Challenges for an integrated strategy of gene banking for farm animals in Europe

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Outline

- From gene banks to biological resource centers

  an infrastructure approach, CRB-Anim in France

- Challenges for gene banks as experienced in CRB-Anim
  - Addressing a range of species
  - Coupling genomic and reproductive material
  - Facilitating access to gene banks
- European initiatives

An infrastructure for gene banking

Genetic diversity:
a heritage and a resource for the future
to meet societal challenges

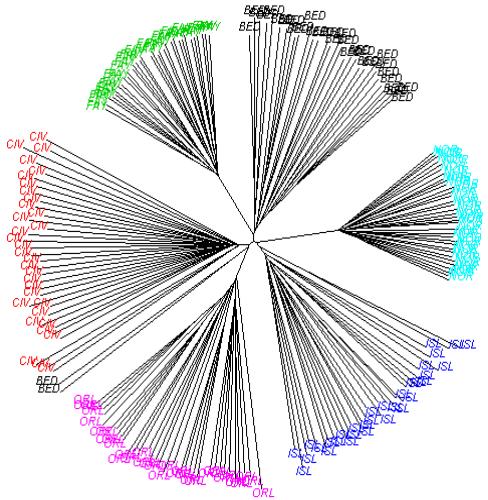
Genomics
Genome an archive of population history
& the basis of phenotype prediction

Cryobanks (*ex situ/in vitro*)
complementary to
***in situ* management**

Progress
in reproductive
biotechnologies

Connect reproductive
and genomic biobanks
→ Biological
Resource
Center

Documented biological samples



From a gene bank to a BRC

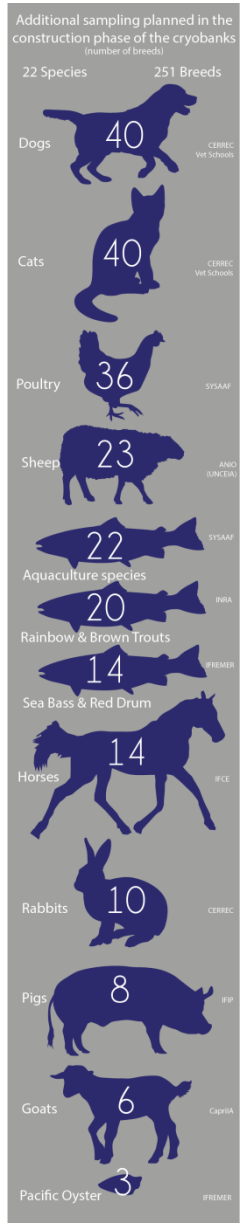
- ✓ **Objectives of gene banks**
  - **breed preservation/back up/reconstruction**
  - **combined *ex situ* / *in situ* management of genetic resources**
  - **monitoring genetic changes,**
  - **creating new breeds**
  - **research**
- ✓ **Requirements**
  - **provide traceability, safety, comply with sanitary regulations**
  - **improve practices and technologies, propose standards,**
  - **disseminate information, facilitate distribution with clear rules (IP)**

// core missions of a Biological Resource Center:
Collect/Characterize/Secure/Distribute biological samples

CRB-Anim

An integrated infrastructure of French gene banks for domestic animals

- WP1 : coordination, scientific committee, stakeholders committee, access rules and fares, communication
- WP2 : technological developments, genomics, reproductive biotechnologies
- WP3 : collections enrichment
  8900 donor animals, 22 species,
  semen, embryos, cells, DNA ; ~ 350 000 samples
- WP4 : information system, Web portal, quality certification
- WP5 : characterization of collections
- WP6 : training (academic, professional, continuous,)
- WP7 : economic exploitation: support to livestock sector, genetic models and diagnostic tests, biotech process



6 partners
11 M€

Labogena

Challenge 1: addressing a range of species

✓ **species-specific issues**

Biology of reproduction	→ sampling and storing procedures
Selection history	→ sampling rules
Legal organisation	→ sanitary regulations, property issues
Breeders' attitude	→ willingness to contribute to gene banking

✓ **main difficulties encountered**

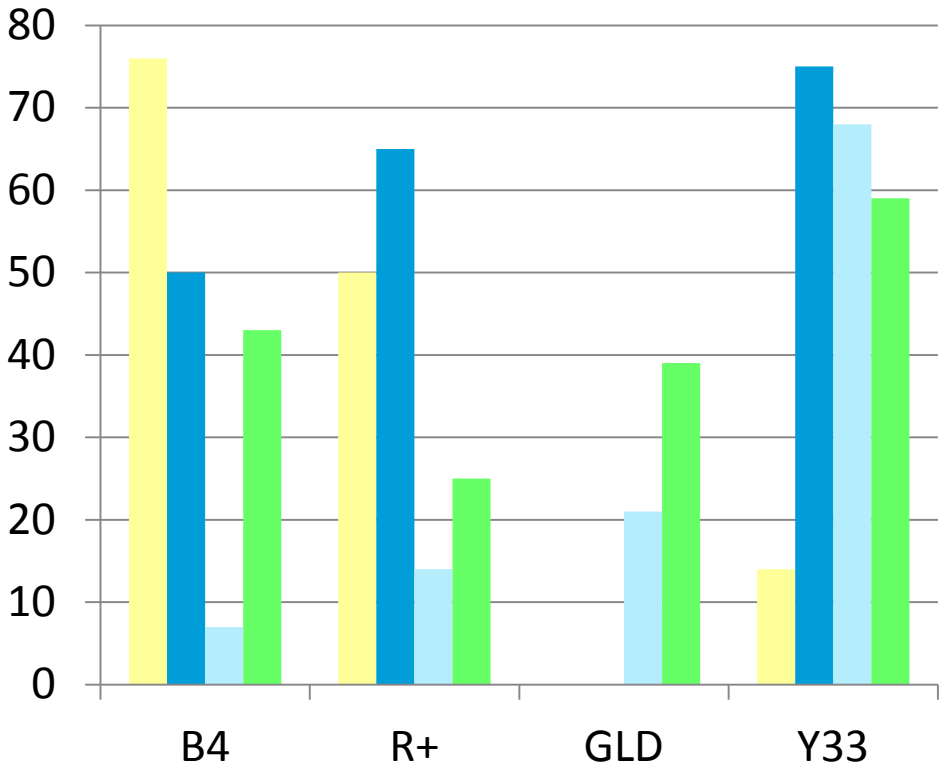
Local breeds cannot generally comply with regulations aimed at securing exports of reproductive material made for transboundary breeds

