The French national breeding program for scrapie resistance

Session 45

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Scrapie : What is it ?

- Sheep and Goat disease.
- Neurodegenerative disease, always fatal.
- Belongs to **T**ransmissible **S**pongiform **E**ncephalopathies group (TSEs).
  - BSE (cattle)
  - Creutzfeldt Jacob (human)
  - Chronic Wasting Disease (cervidae)
  - …

Scrapie and genetic resistance

- Scrapie described in 1732 (U K)
- Genetic resistance : during 70s' (Dickinson *et al* 1968)
  - 2 lines (short vs long incubation period)
  - Incubation period controlled by a major gene
  - BUT which ?
- 1989 : identification of the PrP gene. (Hunter et al 1989)
- 3 codons implicated (136, 154, 171)

PrP polymorphism and scrapie susceptibility in sheep

	1	136	154	171	codons
ARQ		Alanine	Arginine	Glutamine	wild allele
ARH		Ala	Arg	Histidine	mutated allele
VRQ		Valine	Arg	Glut	mutated allele
AHQ		Ala	Histidine	Glut	mutated allele
ARR		Ala	Arg	Arginine	mutated allele

Low to high risk ranking of alleles for scrapie

ARR > AHQ > ARH ≥ ARQ > VRQ

Genetic resistance to scrapie

- 4 alleles used in selection (ARR, AHQ, ARQ, VRQ).
  ↳ 10 genotypes
- ARH, ARK found in French breeds but very scarce
  ↳ considered like ARQ.

Alleles		**ARR**				**AHQ**				**ARQ**				**VRQ**	
Génotype	full	**ARR ARR**	**ARR AHQ**	**ARR ARQ**	**ARR VRQ**	**AHQ AHQ**	**AHQ ARQ**	**ARQ ARQ**	**AHQ VRQ**	**ARQ VRQ**	**VRQ VRQ**
	simplified	RR	RS			SS			VX		
Scrapie status		Resistant	Semi- resistant			susceptible			Very susceptible		

French breeding program implementation

- Late 90s' → BSE crisis
- Scrapie : Human not affected
- BUT scrapie and BSE : same disease group
- Precautionary principle

  ↳ Implementation of a national breeding program for **classical** scrapie resistance

Using the genetic resistance to protect consumers

French breeding program

- The French Ministry of Agriculture launched it in 2001 and funded (partialy with EU since 2004)
- Ruled by a steering committee
  - French Ministry of Agriculture
  - Scientific and technical organisations
  - French reference laboratory
  - all the organisations of sheep production
- Main aim : Protect consumers to BSE risks and eradicate classical scrapie from France

