3) Function:

Identification of the function and role of a particular gene is the end point of functional studies, but is far from being the simplest. The best known approach involves the generation of transgenic mice, in which the gene of interest is either disrupted (knock out) or over expressed (knock in). Targeted modification techniques are also available that allow specific modification in terms of place and time of disruption/over expression. This technique requires a high level of know how for construction of the recombinant DNA used for modification of the gene, for introduction into mice, and for phenotypic analysis of the mice. RNA interference (RNAi) is a new "knocking down" approach that is gaining interest mainly because it is easier to set up. It is based on the inhibition of the expression of the gene after introduction into the cells of RNA sequences complementary to the sequence of the gene to be switched off. New developments are in progress in this domain, which deserve specific attention and will be monitored continuously. Each trait or gene needs the development of a specific approach.

Here again, co-ordination of existing facilities will facilitate existing projects and promote new ones.

3 INFORMATICS AND BIOINFORMATICS

Informatics and bioinformatics are main components of genomics which focus on production, storage and interpretation of data. As for other genomics components, COST Action will facilitate exchange of information, experience and know-how in this field.

(1) Production of material and data

Most equipment used in production of data in genome research is computer driven. In order to limit human errors, and for secure tracking of sample records and data, the different instruments of a platform should be interconnected using LIMS (Laboratory Information Management System). The other point is acquisition of data, for example image analysis of arrays hybridisation. As for data interpretation (see below), the objective could be to establish a common "Pig tool box".

(2) Data storage

Genomic experiments generate huge amount of data: more than 10^{10} bases for genomic sequencing, thousands or tens of thousands expression data for cDNA arrays, thousands of proteins spots on 2D gels. Specific databases have been developed, well established as for sequence data (GeneBank, EMBL, DNA Databank of Japan) or in development for expression data (ArrayExpress from European Bioinformatics Institute). For Pig, there are specific public databases already available ("Arkdb", Roslin Institute[1]; "IMpRH", INRA[2]). There are also private or semi-private databases developed in the frame of collaborative programmes such as resSpecies[3] for QTL and linkage mapping or the Pig genetic diversity database[4]. Last, there are databases developed through a collaboration between public and private laboratories such as "PACE" (Wageningen UR) or "Sigenae" (INRA) that will be at least partly available in few weeks ("PACE", similar to the chicken database "ChickAce" already available[5]) or months ("Sigenae", based on the EMBL-EBI/Sanger Institute Ensembl tools).

As one objective of the network is to share data, a common database should be a useful tool. COST Action will contribute to the evaluation and set up of the integration (interconnection, merging) of existing databases starting with a list of databases, including private ones, and to assess how access could be given to all PigNet partners. Further, the development of a common pig genome database could be foreseen as well as the possibility, not yet evaluated, to join an international database such as that maintained by EMBL at EBI, but its content should be public. This should constitute a new project, specific for PigNet Action, but, unless a specific support can be found, it is dependent on the national resources.

Basically, generic data and knowledge should be freely available, particularly if funded by national agencies. However, pooling all the data implies to deal with IP issues as these data arise from project funded from outside the network. This is not a simple issue, and we need support from both COST and our national agencies in order to address it.

[1] http://www.thearkdb.org
[2] http://www.toulouse.inra.fr/lgc/pig/RH/IMpRH.htm
[3] http://www.resSpecies.org
[4] http://www.projects.roslin.ac.uk/pigbiodiv/
[5] https://acedb.asg.wur.nl/

(3) Data interpretation

The objectives are to transform raw data into biological results (interpretation) then to propose and validate hypothesis. Such activities are clearly the essence of genome research, where the added value is. To take a few examples:

- Aligning BAC fingerprints to build contigs, assembly of whole genome sequence data, SNPs detection, sequence comparisons, annotation of raw sequences, in the field of genome structure;
- cDNA sequences clustering, long oligonucleotides design, hybridisation data processing, expression data clustering, 2D gels protein analysis, in the expression domain.

