A European infrastructure
for farmed animal genotype to phenotype research

Deliverable 4.5

Collaborative framework with EUGENA and industry users

Grant agreement no°: 101094718
Due submission date
2024-June-30
Actual submission date
2024-July-01

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Sensitive: No

This project has received funding from the European Union's Horizon Europe research and innovation programme under grant agreement No 101094718. The content of this report reflects only the author's view. The European Commission is not responsible for any use that may be made of the information it

DOCUMENT CONTROL SHEET

Deliverable name	Collaborative framework with EUGENA and industry users
Deliverable number	D4.5
Partners providing input to this Deliverable	INRAE, EFFAB
Draft final version circulated by lead party to: On date	WP leaders All EuroFAANG parties 28/06/2024
Approved by (on date)	FBN as Coordinator
Work package no	4
Dissemination level	Public (PU)

REVISION HISTORY

Version number	Version date	Document name	Lead partner
Vs1	14/06/2024	Deliverable 4.5_draft report	INRAE
Vs2	29/06/2024	Deliverable 4.5_v1	INRAE
Vs3	01/07/2024	Deliverable 4.5_v2	INRAE
Vs4			
Vs5			

Changes with respect to the DoA (Description of Action)

None

Dissemination and uptake

This is a public deliverable

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1. Executive Summary

Background	EuroFAANG (European Functional Annotation of ANimal Genomes) aims to streamline use of interdisciplinary capabilities for G2P (Genotype to Phenotype) research in terrestrial and aquatic farmed animals and provide transnational access to all of the relevant facilities, expertise and knowledge to European stakeholders. Consolidating biobanking services for cellular models across Europe has been identified as a key component in developing the concept of EuroFAANG Research Infrastructure.
Objectives	To establish a collaborative framework with European organisations such as EUGENA (the European animal gene bank network) and with the private animal breeding sector, with the aim to contribute to safeguarding genetic diversity through biobanking.
Methods	Discussions about the establishment of a collaboration framework between EuroFAANG RI and EUGENA network started in Feb. 2024 and are still ongoing. These discussions included a presentation of EuroFAANG RI and its biobanking component to EUGENA network at the ERFP AnGR Smeeting, on April 23, 2024. Following these exchanges, two forms of collaborations were proposed: - Collaboration through the exchange of the information collected in the network and mutually supporting the development of both initiatives. - Collaboration by integrating individual gene bank of the EUGENA network into the EuroFAANG biobank network based on activities of mutual interest. The connection between EuroFAANG and the industry users was reported using the code EFABAR survey questionnaire (2017 and 2020), which included a section on genetic resources, and was distributed to the breeding organizations of the EFFAB network.
Results & implications	Exchanges between EuroFAANG and the EUGENA network showed that EUGENA members are very positive about their participation in EuroFAANG. To confirm EUGENA's collaboration with EuroFAANG, EUGENA requested for more details on the options that each individual biobank would have for collaboration. Thus, EuroFAANG cannot give final answers to EUGENA at this stage but would rather propose an action plan with a timeline to properly associate all key EUGENA representatives to the ongoing discussions within EuroFAANG. Actions would include: - EUGENA is invited to virtual meetings of think tanks as well as to webinars and trainings. - EUGENA can also be consulted on the business plan, all the more that some biobanks of EUGENA may become members of EF RI in the future. - EuroFAANG RI needs a name list of EUGENA representatives. - An official commitment from a legal entity needed for a gene bank to be part of a European RI. The code EFABAR survey (2017-2020) collected answers from 15 breeding companies (BC) for 4 species or group of species: cattle, pig, poultry, fish. All BC showed a great interest for the preservation of genetic diversity of selected populations. Most of them have their own gene bank, while only 4 of them use a public gene bank. The main issue foreseen for collaborating with breeding companies is data privacy since most of them keep biological material in their own gene bank but do not make this information public because it is considered as strategic. A revised version of code EFABAR survey was launched in 2023. The new template is now available from February 2024 for adoption by EFFAB breeding organisations, which adopt Code EFABAR every 3 years. Then responses will be submitted during the upcoming 3 years by EFFAB members, one by one. A survey with only these aspects of Code EFABAR can be launched to update this deliverable.

Introduction

This deliverable reports the establishment of a collaborative framework of EuroFAANG RI with:
- EUGENA (the European animal gene bank network, managed by the European Regional Focal point) (https://www.eugena-erfp.net/en/) with the aim to contribute to safeguarding genetic diversity through biobanking,
- breeding companies members of the EFFAB.