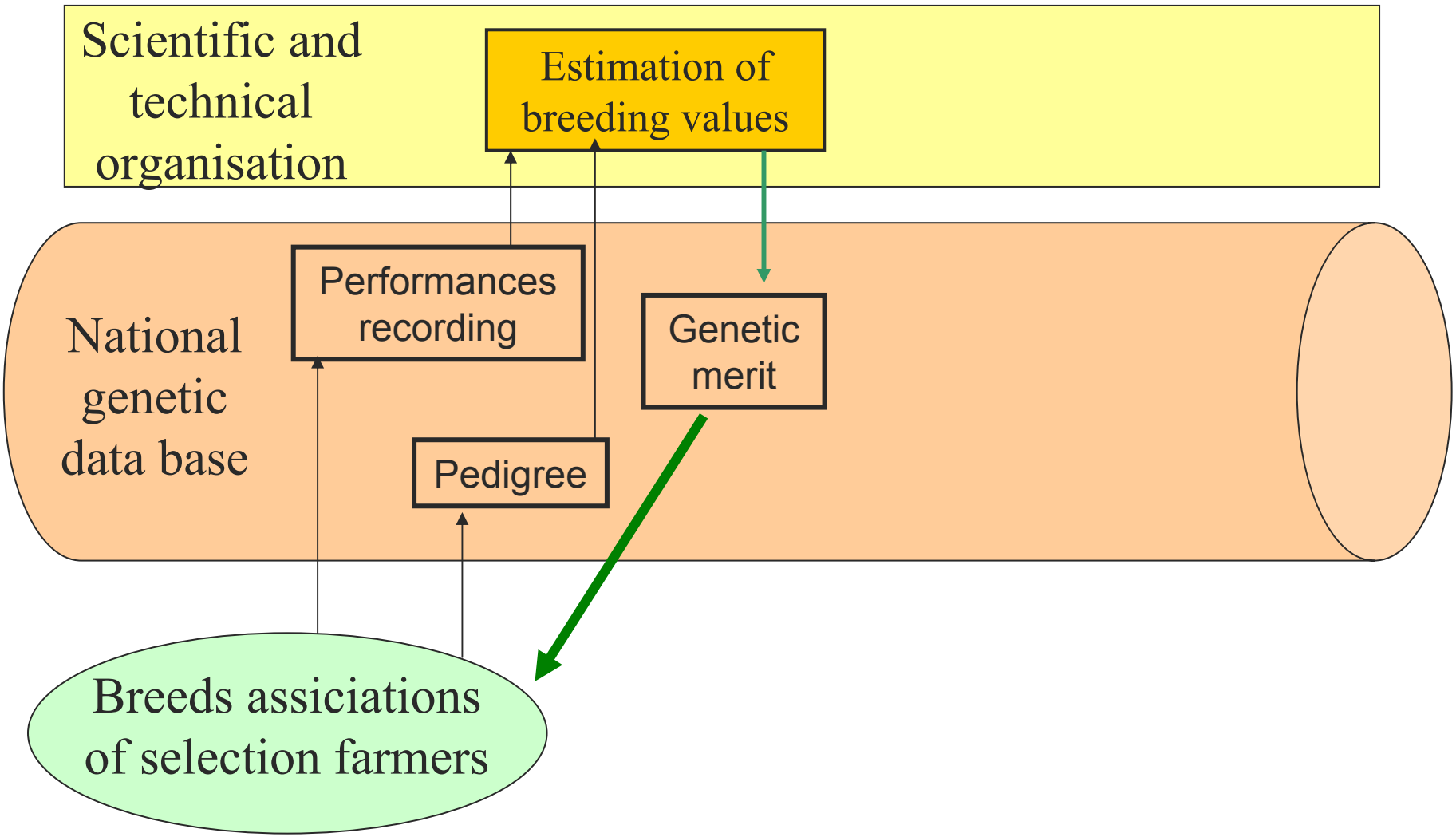
French breeding program implementation

- 4 Objectives :
  - Eliminate VRQ allele in selection flocks
  - Produce resistant animals for affected flocks
  - Selection for ARR allele while maintaining variability and genetic merit
  - Produce ARR/ARR rams for commercial flocks
- All breeds are concerned
- Based on selection flocks

Why in selection flocks ?

- Selection flocks sell reproducers to commercial flocks
- Technical know-how for selection
- National genetic data base
  - Pedigree registration
  - Performance recording
  - …
- Possibilities to make durable genetic progress on scrapie resistance.

Organisation and circulation for genetic information in France (before 2002)



Storing genotyping results

- Setting up of a national molecular data base : INMOLE
- Only laboratories with agreed process could sent results in molecular data base
- **Each result clearly identified**
  - Official N° animal
  - Gene analysed
  - Laboratory
  - Alleles
  - Analysis date
  - Others variables not essential for the identification
- Today more than 670 000 genotypes stored in INMOLE