This field is in full development and some groups have developed expertise in this domain. One objective of the COST Action is to contribute to the development of a common software “Pig tool box” by evaluating and improving existing software or designing new ones. Such “new” softwares might be implemented as add-ons or plug-ins to existing databases (*e.g.* for expression data). Bioinformatics courses for handling of this tool box should be organised.

A last objective that should be considered is the design of tools for using this new type of data in the current animal selection programmes.

More widely, the COST Action will contribute as much as possible to the standardisation and interoperability of existing systems, particularly in view of (i) the quality control of biological resources and experiments with an objective of traceability, (ii) the development of data mining tools that use information across species. Finally, as most if not all bioinformatics questions raised in the frame of PigNet are not pig specific, particular attention should be given to the work done in other species (model or of agronomic interest). This should be facilitated by the fact that most of PigNet members also work with other species, or have connections in their Institutes with people working in other species. Moreover, as indicated below (D.1) for working group 1, these objectives should be approached in relationship with EADGENE network.

4 DISSEMINATION OF KNOWLEDGE AND KNOW-HOW, DIALOGUE WITH SOCIETY

(1) Dissemination of knowledge and know-how

New knowledge and know-how need to be shared and disseminated towards both research and industry. Dissemination towards research will be achieved through classical means such as scientific publications, workshop and conferences and, for people involved in PigNet, through Short Term Scientific Missions. These STSM will allow young as well as senior scientists to learn new techniques or know-how in other laboratories, but also to expand the scope of their research to other, new, fields.

Dissemination towards Pig industry will be achieved directly for breeders involved in PigNet, through general conferences and through EFFAB for others.

(2) Dialogue with society is oriented towards (i) consumer's demands on animal breeding and food quality, and (ii) societal concerns in science that is sustainable breeding and ethics.

Consumer's demands refer to animal welfare and health, environmental considerations as well as food quality and safety. The growing character of this concern can be illustrated by the fact that more than 10 Expressions of Interest concerning animal welfare were published last year following the call for proposals by the European Commission. Beyond a general concern about livestock production, there are specific points to be addressed for pig breeding such as piglet castration, which has a high impact on pig meat quality, animal transport which has also an impact on meat quality or water pollution by nitrates. Genomics can contribute to the development of improved production systems in relation to these topics. Food quality includes traceability that can be improved with the tools developed through genomics studies such as microsatellites or SNP markers.

There are growing concerns about the impacts of scientific and technological developments and thus towards genomics in its economic, legal, social and ethical aspects. This research into and communication of the societal aspects of genomics need to be stimulated and organised. There are

European organisations and networks such as EurSafe (European Society for Agricultural and Food Ethics; http://www.eursafe.org/), SEFABAR (Sustainable European Farm Animal Breeding And Reproduction; www.sefabar.org) or national projects such as the "Centre for Society and Genomics" (http://www.genomics.nl/data/pers/pers_230103_uk.htm) from the Netherlands Genomics Initiative (http://www.genomics.nl/data/international.htm) or the Economic and Social Research Council Centre for Genomics in Society from UK "Egenis" (http://www.ex.ac.uk/egenis/about.htm) that could fulfil this requirement. There are also specific points to be addressed concerning pigs such as those associated with xenotransplantation or the use of pig-based bio-artificial organs.

People involved in the proposed COST Action should promote and participate in research and debate on sustainable breeding and ethical issues involved in pig breeding and its use as a model and resource in human health.

D ORGANISATION

The COST Action will be organised as described in "Rules and Procedures for Implementing COST Actions". In order to meet the objective of the Action, organisation will be set up to allow (i) sharing of the equipment, data and knowledge, (ii) establishing collaborations aimed at improving and accelerating genomic research and reducing costs. Therefore, the management committee will create 5 working groups to facilitate exchange of information, experience and know-how:

1. Working Group 1: Integrating activities

Objectives:

Integration of activities through (i) management of the interactions between working groups, between specialists from different scientific domains, between PigNet and other European projects, (ii) sharing co-ordination for equipment and biological resources (in close relationship with FP 6 EADGENE network of excellence).

