A European infrastructure for farmed animal genotype to phenotype research

Deliverable 7.3
Template of collaboration agreements between EuroFAANG and INFRAIA projects for animal phenotyping

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Table of Contents

1. Executive Summary

Background	EuroFAANG must demonstrate its added value compared to existing research infrastructures (RIs) in the ESFRI Roadmap as well as to completed and on-going INFRAIA projects that are potential future RIs. To address objectives of Genotype to Phenotype research, EuroFAANG has to seek collaboration with research infrastructure projects providing services on animal phenotyping. Added value and reciprocal benefits can be sought at different levels, including tools, protocols, and data; developing complementary services; organizing joint training; fostering cross domain research connections.
Objectives	To map the relevant projects from the INFRAIA, INFRA-DEV, INFRA-SERV, INFRA-TECH actions. To establish a framework of collaboration between animal phenotyping INFRAIAS and EuroFAANG.
Methods	Discussions with each animal phenotyping INFRAIA project were reported previously in MS19 and MS20 that will serve as references. In 2024, the three INFRAIA projects AquaExcel, PIGWEB and SmartCow, submitted an INFRA-DEV proposal, named Pheno-Live. Complementarities between EuroFAANG and Pheno-Live were obvious and it was decided to merge services and resources of EuroFAANG and Pheno-Live in a single RI named GenoPHEnix that was submitted to ESFRI Roadmap on April, 8, 2025. This new proposal integrates all elements required for EuroFAANG to collaborate with animal phenotyping INFRAIA projects.
Results & implications	The scientific study supporting GenoPHEnix application to ESFRI highlighted the important complementarities between services offered by EuroFAANG and Pheno-Live partners. Goals, services, access units and cost units were defined. A common access policy was established. Two examples of research projects combining in vivo and in vitro phenotyping, with biobanking and data sharing are provided. A consortium agreement was signed by 16 institutions to ensure continuous partnership until the expected registration on the ESFRI roadmap. If GenoPHEnix is succesfully registered, the preparatory phase will develop a single portal to access to all services and consolidate the European added value of this new RI for farm animals. In case GenoPHEnix is not accepted by ESFRI, the momentum created by the preparation of the proposal has clearly established the complementarities between *in vitro* and *in vivo* phenotyping services and the need to expand the animal genomics FAANG data portal to phenomics data. Participations in future INFRA-SERV projects will be seeked, in collaboration with existing ESFRI projects or landmarks (as described in D7.2)

2. Introduction

2.1 Discussions with the animal phenotyping INFRAIA projects (MS19 and MS20)

AquaExcel

AquaExcel started as an INFRAIA project and the current consortium is the 3rd project that is established to support high-quality, ethical aquaculture research across countries by providing access to experimental facilities and services. On October 17, 2023, EuroFAANG had a discussion with AquaExcel during its annual assembly meeting. From the discussion, it was gathered that AquaExcel ensures compliance with ethical standards through consistent application of the 3Rs (Replacement, Reduction, and Refinement), accounting for varying national legislations. Aqua-Excel 3.0 is already offering access to some cellular models, including the use of genome editing. So, its objectives are in good agreement with those of EuroFAANG. One strength of Aqua-Excel is its long experience in managing Trans National Access (TNA), which allows researchers (both academic and from industry) to access aquaculture infrastructures across Europe to conduct experiments.

AquaExcel plays a key role in promoting collaboration between academia and industry, with about 30% of its projects coming directly from industrial stakeholders. This enhances knowledge transfer and innovation in the sector.

To support long-term sustainability, AquaExcel seeks diverse funding sources beyond EU support (e.g., ESFRI Roadmap) and aims to keeps the community of partners active and coordinated. While it has some internal biobanking functions, AquaExcel currently operates independently of centralized biobanking infrastructures but sees future potential in such partnerships, especially for the storage and study of infected tissues.

PIGWEB

PIGWEB is a European infrastructure project for experimental research for sustainable pig production and phenotyping. It provides access to experimental and analytical facilities across partner institutions through Transnational Access (TNA) calls. The project aims to harmonize methodologies, support industry engagement, and promote alternatives to invasive procedures. Its long-term goal is to secure sustainability through inclusion in the ESFRI Roadmap.

On December 19, 2023, EuroFAANG had a discussion with Jaap van Milgen, the PIGWEB Project Coordinator. From the discussion, it was concluded that PIGWEB is interested in collaborating with EuroFAANG and sharing community-agreed protocols. In vitro cellular models that align with 3Rs principles are seen as valuable additions. No major obstacles to collaboration were foreseen. While PIGWEB does not have formal biobanking activity, it does sample transport and regroup farm animal samples. A future partnership with a biobanking infrastructure could be beneficial for farm animal research. It was also

mentioned that TNA access is vital but must be carefully managed. Not all facilities are always open to external users, so early dialogue is essential. Regarding quotation for TNA, two cost models discussed included unit cost per facility and actual project costs. Funding via INFRA-SERV grants helps balance national cost disparities and ensures fair distribution using “unit of access“ metrics (e.g., “access to measures on one pig facility for one week“). PIGWEB is not yet connected to ELIXIR. The physiology research community is less familiar with large-scale data infrastructures, and collaboration with EuroFAANG could help bridge this gap.