2. Presentation of ERFP and EUGENA

The European Regional Focal Point for Animal Genetic Resources (ERFP) is the regional platform to support the *in situ* and *ex situ* conservation and sustainable use of animal genetic resources (AnGR) and to facilitate the implementation of FAO's Global Plan of Action for Animal Genetic Resources in Europe. Since 2001, ERFP has served to facilitate the collaboration, coordination of work and exchange of information and experience between different European countries and governmental and non-governmental organizations, including research organisations. The secretariat of ERFP is currently hosted by France, with IDELE (https://www.eurc-eab.eu/idele) and INRAE.
The ERFP network developed an AnGR strategy for Europe and elaborated an Action Plan. The objective is to streamline the actions to be adopted by the European countries to ensure the long-term availability and use of Animal Genetic Resources.

The ERFP objectives are:

- To support the *in situ* and *ex situ* conservation and sustainable use of AnGR in European countries.
- To facilitate the implementation of the Global Plan of Action for AnGR in Europe.
- To assist and enhance the AnGR activities of NCs at the European level.
- To develop and maintain regular contact and exchange of relevant information on AnGR horizontally between European NCs and EAAP and vertically with the Global Focal Point in Rome using existing structures.
- To stimulate the funding and organisation of regional projects, research, workshops and national programmes for AnGR within the European Region.
- To maintain an appropriate liaison with the European Commission, the FAO Commission on Genetic Resources for Food and Agriculture, the Secretariat of the Convention on Biological Diversity and regional and international NGOs. For scientific aspects, it is supported by the European Association of Animal Production's Working Group on Animal Genetic Resources (EAAP WG-AGR).
- To stimulate and coordinate the maintenance and further development of national and regional AnGR databases and to encourage European information networking on AnGR.

One of the ways ERFP operates is through Working Groups, which are established by the Assembly on a permanent basis to work on long-term tasks. Currently, there are three Working Groups :

- *Ex situ* conservation (cryo-conservation), the one particularly targeted by EuroFAANG RI
- Documentation and Information
- *In situ* conservation and valorisation of Animal Genetic Resources

The ERFP Working Group *Ex situ* conservation incubated the set-up of the European Gene bank Network for AnGR (EUGENA).

What is EUGENA?

The European Gene bank Network for AnGR (EUGENA) is a network of National Gene banks in European countries with the aim to support the ex situ conservation and sustainable use of AnGR, and to facilitate the implementation of the FAO Global Plan of Action at national and pan-European level. Exchange of knowledge and experiences, and facilitating access (Nagoya protocol for Access to genetic resources and Benefit Sharing, ABS) to information about gene bank collections in Europe are the main objectives of EUGENA.

Development of EUGENA was initiated by the ERFP in 2016, and since then the network has grown constantly in terms of number of countries, Member Gene banks and information collected on the collections. EUGENA itself does not constitute a legal entity but operates by its Member Gene banks collectively to reach the main objective to drive the collaborative work between all the ex situ collections of AnGR in Europe, and to promote the relevance of the gene banks in the conservation of AnGR.

The EUGENA activities are coordinated by a Steering Board, comprised by one representative of the gene banks per Member Country. The Steering Board is supervised by the ERFP Assembly and assisted by the ERFP '*Ex situ* conservation' Working Group. The ERFP Working Group on Documentation and Information supports the Steering Board to document collections of EUGENA. The ERFP Secretariat provides technical and administrational support to EUGENA.
The EUGENA Portal is managed under the umbrella of ERFP and contains data for Europe only. Data on collections are provided by the individual gene banks.

The objectives of EUGENA are:

- To support gene banks in European countries to fulfil their individual roles and objectives;
- To improve monitoring and assessment of AnGR kept in *ex situ* collections in European countries by sharing information on gene bank collections;
- To improve gene bank operations and procedures in European countries by sharing information;
- To develop synergies for *ex situ* conservation and sustainable use of AnGR by joint activities of gene banks in European countries, including research;
- To increase the efficiency of *ex situ* conservation and sustainable use of the genetic diversity of transboundary breeds;
- To promote harmonization of acquisition and access terms for *ex situ* conservation and sustainable use throughout the gene banks in European countries;
- To facilitate quality management of the gene banks in European countries;

- To create an element of the European research infrastructure for conservation and sustainable use of AnGR;
- To facilitate a regional European approach for international cooperation and exchange of AnGR in the context of the implementation of the Nagoya Protocol for Access and Benefit Sharing.
- To support countries in the achievement of target 2.5 of the Sustainable Development Goal (SDG) #2, and in the monitoring of indicators SDG 2.5.1.b and 2.5.2.
- To facilitate the implementation of the exception for movements of germinal products between gene banks in different countries of the EU, foreseen in Regulation 2020/686.