Management of the interactions

As stressed elsewhere (A.3.2, D.7, D.8) to reduce overlaps and to create synergies, there is a need for interactions between research programmes (COST Actions 846, 925; EADGENE network), working groups or scientists from different disciplines. The various meetings provided by the COST Action will allow such interactions, but, in order to formalise those, we propose to prepare annual reports to describe how these interactions take place and how they are of benefit to the network.

Sharing co-ordination

One goal for the COST Action PigNet is the sharing of biological resources and equipment. Such sharing will provide access to material and techniques for pig genomic research for a wide number of research groups, improving and accelerating genomic research, as well as reducing costs. To achieve this goal, a first task will be to identify and list biological resources and technical facilities, experimental protocols and quality control procedures. Further, we should promote, as far as possible, the choice and set up of common standard operating procedures (SOPs), quality processes (QA/QC) protocols. The resulting materials should then be standardized and quality controlled to the highest standard to allow access to material in as homogeneous a manner as possible, even if obtained on different platforms. Such "standardisation", achieved through collaboration and coordination, provides considerable potential for integration and will result in a virtually unique facility. It will be established through a close collaboration with the EADGENE project that has similar objectives. Short-term scientific missions will facilitate this sharing and standardisation goal.

	WG1 deliverables	Indicative months
	Interactions	
1	Annual report on interactions between genomics and other sciences	1 – 60
2	Annual report on interactions between working groups	1 – 60
3	Annual report on interactions between relevant European programmes	1 – 60
4	Meeting reports	1 – 60
	Sharing co-ordination	
5	List of biological resources, technological facilities	1 – 12
6	Selection of a common set of standard operating procedures, quality process and protocols	12 – 24

2. Working Group 2: Structure of the genome

Objectives:

Mapping and sequencing projects as described in the scientific programme (C.1)

	WG 2 deliverables	Indicative months
1	Physical map: BACs fingerprint and contigs, contig anchorage on maps	1- 24
2	Genome sequencing: BACs ends sequencing	1- 24
3	SNP sets, evaluation, set up and maintenance of a common SNP database	1- 60
4	QTL identification	1- 36
5	cDNAs and genomic sequence data publications	1- 60
6	Meeting reports	1- 60

3. Working Group 3: Functional genomics

Objectives:

Exchange and development of expression analysis tools and data as described in the scientific programme (C.2)

	WG 3 deliverables	Indicative months
	Transcriptome	
1	Set up of a common list of unique sequences with available corresponding cDNAs	1 - 24
2	Set up of “whole genome” microarrays	18 - 36
3	Availability of specialised microarrays	6 - 60
4	Evaluation and set up of long mers arrays	18- 36
5	Proteome	
6	Protein maps of muscle, liver, intestine and serum	1 – 36
7	Function	
	List of projects (updated yearly)	
8	Meeting reports	1 - 60

4. Working Group 4: informatics and bioinformatics

Objectives:

Exchange of information, experience and know-how in informatics and bioinformatics in order to facilitate data management.

The scientific objectives of this WG concern data production, storage and interpretation, including improvement and design of software as described before. A major goal is the evaluation and set up of common tools and databases, integrating existing ones and those newly developed within the project. Besides this major activity, this working group will also be in charge of the development, set up and maintenance of a Web site specific for the PigNet COST Action. Its contents will be provided by WG 5. Finally, this WG will provide support for the use of software for genomics through courses.