Cost of using gene bank material : logistics, know-how

Very variable fertility rate obtained from gene bank material

⇒ **the endangered breeds are often the main motivation for gene banking but they encounter the most technical difficulties to benefit from gene banks**

Variability of fertility and consequences for sampling : exemple in chickens



Blesbois et al., 2007

B4	R+	GLD	Y33
473	**973**	**492**	**536**

Number of straws to restore the line (n=40) to 97-98% identity after backcrossing

To answer these issues : improve methods to use cells with reproductive potential from gene banks

Main critical points:

Reproductive potential of cryopreserved cells

Safety conditions (storage media)

Epigenome integrity following cryopreservation

Cells/tissues concerned:
(from oyster to horses,
The « difficult « cases)

- **mature gametes (semen)**
- **Embryos and larvae**
- **Diploïd germ cells (isolated or in gonadic tissus)**
- **Somatic cells and tissues**
  To be reprogrammed in germ cells

Current approaches to improve predictability of fertility results of frozen semen for chickens

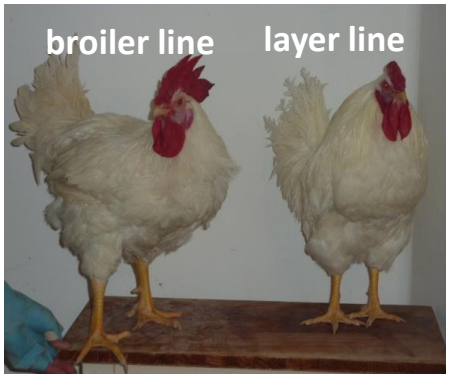
Find a fast, reliable and simple method for fertility screening


Available online at www.sciencedirect.com
ScienceDirect
www.elsevier.com/locate/jprot
ELSEVIER
PROTEOMICS
Qualitative and quantitative peptidomic and proteomic approaches to phenotyping chicken semen
Valérie Labas[a,b,c,d,e], Isabelle Grasseau[a,b,c,d], Karine Cahier[a,b,c,d], Audrey Gargaros[a,b,c,d], Grégoire Harichaux[a,b,c,d,e], Ana-Paula Teixeira-Gomes[a,d,g], Sabine Alves[a,b,c,d], Marie Bourin[a,b,c,d], Nadine Gérard[a,b,c,d], Elisabeth Blesbois[a,b,c,d,*]

- ✓ **Pilot study with proteomics**: Labas et al., 2014
  - ✓ Intact cell MALDI-TOF mass spectrometry (ICM-MS) = fast, reliable and relatively inexpensive tool to **phenotype male chicken fertility**
  - ✓ Molecular basis of infertility

1- Use of ICM-MS in a larger rooster population including different genetic backgrounds
⇒ **reproductive phenotyping**

2- Identify and characterize biomarkers
Linked to fertility ⇒**fertility molecular signatures**