3. Collaborative framework between EuroFAANG RI and EUGENA

- **Calendar of exchanges between EuroFAANG RI and the EUGENA network:**
  - 2023: some biobanks of EUGENA answered the EuroFAANG biobanking survey (see below)
  - Feb. 2024: EUGENA network made a presentation to EFFAB members (Semen collection centers)
  - April 23rd, 2024: presentation of WP4 of EuroFAANG RI to ERFP *ex situ* working group.
  - April 26th, 2024: meeting between the SG of ERFP on AnGR and the *ex-situ* WG chair, after WP4 EuroFAANG RI presentation.
  - May 28th 2024: feedback to EuroFAANG RI from EUGENA by email, ahead of EUGENA Steering committee.
  - June 7th, 2024: answer from EuroFAANG RI to EUGENA Steering Committee.

Four EUGENA biobanks are ready to deliver at least one biobanking service to EuroFAANG, and **five EUGENA biobanks** are interested to contribute biobanking services to EuroFAANG (**in purple** are those who answered the second survey including information system, quality management, fee policy):

Table 1: EUGENA Biobanks that are ready to deliver at least one biobanking service to EuroFAANG

Biobank ID	Country	EUGENA member	Biobanking services (at least one of the services
National Research Institute of Animal Production, National Bank of Biological Material	Poland	Yes	Yes
Research Institute for Farm Animal Biology	Germany	In the process	Yes
French National Cryobank	France	In the process	Yes
Centre for Genetic Resources, the Netherlands	Netherlands	Yes	Yes

Table 2: EUGENA Biobanks that are interested to contribute biobanking services to EuroFAANG

Biobank ID	Country	EUGENA member	Biobanking services (at least one of the services)
Natural Resources Institute Finland	Finland	In process	Possibly
The Farm animal cryobank IBBA-CNR	Italy	In the process	Possibly
Agricultural Research and Education Centre Raumberg-Gumpenstein	Austria	Yes	Possibly
Banco de Germoplasma BIOMEJAN AGR218	Spain	In the process	Possibly
University of Ljubljana, Biotechnical faculty, Jamnikarjeva ulica	Slovenia	In the process	Possibly

Presentation of EuroFAANG to EUGENA on April 23, 2024.

Members of EUGENA have expertise in cryopreservation of germ cells; sanitary aspects, quality control, FAO policy on animal genetic resources. But objectives differ:

- EUGENA: *ex situ* conservation of animal genetic resources for sustainable use of livestock in Europe. Supporting research comes as an objective but with lower priority level
- EuroFAANG: supports research on animal genetic resources for improved knowledge and support to sustainable breeding in Europe. This comes as the main priority.

Thus, the objectives of EUGENA and EuroFAANG are complementary. However, more precise collaboration can be achieved if EUGENA members can contribute to a research infrastructure and not only to conserve biological material from heritage breeds or breeding populations. Specifically:

1. Biobanks of EUGENA could be integrated individually in the EuroFAANG project to collaborate more closely on activities that would be of mutual interest. This approach can be achieved by:
   - Subscribing to access policy
   - Applying quality control protocols
   - Participating in the governance of the RI by institutional membership

2. EUGENA could collaborate with EuroFAANG RI as a whole by:
   - Sharing protocols
   - EUGENA gene banks acting as mirror sites
   - Communicating on each other: one improves the notoriety of the other
   - Joining different users' communities across a large number of countries

Exchanges between EUGENA and EuroFAANG RI between April and June 2024

- **EUGENA feedback from the meeting on April 23.**

EUGENA members were very positive about their participation in EuroFAANG RI. The following forms of collaboration were considered:

1. EUGENA can collaborate with EuroFAANG directly, exchanging the information collected in the network and mutually supporting the development of both initiatives.
2. Each gene bank in the network could be integrated individually in the project, and collaborate more closely on activities that would be of mutual interest.
3. EUGENA Steering committee requested more information on the services expected by EuroFAANG RI from EUGENA gene banks, on the benefits that its gene banks would get from joining EuroFAANG, on the possible financial support from EuroFAANG RI for EUGENA gene banks to participate in training sessions, and on the procedure to become a member of the RI.