	WG 4 deliverables	Indicative months
1	Web site	1 – 6
2	List of informatics tools used by the different partners	1 – 12
3	Evaluation of the feasibility of a specific, common, "pig tool box" and set up if feasible	6 – 60
4	List of databases, including private ones	1 – 12
5	Evaluation of how access to databases could be given to all PigNet partners, if interoperability could be set up, and if a common database can be foreseen, including IP issues	12 –60
6	New software or add-on about missing tools for the existing databases (*e.g.* about expression data management).	36 – 60
7	Bioinformatics courses	1 – 60
8	Meeting reports	1 – 60
9	New tools for animal selection programme	1 – 60

5. Working Group 5: dissemination and dialogue with society

Objectives:

Dissemination of knowledge and know-how, dialogue with society

The Web site will publish on the home page the objectives of the Action, its organisation as well as information on the activity of the WGs. Agenda and a brief outline of the various meetings will also be available. A private, intranet, part of the Web site will serve as a forum for the scientific projects,

but also for dissemination of the information, mainly reports, for the participants to the COST Action. The MC will decide what information should be public or not.

This working group will be also in charge of the dissemination of the knowledge and know-how developed through the network by the way of STSMs, meetings, conferences as well as informal contacts. The EFFAB (European Forum of Farm Animal Breeders; http://www.faip.info/), which is an independent forum for farm animal reproduction and selection organisations, should play a major role in dissemination towards breeders.

Another essential task assigned to this working group in close relationship with WG 2, 3 and 4 will be the scientific and technological surveys in the corresponding domains to keep on the leading edge.

Dialogue with society will be undertaken through collaboration with specific projects and organisations as described in C.4.

	WG 5 deliverables	Indicative months
	Dissemination	
1	WEB site for dissemination of information, diffusion list (already active)	1 – 60
2	Scientific surveys	1 – 60
3	STSM for doctoral and post-doctoral students	6 – 60
4	STSM, regular scientific publications and PigNet conferences for researchers	1 – 60
5	PigNet conferences and EFFAB meeting for pig industry	1 – 60
	Dialogue	
6	EFFAB meetings and Actions	1 – 60
7	Conference(s), meeting(s) with other national or European organisations such as Eursafe, SEFABAR, Centre for Society and Genomics (NL) or Economic and Social Research Council (UK).	1 – 60

6. Meetings and Short Term Scientific Missions

The WG co-ordinators will be responsible for organising their working groups, co-ordinating meetings and producing reports within their groups. WG meetings will be followed by the MC meetings at the same place in order to reduce costs (see figure 3). A general conference involving all working groups will be held soon after the beginning of the Action. This “initiation” workshop

will provide the “state of the art” knowledge for all participants, allow refining goals and initiate the work programme for each WG. It will be open to the whole scientific community and representatives from the industry may be invited to participate if the MC has decided so. This general conference will be repeated during year 3 and at the end of year 5 of the Action. If relevant, the meetings will also include people from other projects such as COST Actions 846 and 925 or European project such as Pordictor or EADGENE.

In order to facilitate interactions between participants, working groups and relevant sciences and to share genomics technologies, Short Term Scientific Missions will be encouraged for both young and senior scientists. Applications will be made by the MC, which will also review the reports of these STSMs. The objective is that 10 scientist exchanges will take place per year.

7. Interactions between working groups

Genomics is not carried out for itself, but rather used as a tool or a suite of technologies for solving specific problems related to biological or zootechnical questions. All the components of this suite are more or less dependent on each other, or at least related. So that, in PigNet, the working groups devoted to these different components are “naturally” interacting (Fig. 2).