Challenge 2: Coupling genomic and reproductive material

DNA banks and reproductive gene banks are poorly connected

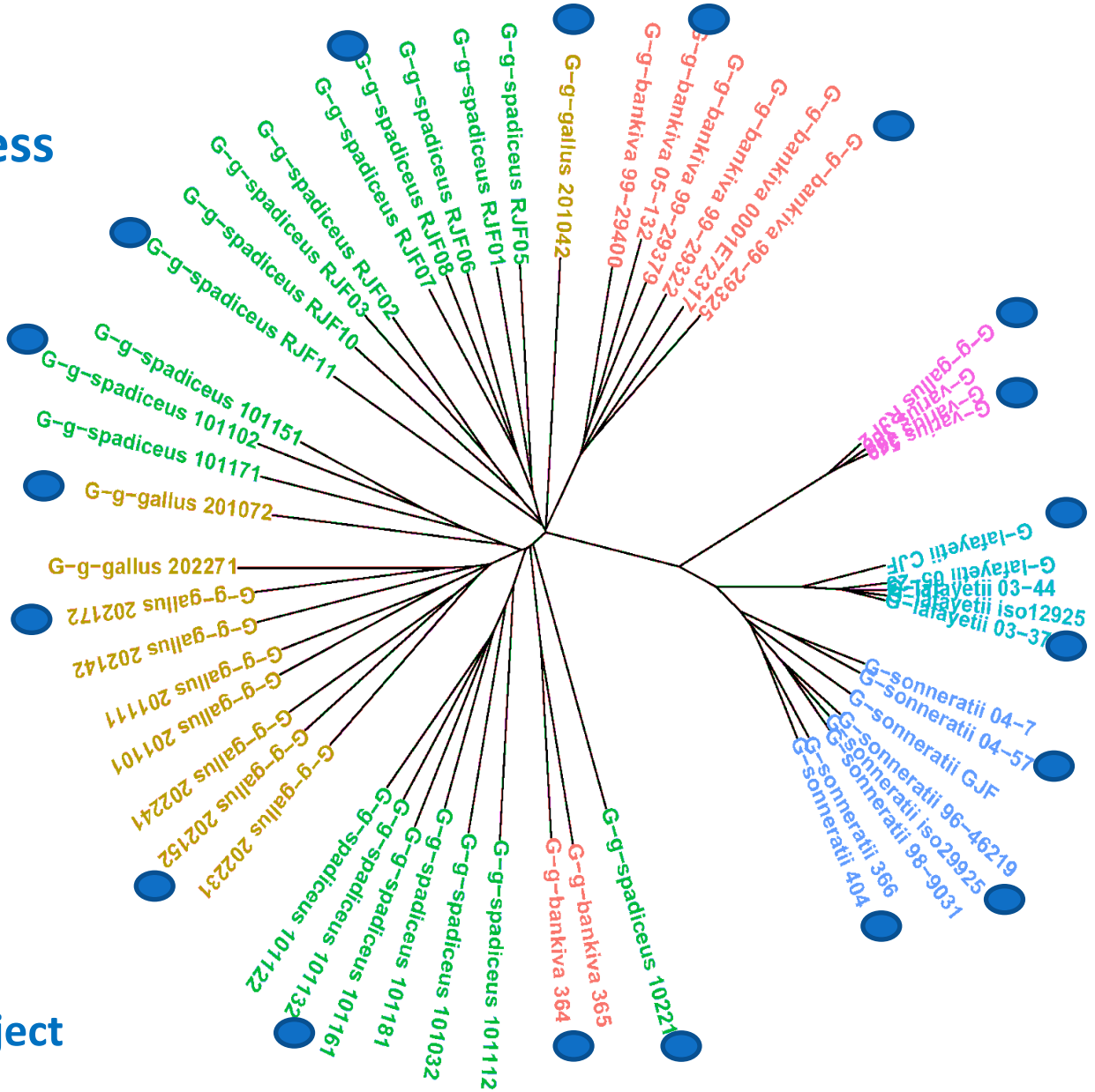
- Many advantages
  - Enhance knowledge about gene bank collections
    - assess their representativness
  - Enhance the scientific value of collections
    - including the characterization of genetic defects
  - Marker-assisted sampling/ marker-assisted use
    - refine the choice of animals on the basis of genotypes
- Major difficulties
  - Genotyping cost (lower cost/marker)
  - Data sharing policy
  - Database interoperability, , standard descriptors