- **Answer from EuroFAANG to the questions of the ERFP AnGR SC meeting.**

EuroFAANG RI answered that each gene bank can choose its level of commitment.
EuroFAANG is aware that the gene banks of the EUGENA network have different levels of resources and implementation which could be improved. EuroFAANG RI is also aware that the main material stored in the gene banks is frozen semen for the purpose of preservation, R&I and further use if needed.

EuroFAANG RI would expect that gene banks provide at least one of the services listed below (this is a very broad and ambitious list, as defined also for other biobanks than those of EUGENA):

- Store and distribute at least one of available immortalised cell lines, stem cells (adult and embryonic stem cells, pluripotent stem cells), primary cells and/or gene-edited cells provided by researchers; if some biobanks can prepare stem cells themselves, all the better;
- host the researchers willing to prepare themselves organoids from stored stem cells
- host the researchers willing to prepare themselves gene-edited cells
- host the researchers willing to prepare themselves immortalised cell lines
- prepare organoids from stored stem cells and distribute them
- prepare gene-edited cells and distribute them

Except for the first option, all services require access to a cell culture lab and related expertise, but several biobanks declared in the survey that this was indeed the case.

EuroFAANG RI also expects sharing the data/metadata/protocols of access on EUGENA gene bank collections with the EuroFAANG biobank directory. The guidelines that the Ex-situ WG is developing to have access to and to use the material stored in gene banks could be part of it too.

In return EuroFAANG RI would propose to each gene bank: (not only EUGENA, this is very wide)

- centralized visibility and recognition on its portal & network participation; TNA (TransNational Access) options later on
- training on biobanking procedures
- training on metadata and data standards
- harmonization of European metadata- and data standards with one biobank directory portal
- participation in the development and testing of new methods
- training on these new methods
- Access through the EuroFAANG RI to new technologies such as genome-wide CRISPR screens and new networks of collaborators who wish to access the biobanks to apply these.
- Participation in EU -funded research projects as INFRA-SERV or INFRA-TECH. This would be possible only when EuroFAANG RI has completed its construction phase and has its own budget (from member fees and from EU-funded projects, such as INFRA-SERV or INFRA-TECH projects)
- access to results obtained from the use of another biobank within EuroFAANG RI (i.e. transnational access), with a non-disclosure agreement

Regarding the costs of attending EuroFAANG training workshops (if held physically), at present, they are open to EUGENA members but the INFRA-DEV project has not sufficient budget to cover traveling and local accommodation of non-partners. Yet, all the costs related to training material on-site are covered by EuroFAANG RI. Moreover case by case discussion could be possible. The next EuroFAANG training workshop is planned at INRAE Jouy-en-Josas in February 2025 (https://eurofaang.eu/g2p-in-a-dish/) and is open to registration at no fee.

On the question of the procedure for EUGENA gene banks to become members of EuroFAANG RI in the future, we foresee two possibilities:

- the institution hosting the gene bank becomes a member of EuroFAANG RI if the RI is managed as an association of institutions
- the Member State hosting one or several gene banks becomes the member of EuroFAANG RI if the RI is managed as European Research Infrastructure Consortium, (ERIC), this means that a government representative validates the ERIC statutes;

It is totally premature to decide about the fee that one institution or one country will have to pay in order to join EuroFAANG RI. In anycase, EUGENA could not integrate the EuroFAANG RI at the present time because EuroFAANG RI is at its conceptual phase.

Yet, if EuroFAANG RI is established after this phase as a European Research Infrastructure, it will fund “TransNational Access” (TNA) that covers the cost of using the services, i.e.: the costs of asking biological material to a biobank would be covered by TNA budget or by the users (own project money), but in no case by the biobank itself. This will imply for adhering biobank to make a full cost analysis in order to calculate a fee for users.

- **Conclusions:**

EuroFAANG RI cannot give final answers right now to EUGENA but would rather propose an action plan with a timeline so that EUGENA representatives become associated to the discussions we have within EuroFAANG, as follows:

- EUGENA members are invited to virtual meetings of think tanks as well as to webinars and trainings.
- EUGENA will be consulted on the business plan. This would be particularly important because EUGENA includes several biobanks that could join the RI in the future.