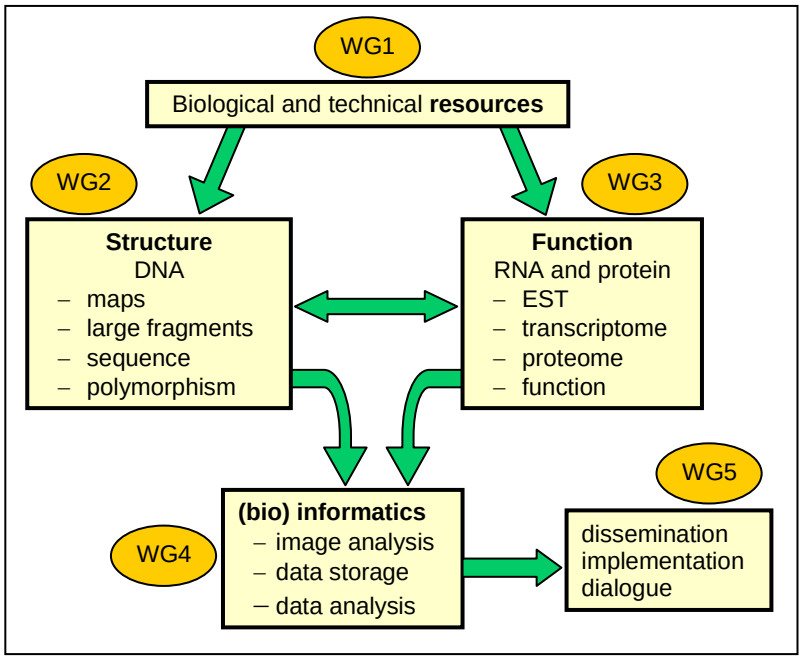


Figure 2 Interactions between Working Groups

The main components of genomics, structure and function are the two sides of the same coin, which are complementary approaches that can be used to answer the same question. Even if they can be considered independently, there is an obvious benefit to take advantage of both. The IGF2 example given above relies on the QTL mapping as a structural element, and on the known role of IGF2 in muscle development as a functional element. We hope to get more examples in the future, through the activity of working groups 2 (structure) and 3 (function). Both approaches necessitate resources and technological facilities that should be identified and co-ordinated through working group 1. Those genomics approaches produce a large number of data that have to be stored, managed and interpreted through informatics and bioinformatics tools and resources (working group 4). Finally, working group 5 that disseminate this new knowledge clearly relies upon activities of WG 2, 3 through WG 4.

Moreover, two thirds of the scientists expressed their interest in more than 3 working groups, which will insure that each working group will not be considered independently from the other ones, and will also reinforce the complementarities between these working groups. Particularly, when considering the number of scientists involved in either the WG 2 (structure of the genome), the WG 3 (functional genomics) or both, more than 50 % expressed their interest in both WGs.

Finally, all the working groups will meet together during the 3 general conferences. The first two (beginning of year 1, year 3) will particularly allow coordination of activities between the different working groups. Other meetings with all working groups could also be organised if the management committee find it useful for the progress of the Action. Working Group 1 will be in charge of this important co-ordination activity and specific reports on working groups' interactions will be produced each year.

8. Interactions between genomics and other sciences

Traits improvement needs to take into account not only biological factors such as genetics, physio-pathology, nutrition, etc but also other factors such as feeding and housing of animals and processing of the carcasses and fabrication of products to give a few. As stated earlier, genomics is a global approach that allows taking into account various factors, not only related to the "biological" status of the animals, but also related to the environment or the production. Moreover, genomics is not carried out for itself, but is rather done by scientists who have specific projects in

meat quality, pathology, nutrition and so on. They all start from a biological or zootechnical question and they try to solve it using the available tools and methods, as they have always been doing; today, current tools and methods are called "genomics". So, very few in the PigNet group define themselves as “genomicists”, but are mainly geneticists, and also biochemists, molecular biologists or physiologists. As their research projects are oriented towards breeding or production improvement, their groups collaborate with or include specialists in physiology, pathology (microbiology/virology/immunology), biochemistry, nutrition, meat processing and even “pure” genomics.

To increase these interactions, we propose to organise transversal meetings on specific topics that go across different disciplines in order to bring together every people interested in, even if these people are not permanently in the network. These people are present in the organisations participating in PigNet, such as INRA, ID Lelystad, DIAS, Roslin Institute … These meetings will also include people from other projects such as COST Actions 846 and 925 or European projects such as Pordictor or EADGENE. Such meetings should also benefit from inputs from other species as, beside model species, genomics develops also in other farm animals.

Working Group 1 will be in charge of this important co-ordination activity and specific reports on interactions between genomics and other sciences will be produced each year.