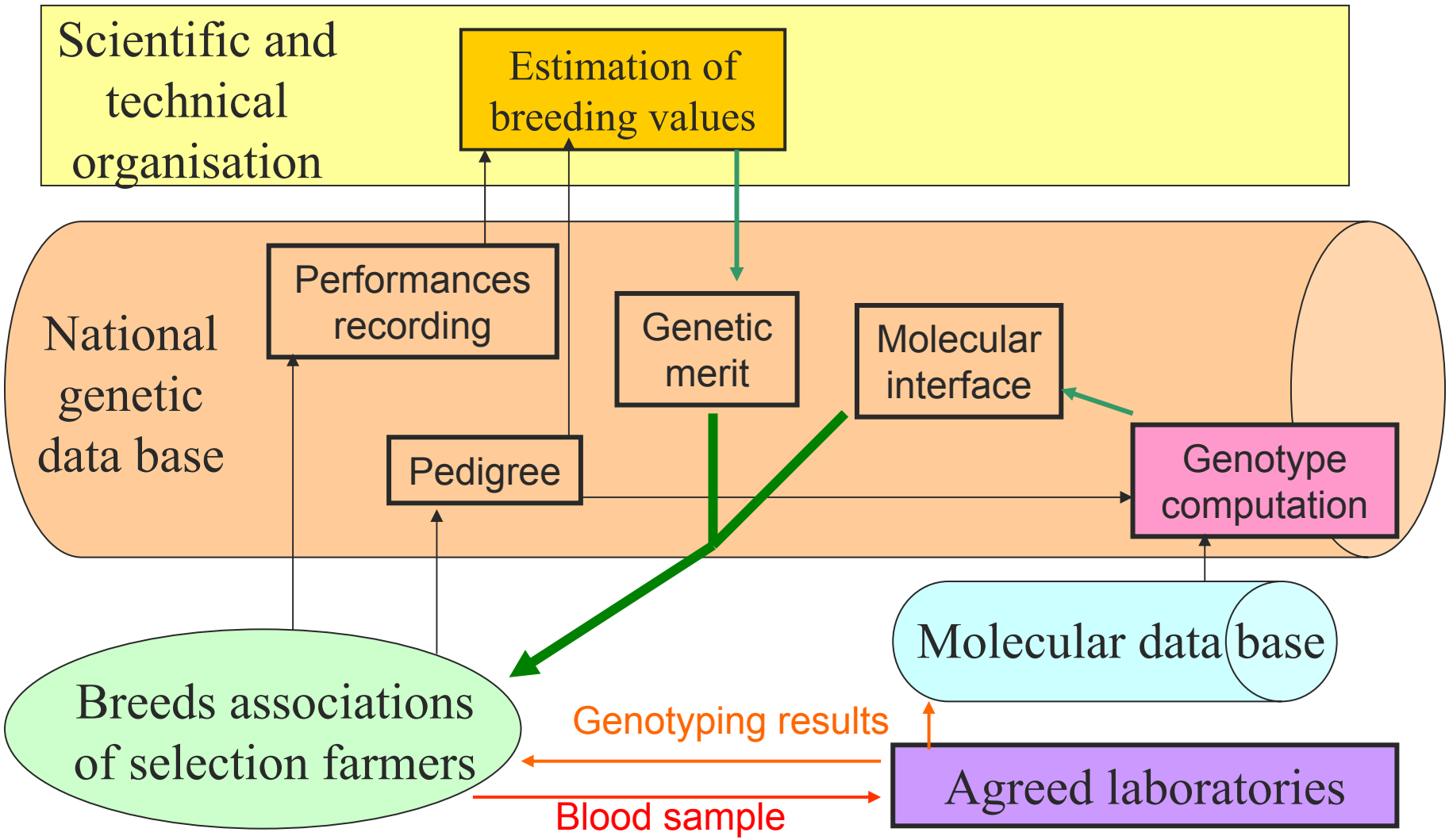
Why the centralization of genotyping results ?

- Communication between national genetic data base and molecular data base

  ↳ setting up an interface

- Now thanks to a breeding software, farmers associations have for each animal :
  - Pedigree
  - Zootechnic performance
  - Genetic merit
  - **PrP genotype**

Organisation and circulation for genetic information in France (after 2002)