SmartCow

The former INFRAIA project named SmartCow was the first to be supported as an INFRAIA for cattle phenotyping, with similar objectives as those of PIGWEB, on a ruminant species. SmartCow proposed to test technological developments in various areas of animal nutrition: 1) Feed additives to reduce methane emissions, 2) New strategies for supplementing rations with synthetic essential amino acids, 3) Probiotics to improve the digestive health of animals, 4) Mineral supplements and 5) Animal activity sensors. Several projects have led to additional collaborations between industrial partners and the research infrastructure, mobilizing additional resources for the SmartCow project to complete the research. SmartCow also supported standardization of protocols and provided access to experimental facilities for cattle, either dairy or beef. It was not connected to biobanking, neither to ELIXIR. It was terminated before the start of EuroFAANG but is still offering some of its services of cattle phenotyping in the frame of INFRA-SERV AgroServ project.

These three INFRAIA projects were all coordinated by INRAE institution, France, and had some partners in common with EuroFAANG, such as FBN, WUR and EFFAB.

In conclusion, it appeared that services proposed by EuroFAANG and services offered by these INFRAIA projects could be highly complementary, regarding the scale of study from cellular to whole organism, as well as the interplay between *in vitro* and *in vivo* approaches. Furthermore, there was no equivalent to the EuroFAANG data portal for phenotyping data, so that there was an obvious advantage for animal phenotyping infrastructures to benefit from the expertise developed by EMBL-EBI for the EuroFAANG data portal.

2.2 Building the GenoPHEnix ESFRI proposal

In April 2024, partners of the three INFRAIA projects, Aqua-Excel, SmartCow and PIGWEB had put together an INFRA-DEV project, named Pheno-Live, to prepare an ESFRI proposal on animal phenotyping. This project was referring to EuroFAANG for services on

biobanking and cellular models, and was raising similar issues on data fairness. However, this project was not selected. Following this event, some EuroFAANG partners, namely INRAE and FBN, suggested that Pheno-Live and EuroFAANG may work together to prepare a common ESFRI proposal for an integrated research infrastructure on farm animals, combining phenotyping, biobanking and data services.

In October 2024, both consortia met in Brussels and decided to join their efforts to elaborate a unified proposal for the ESFRI roadmap, which has been named GenoPHEnix, in order to submit it at the call of the ESFRI roadmap update 2026, with the submission of the proposal on April, 8, 2025.

At this moment, collaboration between EuroFAANG and animal phenotyping INFRAIA projects engaged into a strategy of long-term partnership. Indeed, GenoPHEnix has been designed considering the needs expressed by:

- Users of existing INFRAIA projects (SmartCow, PIGWEB, AQUAEXCEL 3.0),
- Responses to biobanking and technology surveys conducted by the INFRA-DEV EuroFAANG project, - Recommendations from expert Think-Tanks on cellular models and genome editing.
- the outcomes and expectations of six EuroFAANG Horizon 2020 projects (BovReg, GeneSwitch, Rumigen, Holoruminant, AquaFAANG, Geronimo),

To prepare the submission of GenoPHEnix proposal, a **consortium agreement** has been signed by 16 research institutions from 12 countries, which states in its preamble: "*that said Pan-European distributed research infrastructure's mission and tasks would consist in (a) providing users from both the research/academic world and the business/industrial world with access to research, development, training and advisory services, and through those services, to resources such as, but not limited to, research facilities, expertise and data; (b) coordinating the efforts of the farm/aquafarm genomics and phenomics community through the adoption of a community-wide Scientific and Technological Agenda; (c) advancing scientific knowledge and technologies through joint research and development activities involving Members; (d) harmonising methods and protocols in the scientific community through the adoption of common standards and practices; (e) contribute to a more innovative Europe through collaborations with relevant industries; (f) training researchers and technical personnel in advanced methods of genomics and phenomics; (g) promoting multi-disciplinary research in association with research infrastructures in related and/or complementary fields*;".

Thus, this agreement provides a basis for establishing a long-term collaboration between animal phenotyping services and EuroFAANG services. Its aim is '*to design a future pan-European legal entity invested with the mission of producing services for R&D&I stakeholders in the field of farm and aquafarm animal genomics and phenomics*'. Services proposed by EuroFAANG as well as animal phenotyping services are listed in the annex of this consortium agreement which will be into force at least until the ESFRI decision to include, or not, GenoPHEnix on its roadmap.