Assessing Representativness

Ex: NJ tree on wild *Gallus*

57K SNP chip

Choosing animals for further study &/or sampling



Agence Nationale de la Recherche ANR **Domestichick project**

Enhancing the scientific value of gene bank collections

Screening a DNA bank to identify an IBD region for a genetic defect

Candidate region from linkage analysis

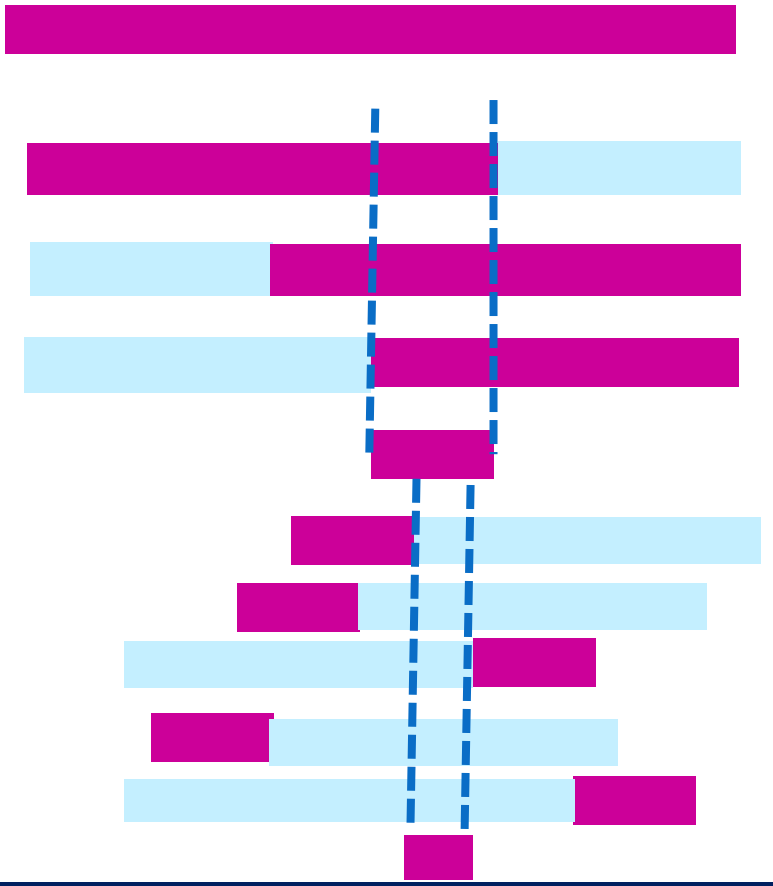
Mb scale

Genotyping or partial sequencing of the candidate region In carriers animals

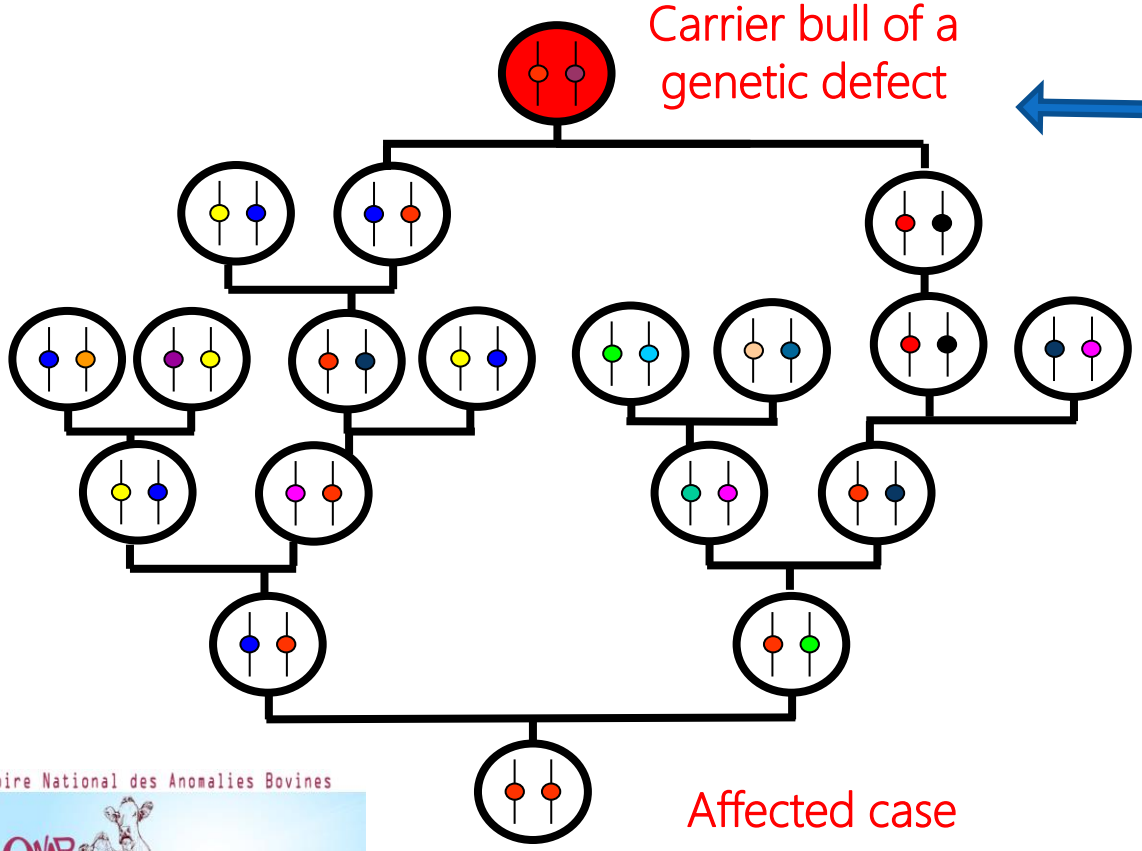
Find a common region

Scan non carrier populations