To achieve these actions, EuroFAANG RI will obtain the names of EUGENA representatives to be invited at virtual meetings.
It is to be reminded that an official commitment from a legal entity (either an institution or a State) will be needed for a gene bank to be part of a European RI.

4. Collaborative framework between EuroFAANG RI and breeding companies

The code EFABAR survey (https://www.effab.info/modern-animal-breeding/responsible-breeding/code-efabar) was analyzed to draft a collaborative framework between EuroFAANG and breeding companies (BC). EFFAB members adopt Code EFABAR every 3 years. Responses from 2017 and 2020 adoptions were considered. A new version of Code EFABAR for all species has been, published for adoption by members early 2024. BC will adopt it when their previous certificate expires. To have more consistent data from this network of breeders, we can perform a short survey on this aspect of Code EFABAR. .

The answers to the following questions were extracted from the survey:

- Genetic diversity monitoring within commercial breeds or purebred lines
- Gene conservation for commercial breeds, either *in situ* or *ex situ*
- Gene conservation for rare and threatened breeds
- Provision of mating programs for farmers to control inbreeding
- Does the BC have or contribute to a gene bank for commercial breeds?
- Does the BC contribute to the conservation of genes of rare and threatened breeds?

In addition, specific questions were asked according to species:
For cattle

- Crossbreeding programs

For poultry:

- Does the company maintain non-core product lines?
- Does the company hold lines in suitable locations to ensure security of the genetic diversity?

For Fish:

- Initiation of domestication or genetic selection of new species with an initial large genetic variation
- Mid-term live backup

a) Answers for cattle

Four companies answered.
They all recognized that genetic diversity is needed to maintain sustainable breeding and that they were monitoring inbreeding, either with specific indices or by maintaining a sufficient number of sires. All companies provide mating programs and/or recommendations to farmers to manage inbreeding.
Two companies see an interest in using crossbreeding programs.
All companies are storing frozen semen, one mentioned that it was providing biological material to the National Gene bank whereas the others only mentioned their own gene bank. One company declared taking action in favor of rare breeds, including semen cryoconservation in their company gene bank.

b) Answers for pig

Three companies answered.
Two companies are using methods to monitor inbreeding and optimize mating plans, using pedigree information, and for one of them, genomic information.
The other company is maintaining a large number of sires to avoid inbreeding.
All companies provide mating programs and/or recommendations to farmers to manage inbreeding.
In situ preservation of lines appeared to be preferred by all companies, but one company mentioned the use of frozen semen, in particular to preserve lines which are not used any more for commercial breeding. One company is conserving 2 lines of threatened breeds
Two companies use a gene bank, one contributes to a National Gene bank, the other has its own gene bank.

c) Answers for poultry

Three companies answered.
Two companies keep a large number of lines to preserve genetic diversity of their breeding material. The other one is securing a core population size of its key lines. They apply protocols to control inbreeding but do not provide mating plans to farmers who are producing the commercial animals but are not involved in breeding activities.
Two companies are using *in situ* preservation of lines and one mentions storing germplasm. The three companies declare that lines are spread over different locations for safety issues. In addition, they all declare having their own gene bank but do not detail what type of material is preserved (i.e. frozen semen or DNA for instance). No company declares taking action for rare or threatened breeds, one mentions this is the responsibility of government.

d) Answers for fish

Five companies answered.
Regarding the initiation of domestication or selection, two companies answered: one declared it is initiating domestication for one fish species, and the other one declared it is maximizing genetic diversity of the founder population (at the start of the selection).
All companies declare monitoring inbreeding to keep it below 1% per generation.
In situ conservation is performed in various ways: one declared getting public support for the conservation of the wild ancestor species, two are spreading the population over two different locations for safety (as done in poultry), another one is conserving the founder generation as a live flock.
Three companies use semen cryoconservation which is performed for all selected males.
Three companies are using a gene bank, either public or private. One of them is using both a private and a public gene bank.
The concept of rare breeds do not exist in fish breeding, but wild resources can be threatened and one company declares an action for the preservation of a wild species.