In the following, this deliverable will present access to services already achieved by animal phenotyping INFRAIAs and by the FAANG data portal and provide case studies illustrating how EuroFAANG and animal phenotyping services could be merged.

3. Access to services

3.1. TNA experience of animal phenotyping services.

Animal phenotyping INFRAIA projects (AQUAEXCEL 3.0, SmartCow, PIGWEB) have a strong experience in managing access to their services and are members of two INFRASERV projects, AgroServ and AQUASERV.

The process is described below:

The possibility to propose a TNA project is widely disseminated through networks and presentations at international conferences. A procedural manual is available online to any potential user describing the principles of TNA, the types of facilities and expertise offered, the research priorities and the procedures to apply for TNA access.

For each TNA call an initial evaluation for eligibility (participation rules) and feasibility (availability of facilities) is conducted by the Access Management Team and facility managers in order to give applicants a rapid response and decision on whether they should work on a full proposal. Each of the eligible Full Proposals is independently evaluated by internal reviewers (i.e. from a project partner not involved in the proposed work/facility) and external reviewers in order to rank them based on their scientific value, originality, plans for dissemination and optimal use of facilities. Proposals are also checked by the Ethics Committee (reviewers are asked to flag any specific issues, but on this occasion the Committee looks at all applications). Evaluation scores and ranking are then considered alongside the availability of space at each facility and discussions amongst the Access Management Team identified options for alternative (second preference) facilities in some cases. These options are then discussed with Facility Managers and a final list of approved projects and available facilities is drawn up.

Characteristics of TNA projects from the three INFRAIS projects are summarized here:

Project	Years	Number of TNA projects		Acceptance rate	TNA budget (k€)	
		submitted	selected		Total	/ Project
AQUAEXCEL	2011-2015	136	98	72.1	2 800	28.6
AQUAEXCEL2020	2015-2020	179	136	76.0	3 900	28.7
AQUAEXCEL3.0	2021-2025	188	142	75.5	4 900	34.5
SmartCow	2018-2022	48	24	50.0	1 500	62.5
PIGWEB	2021-2026	70	30	42.9	1 500	50.0
Total / mean		**621**	**430**	**69.2**	**14 600**	**34.0**

3.2. EuroFAANG experience in data services

The FAANG Data Portal (https://data.faang.org/) has been developed and managed by EMBL-EBI to offer a centralised access point for farmed animal datasets. The Data Portal acts as a brokering tool, that facilitates both metadata and data submission and validation into EMBL core data services. It also acts as a single centralised point of access to data stored within EMBL core data services, consolidating and improving the findability and accessibility of the datasets for the user community. Data can be searched based on multiple criteria including, species, tissue, developmental stage, submitter, assay type etc. Users can submit complex search queries in the same session and could search for, as an example "all RNA-Seq datasets from mammary gland tissue for cattle [RNA-Seq; cattle; mammary gland]". This search function means that users do not need to make multiple queries across several data repositories to find the datasets they are looking for.

The data portal is also highly scalable for the increasing amount of data that is being produced for farmed animals and will be expanded for GenoPHEnix to include additional data types such as qualitative measurement data for phenotypes and image data.

For any researcher planning a new experiment, the portal also makes it possible to find existing protocols. The choice of samples, and recording useful and detailed metadata, are key steps to be able to produce new and useful data that can be merged with existing datasets. Thus, a set of metadata standards has been defined for researchers in the FAANG consortium (https://doi.org/10.1111/age.12736). These rules include information about sample type, derivation and are based on standardised ontologies. To facilitate metadata and data submission, the FAANG portal provides an on-line service for validation of the metadata associated with samples before submission to the Biosamples database.

4. Merging animal phenotyping services and EuroFAANG services in GenoPHEnix

The GenoPHEnix proposal has identified five categories of services:

- Experimental services, provided by INFRAIA projects
- Laboratory services, provided by INFRAIA and EuroFAANG projects
- Data and associated services mainly provided by EuroFAANG project
- Biobanking services provided by EuroFAANG project
- Training services, provided by INFRAIA and EuroFAANG projects

A table of services is provided in annex. List of services offered to RIA projets is discussed in D7.4.

The examples below are taken from the scientific study design of GenoPHEnix.

4.1 Service integration case #1 *– Feed efficiency: Phenotyping of feed intake, digestive and metabolic functions using gold standard methods, proxies, in vitro methods and biobanking*

Background: Nutritional studies aim to assess the nutrients provided by feeds and diets (feed evaluation) on the one hand, and the nutritional requirements of animals on the other, with the objective of aligning them to enhance nutrient use efficiency.