Final interval : kb scale



Trace the history of a recessive mutation



Storing DNA and semen in a BRC

↓

candidate mutation

↓

Produce carriers to study the mode of action

↓

Develop a genetic test

↓

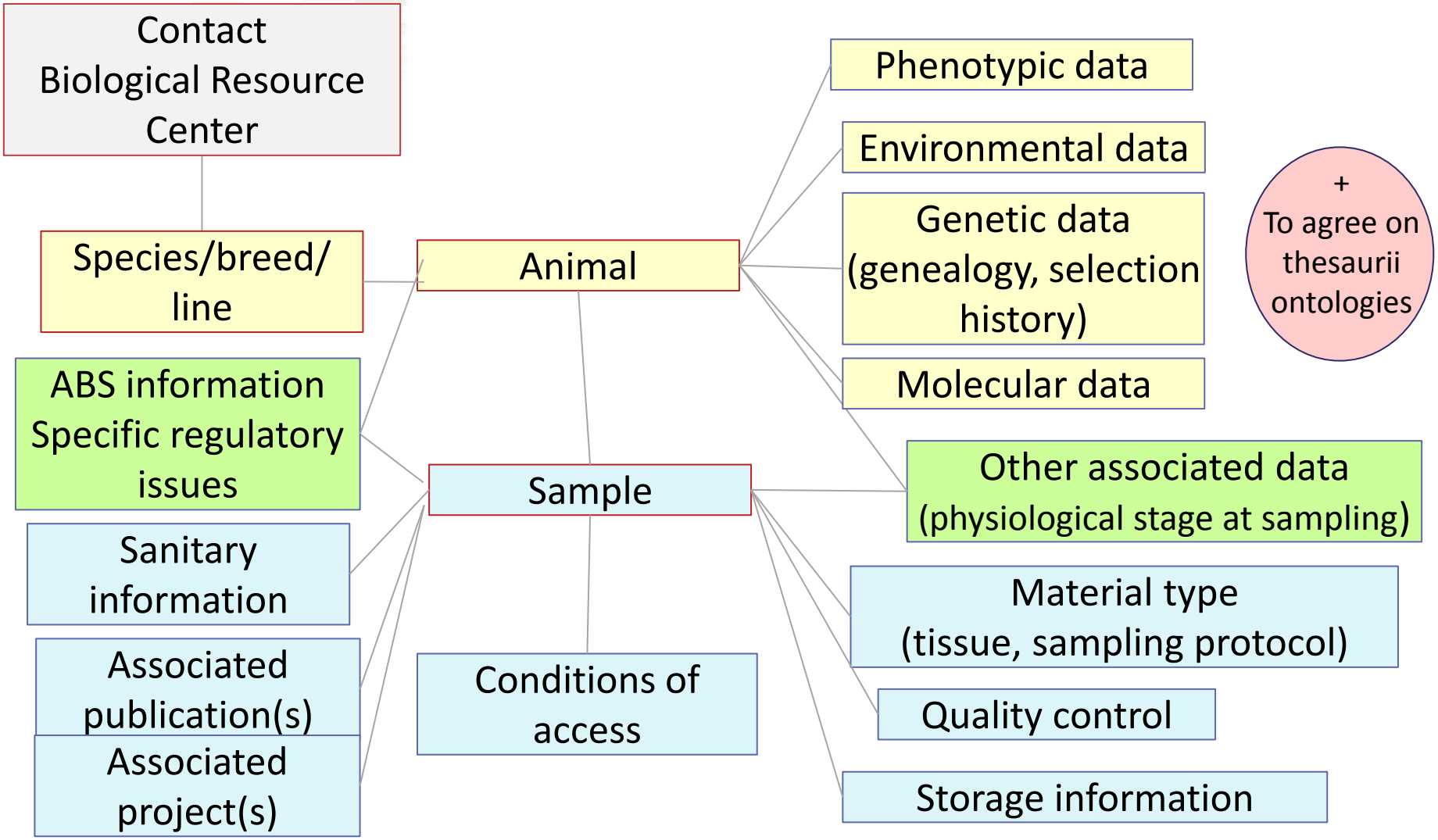
Check other gene banks' collections

Modify the population management

Observatoire National des Anomalies Bovines

French National Observatory for cattle genetic defects

Coupling gene banks: agree on common descriptors



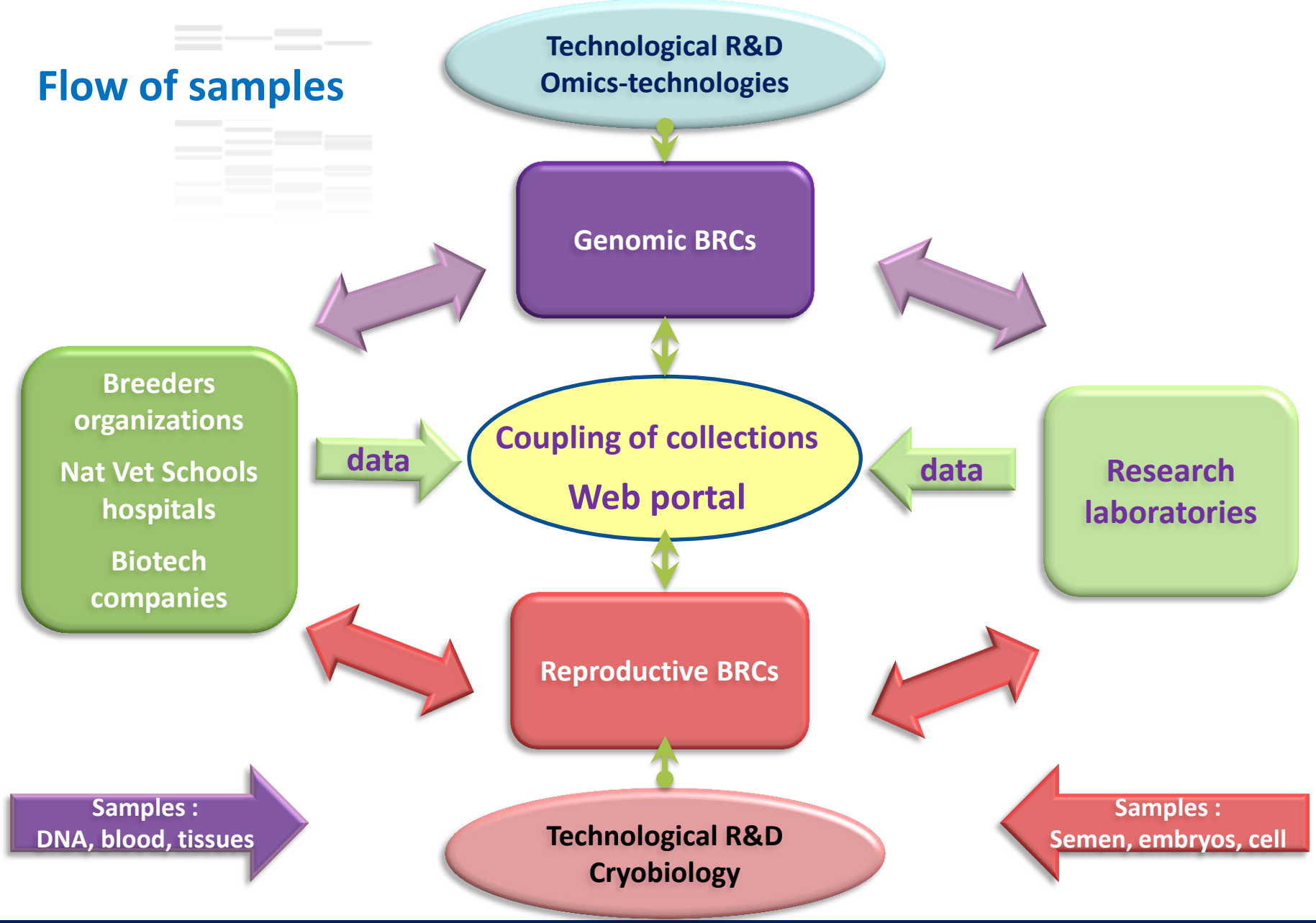
Challenge 3:
Facilitating access to gene banks