E TIMETABLE

According to the wide scope of this Action, a five year programme is proposed.

The timetable of the project is depicted in figure 3 that differentiates management and integration activities from scientific activities and some comments are given below.

Management and integrating activities should start as soon as the first MC meeting takes place. A MC meeting will be held at least twice a year, with a progressive shift in order to have the last one at the end of the project. WG 1 activity will be very important, during the first two years for sharing facilities and resources, and during the whole Action for promoting and maintaining interactions between working groups, between genomics and other sciences, between PigNet and

other relevant European projects. WG 4 is partly concerned with integrating activities and management through the Web site that should be set up as soon as possible. Maintenance of this site is also part of WG4 activity and is roughly indicated as taking place twice a year, which rather corresponds to a regular, low level activity. For WG 5, if STSM, scientific publications and conferences are clearly scientific activities, dialogue and dissemination as well as updating the Web site can be considered as integrating activities. This is indicated in the figure by alternating both kinds of activities, roughly 50/50.

Scientific activities will start after the first general conference as one of its objectives is to refine goals according to the state of the art. This conference will also allow the establishment of a more precise deliverable list and time table. Activity devoted to the structure of the genome (WG 2) could probably start rapidly as the goals are well defined and the materials are available. This is not the case for functional genomics (WG 3) that is more dependent on technological co-ordination and standardisation, both achieved by WG 1. We thus anticipate a 5 to 6 month delay. Scientific activities will run continuously up to the end of the Action. Regular meetings will punctuate this scientific activity together with the two general conferences during year 3 and slightly before the end of the Action (year 5). Although primarily scientific in nature and indicated as such, the STSMs should also participate in integrating activities within WG 1 for promoting and maintaining interactions between working groups, between genomics and other sciences, between PigNet and other relevant European projects.

Meetings

As an objective of the PigNet COST Action is to address the fragmentation of European pig genomics research it is necessary to give people opportunities to meet, to exchange, in order to avoid duplication of effort and, if possible, to build common new projects. Thus, meeting twice a year seems to us a good frequency; working groups and management committee meetings will take place in two following days as indicated by vertical dotted lines, in order to reduce costs. Moreover, according to the needs, some of the planned meetings may evolve towards transversal meetings as proposed above.

F. ECONOMIC DIMENSION

The following COST countries have actively participated in the preparation of the Action or otherwise indicated their interest:

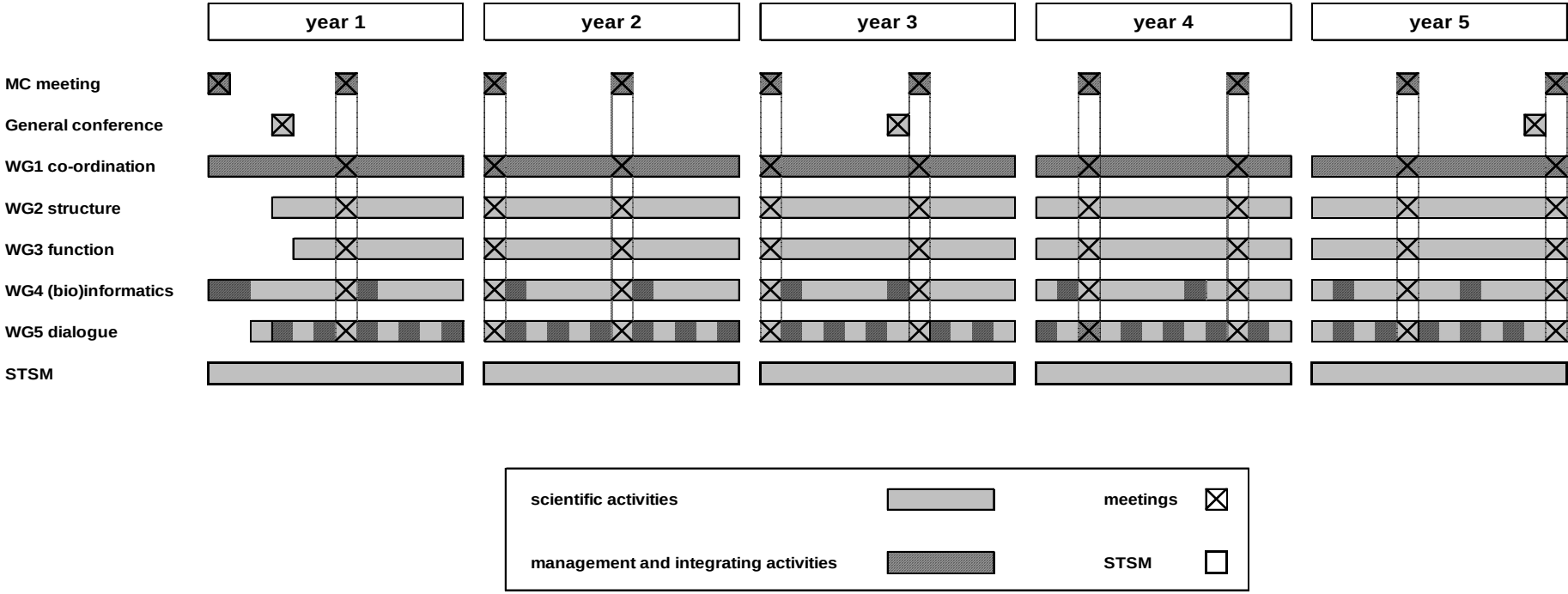
Austria	Greece	Spain
Belgium	Hungary	Sweden
Czech Republic	Italy	Switzerland
Denmark	Poland	The Netherlands
France	Portugal	United Kingdom
Germany	Slovenia	

These countries represent nearly 34 different institutes, with about 215 scientists involved in pig genomics. On this basis, the economic dimension of the activities to be carried out under the Action has been estimated, in 2003 prices, at roughly Euro 13 millions per year.

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.

Outside Europe, the Beijing Genomics Institute in China has indicated its interest in this Action, with more than 50 people involved in the pig sequencing project.

Figure 3 Timetable



G DISSEMINATION PLAN

As the objective of this COST Action is to increase our knowledge on the structure, expression and regulation of the genes involved in pig development, growth, pathology and reproduction as a basis for pig breeding and use as a model or resource in human health, the results of the Action will be disseminated to i) researchers working in the field or in related fields, ii) breeders, iii) society.

A common dissemination tool is the electronic network (e-mail, diffusion lists, intranet and internet Website) which will be set up and will be used for both internal information (scientific and administrative) and results dissemination.

(i) dissemination towards scientific audience will be achieved mainly through publications from the participants, preferentially in groups from different institutes, in high quality scientific journals. Reciprocally, reputed researchers working in the field will be invited for seminars and conferences during the meetings of the Action. All the reports (annual reports, meetings, workshops or conferences) will also be available through the electronic network of the project, either intranet or internet, according to the nature of the information and to the decision of the MC.

(ii) dissemination towards breeding companies deserves a special attention as they are mainly SMEs. As such, they do not have the knowledge and technologies that are necessary for the implementation of genomics into animal breeding. For example, the evaluation of potentially valuable genes specifically for their own breeding programmes is a problem for breeding companies. For this dissemination towards breeders, the EFFAB (European Forum of Farm Animal Breeders), an independent forum for farm animal reproduction and selection organisations, should play a major role. Besides EFFAB, four private companies have expressed their interest in this COST Action.

(iii) dissemination towards society includes at least two different aspects. One is related to animal breeding (welfare, environment) and the other to consumer's demand (quality, safety, traceability). Ethical aspects of the use of pig as a model or resource for human health may also be considered. These aspects will be addressed through specific meetings and workshops in partnership with specific European organisations and networks such as EFFAB, EurSafe, SEFABAR or national projects such as the "Centre for Society and Genomics" in the Netherlands.