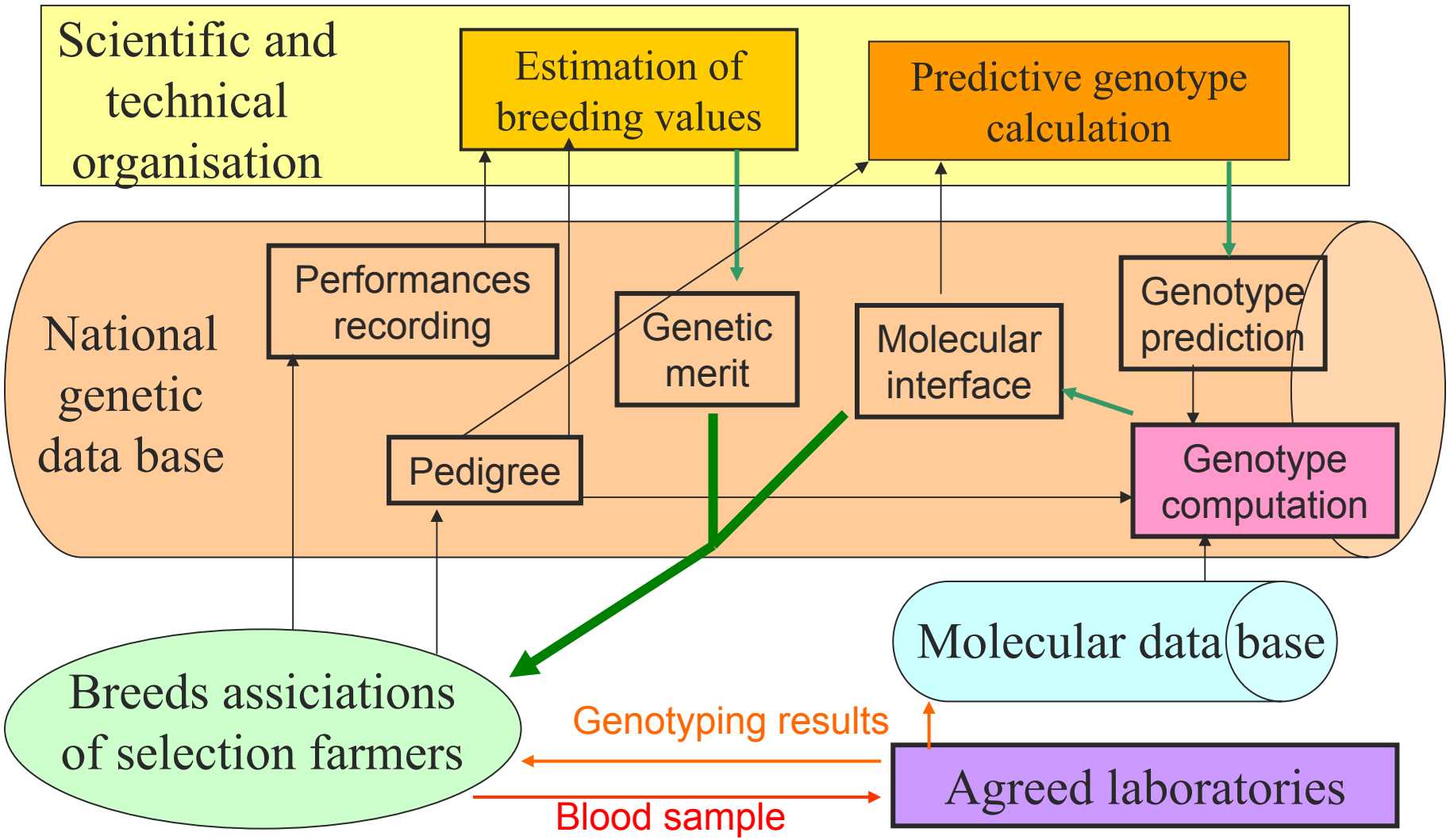
Development of genotype prediction method

- In order to give value to the pedigree information and molecular one
  - ↳ developpment of a predictive genotype method
    - Decrease of genotype analysis → less expensive
    - Best choice for animals to select
- An information reliable.
  - ↳ Almost 276 000 animals have a genotyping result and a prediction. Only 0.6% with incompatibility
- An information to store in the molecular interface