- Provide easy access to useful information : **web portal**
  to search for desired samples
  define options/criteria with users'groups
  Main request will rely on species/aim/ type of material

- Provide clear rules for entry/ distribution of samples
  Rely on a quality management system

- A demonstration project of CRB-Anim on local pig breeds

Flow of samples



What is Quality ?
Why do we need it in a gene bank ?

Quality system

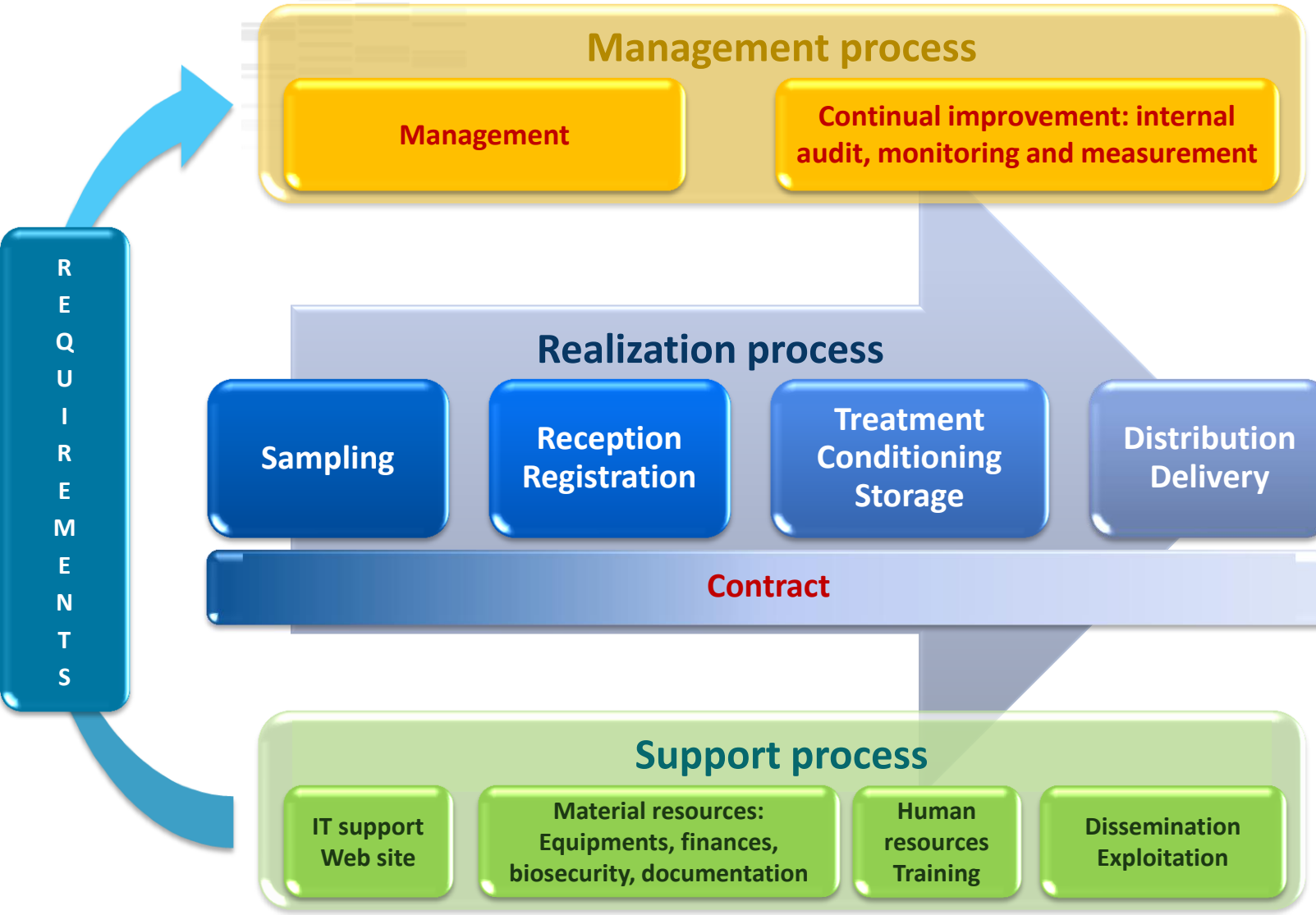
Customers requests

Products and services

Satisfy requirements of customers

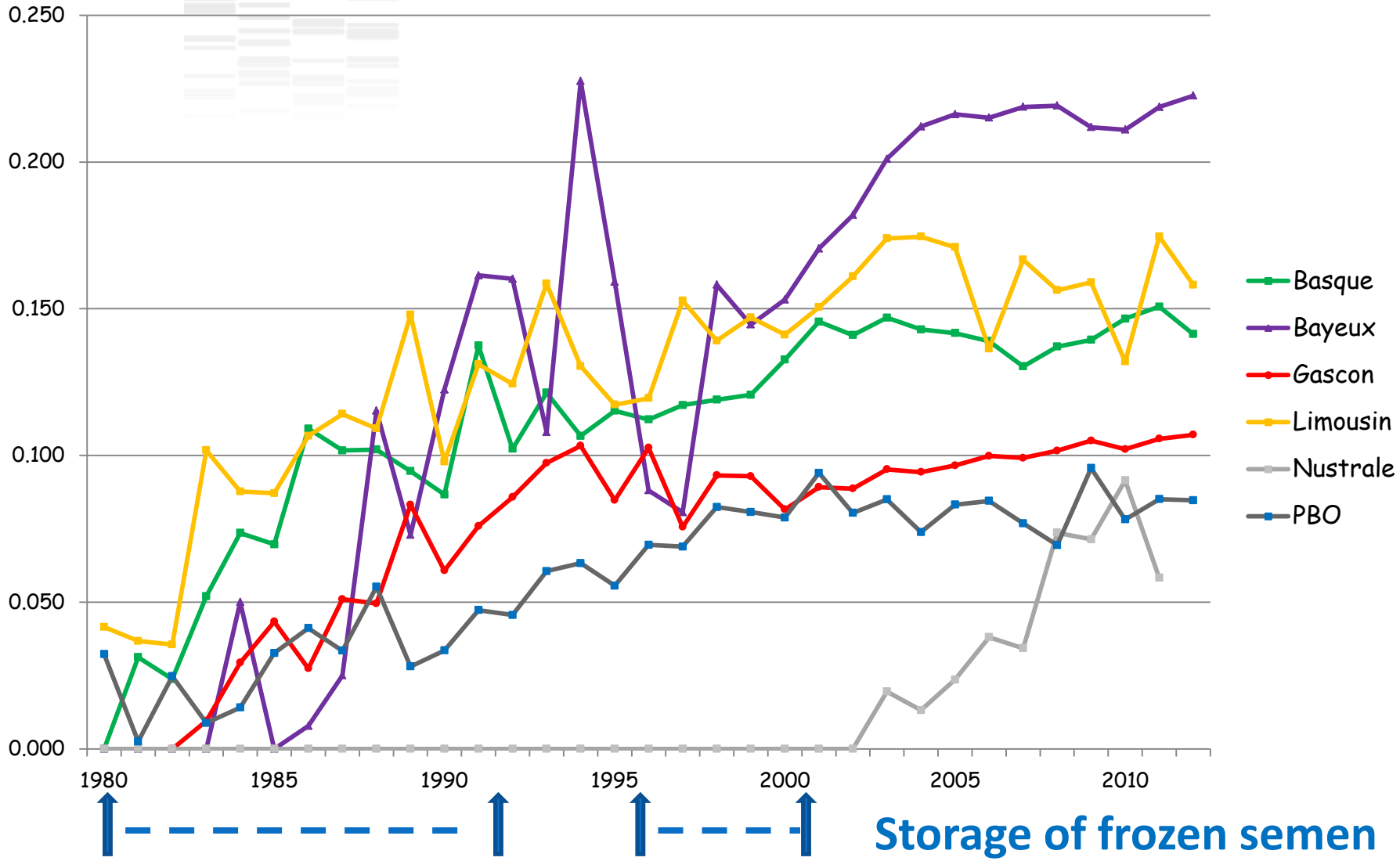
- **Guarantee traceability**
- **Transparency of procedures**
- **Satisfaction of user and of BRC staff**

BRC quality management system



Using a gene bank : a demonstration project with French pig local breeds

Trends in inbreeding



Current results

- Using 'ancient' frozen semen
  - Cul Noir Limousin , 4 boars
    - Round 1: 42% of IA were successful
    - Round 2: 62%
    - 7.2 born alive / litter, 4.7 weaned
  - Gascon (3 boars)
    - Round 1: 33%
    - Round 2 : 50%
    - 5 born alive / litter, 2.7 weaned
- New entry of frozen semen in the gene bank
  - Cul Noir Limousin : 2 boars, 162 doses
  - Gascon : 2 boars (on-going)

From a national network of Gene banks to a European Network

CRB-Anim: 2 BRC for reproductive material of different species (farm/dogs)
4 BRC for genomic material with some species in common
mostly 'specialized BRC'
sharing procedures, information, defining a common portal: effort!
impact on distributing samples: not yet !