5. Conclusions

In total, 15 breeding companies adopted code EFABAR. All of them declare monitoring inbreeding to limit the loss of diversity. In addition to *in situ* conservation programs, most of them are using gene banking for *ex situ* conservation but only four are storing samples in a public gene bank, generally the National Gene bank, which could be part of EUGENA already, but this information is not reported in Code EFABAR.
Thus, the main issue foreseen for collaborating with breeding companies is data privacy since most of them keep biological material in their own gene bank but do not make this information public because it is considered as strategic. Yet, it is positive to see that they are already investing in gene banking, and aware of the usefulness of it.
Regarding the issue of rare or threatened breeds, the situation varies according to species: most cattle breeding companies are concerned about rare breeds, only one pig breeding company declares this concern whereas no poultry breeding company contributes to preserving rare breeds. In fish, at present, threatened populations seem to be wild, and one company takes action for the preservation of a wild species.

This result will be updated when all answers from the 2023 survey version will have been collected. This survey includes additional questions, as listed in Appendix 1

6. Appendix 1: Questionnaire for the ongoing Code EFABAR 2023 version

Code EFABAR 2023 Version	
Have the following breeding elements been implemented in the BC breeding programme?	
Species	**Breeding elements**
Aquaculture	Initiation of domestication or genetic selection of new species with an initial large genetic variation. Management of genetic variability in selected lines to limit increase of inbreeding rate. In-situ conservation of genetic resource. Mid-term live backup. Long-term cryo-banking of genetic resources (germ, stem cells, sperm, oocyte or larvae. Amount of cyro conservation (% male nucleus frozen). Use of pedigree to manage inbreeding. Use of a minimal number of parents per generation and appropriate measures to minimise inbreeding in respecting < 1% of increase in the rate of inbreed. **Are there any other breeding elements that are important to your BC and should be considered?**
Pig	Is the genetic diversity within purebred lines recorded? (Preventing inbreeding at population and individual levels)? Is the conservation of alleles of purebred lines implemented? (in situ or ex situ)? Is there a programme for conservation of alleles of rare and threatened breeds? Does the BC provide a mating program for farmers to manage inbreeding?(rate of inbreeding per year, FAO)? Has the BC implemented optimum contribution selection (or other methods to balance genetic progress and rate of inbreeding increase)? Is a genomics-based parentage testing implemented (using STR or SNP markers)? **Are there any other breeding elements that are important to your BC and should be considered?**
Poultry	Genetic variation within purebred lines. Conservation of genes of purebred lines (in situ or ex situ). Limiting inbreeding (balancing rate of inbreeding with rate of genetic change). Preservation and improvement of local breeds. **Are there any other breeding elements concerning genetic diversity that are important to your BC/O and should be considered?**
Ruminants	Maintaining genetic variation in commercial breeds. Conservation of genes of commercial breeds (in situ or ex situ). Cross breeding (programs): for hybrid vigour, rescue rare species. Maintaining pure breed populations. Conservation of genes of local and indigenous breeds. Provision of mating programs for farmers to control inbreeding. Genomics-based parentage testing implemented (using STR or SNP markers)

Code EFABAR 2023 Version	
Have the following management elements been implemented in the BC breeding programme?	
Species	**Management elements**
Aquaculture	Does the BC operate its own or contribute to a public gene bank for commercial breed? Does the BC operate its own or contribute to a public gene bank for commercial lines? Does the BC contribute to the conservation of genes of rare and threatened breeds? Does the BC use pedigree management using physical tagging and genomic selection? **Are there any other management elements that are important to your BC and should be considered?**
Pig	Does the BC operate its own or contribute to a public gene bank for commercial pig breeds/lines? Does the BC contribute to the conservation of alleles of rare and threatened pig breeds? Are there any other management elements that are important to your BC and should be considered? Does the BC/O safeguard valuable genetic resources against future disasters such as disease outbreaks? **Are there any other management elements that are important to your BC/O and should be considered?**
Poultry	Does the BC/O record and monitor the inbreeding level in its pure lines? Does the company maintain non-core product lines? Does the company hold lines in suitable locations to ensure security of the genetic diversity? Does the BC/O have or contribute to a gene bank for commercial breeds? Does the BC/O contribute to the conservation of genes of rare and threatened breeds? **Are there any other management elements concerning genetic diversity that are important to your BC/O and should be considered?**
Ruminants	Does the BC/O have or contribute to a gene bank for commercial breeds? Does the BC/O contribute to the conservation of genes of local and indigenous breeds? Does the BC/O safeguard valuable genetic resources against future disasters such as disease outbreaks? **Are there any other management elements that are important to your BC/O and should be considered?**