Novel methods for evaluating feed and animal nutritional requirements:

There is consensus that alternative, less-invasive tools are needed to replace conventional "Gold Standard" methods, which are not always suitable to all farming systems, particularly extensive or semi-intensive conditions (i.e. outdoor). Different proxies will be proposed for the evaluation of feed and animal requirements, based on:

- Individual measurement or prediction of feed intake even if animals are raised in groups using automatic devices, animal sensors, image analysis or proxies.
- Faecal spot sampling to predict the whole-tract digestibility from Near Infra-Red Spectrometry (NIRS) analysis and then the absorbed nutrients.
- Blood and saliva sampling to monitor metabolic profiles and isotopic signatures to characterize the metabolic use of protein and energy for growth and lactation as well as for the composition of body weight (BW) gain.
- Use of gut organoids to test digestibility of feeds differing in composition
- Analyses of respiratory gas exchanges via spot sampling at feeding as proxies of whole-day energy expenditure and metabolic balance.

Actions:

1. Cataloguing EU laboratories and databases on the prediction of diet digestibility from faecal NIR spectra.
2. Biobanking faeces for future microbiota studies
3. Biobanking blood for future genetic analyses
4. Standardisation and validation of NIR spectra methods for prediction of diet digestibility.
5. Multi-species guidelines for predicting diet digestibility with alternative methods.

6. For each animal species, inventory of candidate and reliable blood or saliva biomarkers that translate the metabolic use efficiency of energy and protein and the composition of body weight gain.
7. Searching for biobank samples of faeces, or blood or saliva coming from animals with phenotypic information on feed efficiency and use them to validate biomarkers
8. Identifying universal biomarkers across species to evaluate both the metabolic use efficiency of protein and energy and the composition of BW gain, and evaluate their validity, precision, variability, robustness and harm/benefit.
9. Correlate these biomarkers with genotypes of animals
10. Building a multi-species database of spot measurements of gas exchanges together with whole-day values of energy expenditure and metabolic balance.

4.2 Service integration case #2 – *Body composition: Phenotyping of body composition and its temporal variations through non-invasive methods and linking with biobanking*

Background: Body composition and its temporal changes are major determinants of the efficiency (including feed use efficiency) and resilience of farm animals. Body composition traits are common across different species, but their phenotyping remains complex, especially when considering temporal changes. Potential methods for phenotyping body composition and its changes over time would include:

- Frequent BW measurements (usually performed in dairy and beef cattle on experimental farms): need to explore the potential of these frequent and temporal measurements in other species (monogastric animals).
- Body Condition Score (BCS): existence of different scales and different measurement sites: need for re-scaling at the European level (a common scale to be linked to other body composition measures), objectification of body condition using 3D imaging.
- Ultrasound measurements of backfat thickness: need to automate image analysis, use of non-contact methods.
- Imaging for carcass quality on the live animal (2D/3D and advanced data analytics, automation using AI).
- Deuterium oxide dilution measured in e.g., saliva to predict total body fat and its changes over time.
- Milk spectra: prediction of fatty acids and other metabolites related to body reserve mobilisation and metabolic status.
- "Volatolomics" and other omics techniques applied to breath, milk, blood or other body fluids to test the applicability of this method to assess energy balance, body composition and its variation over time.
- Rapid and sensitive methods to measure blood or milk proteins identified as biomarkers of body composition or negative energy balance (or inflammatory status).

Actions:

1. Mapping phenotyping capabilities across species from gold standard methods (e.g., standardisation of manual BCS, chemical analyses of animal body components including carcass) to new less or non-invasive methods (e.g. deuterated water tracer method, ultrasonography, 3D imaging, etc.)

2. Characterizing the environment of the animal: feed composition, climatic parameters
3. Searching for biobank samples of tissues, saliva or milk coming from animals with phenotypic information on body composition and use them to validate biomarkers
4. Exploration of multi-species approaches to evaluate body composition (including tests on the relevance of a method used in one animal species for another species, comparison with a gold standard method)
5. Use of well-established methods to evaluate the development of more exploratory approaches (proxies/biomarkers) and to assess their impact on AW
6. Creating and sharing large datasets dedicated to analysis of GxE interactions to support data processing, standardisation and curation

5. Conclusions

The framework of collaboration between animal phenotyping INFRAIAS and EuroFAANG is now embodied in GenoPHEnix, with a long-term perspective.

Even if the proposal would not be accepted by ESFRI, the momentum created by the preparation of the proposal has clearly established the complementarities between *in vitro* and *in vivo* phenotyping services and the need to expand the animal genomics FAANG data portal to phenomics data. Critical elements to run collaborative projects have been developed for GenoPHEnix with a typology of services, cost units, number of units. The next challenge will be to create a user interface facilitating the combination of the proposed services. Elements to be listed in a template would include goals, types of service, steps, cost units, duration, added value and exploitation.