European level: **EUGENA initiative of the European Focal Point**
a European gene banks network
☺ same range of species, same biological and genetic issues
☺ same interest in coupling reproductive/genomic gene banks
☺ in sharing technical solutions, miror collections

☹ **complex governance:** national policy / autonomy of decision
☹ **legal issues**, different property rules, different funding rules

Goals and objectives of the European project IMAGE (submitted)

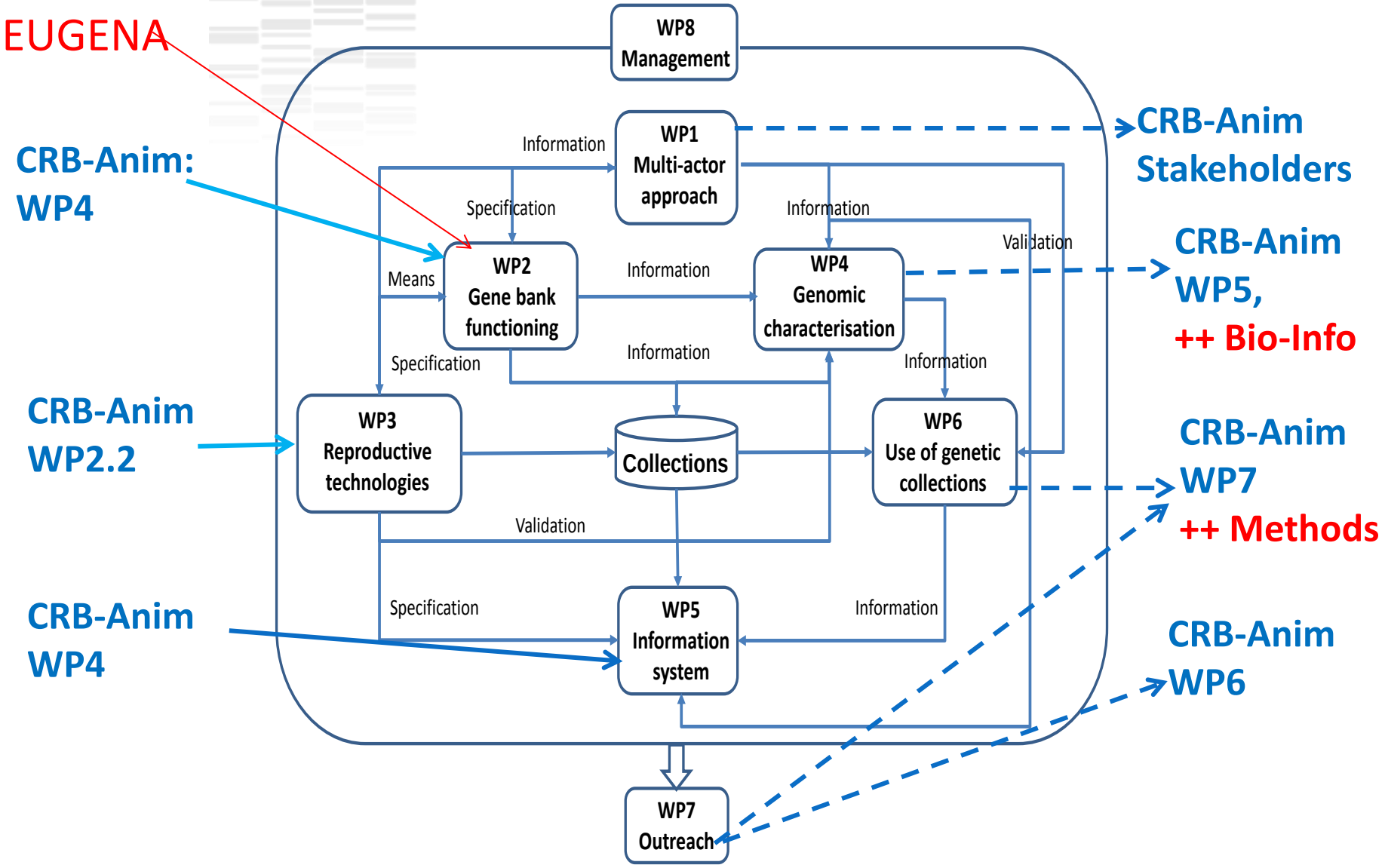
→ to **upgrade animal gene bank management through genomics and bio-informatics**

to demonstrate the benefits brought by gene banks to the development of more sustainable livestock production systems, by:

- ***Enhancing the usefulness of existing genetic collections*** *to allow the livestock sector to respond to new environmental constraints and market needs while minimising genetic accidents such as abnormalities or loss of genetic variability*
- ***Optimising complementarity between ex situ and in situ conservation*** *to maximise resources for the future.*

28 partners 3 SMEs, 3 NGOs, FAO, 9 research institutions,
11 higher education and research, INRA Transfert.
13 EU countries + Switzerland + Argentina, Columbia, Egypt, Morocco

IMAGE: breakdown of activities into 8 main WP



Conclusions

- **Promote a dynamic management of gene banks**
  - **Developing complementarity between *in vitro*/ *in situ* conservation is more valuable than « storing without using «**
  - **Reintroducing diversity in selected populations, to monitor inbreeding is currently more cost-effective than breed restoration because of limited or unpredictable efficiency of reproductive technologies in many species**
  - **Innovative uses : combine old and new genotypes for new needs?**

- **To achieve this: cooperation is needed between gene banks**
  - **Develop standard procedures , explain rules of access**
  - **Share data and metadata thanks to web tools**
  - **Funding needed : H2020, genetic resources focus group discussion**

Acknowledgements

Nicolas Coudert, Président du LIGERAL
Marie-José Mercat, IFIP,

All members of CRB-Anim

Coralie Danchin-Burge, Idele ,
Delphine Duclos, Idele, National Cryobank

Aurélie Delavaud, FRB,
Sylvain Marthey, INRA

Elisabeth Blesbois, INRA
Aurore Thélie, INRA
Laura Soler Vasco, INRA, Agreenskills

Maelle D'Arbaumont, INRA