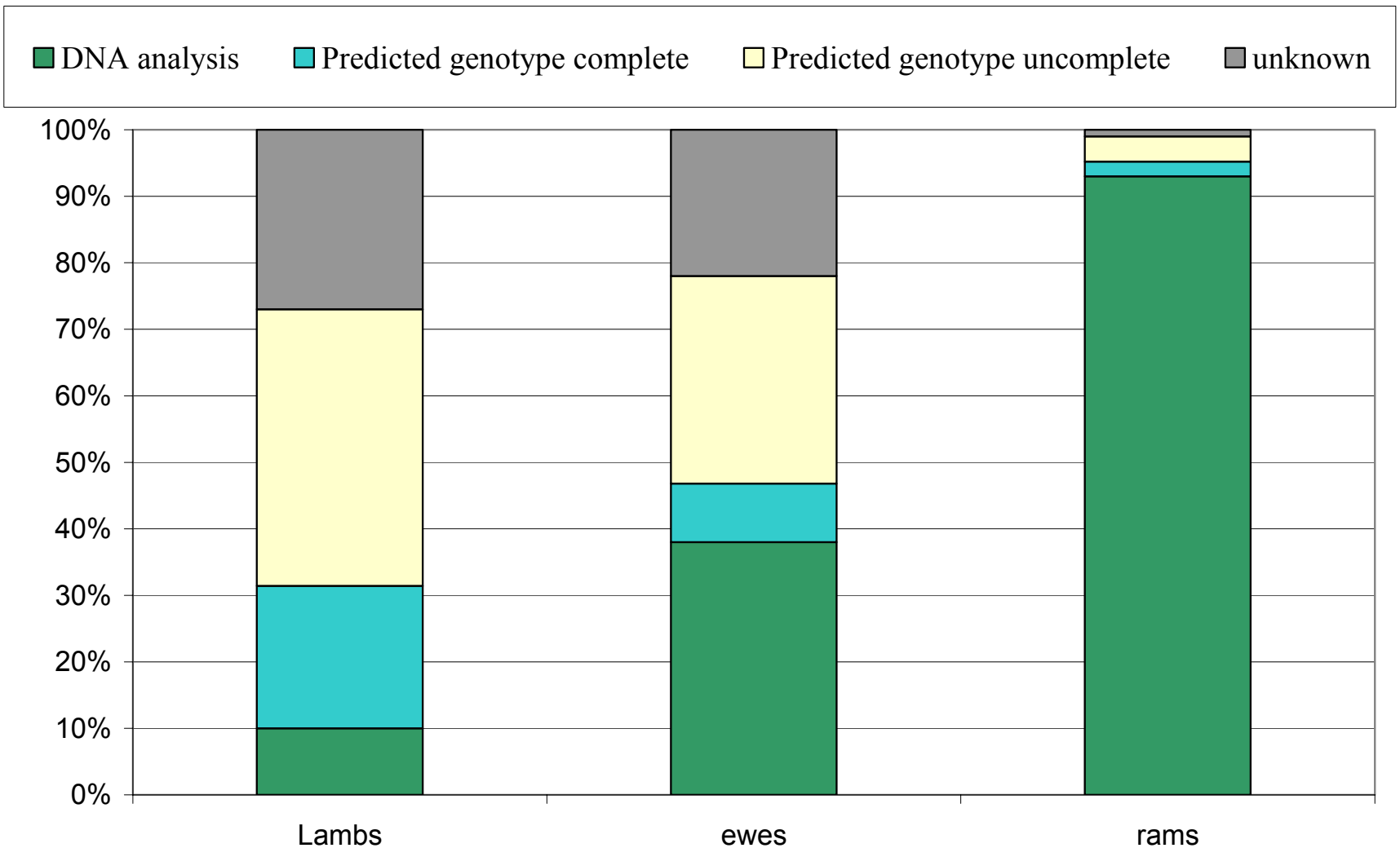
Informations stored in the molecular interface

- DNA analysis and genotype predictions clearly identified
  - Official animal n°
  - Analysis date
  - Prediction date
  - Alleles
  - Prediction indicator (0= DNA analysis , 1=genotype prediction)
  - Others variables not essential for the identification

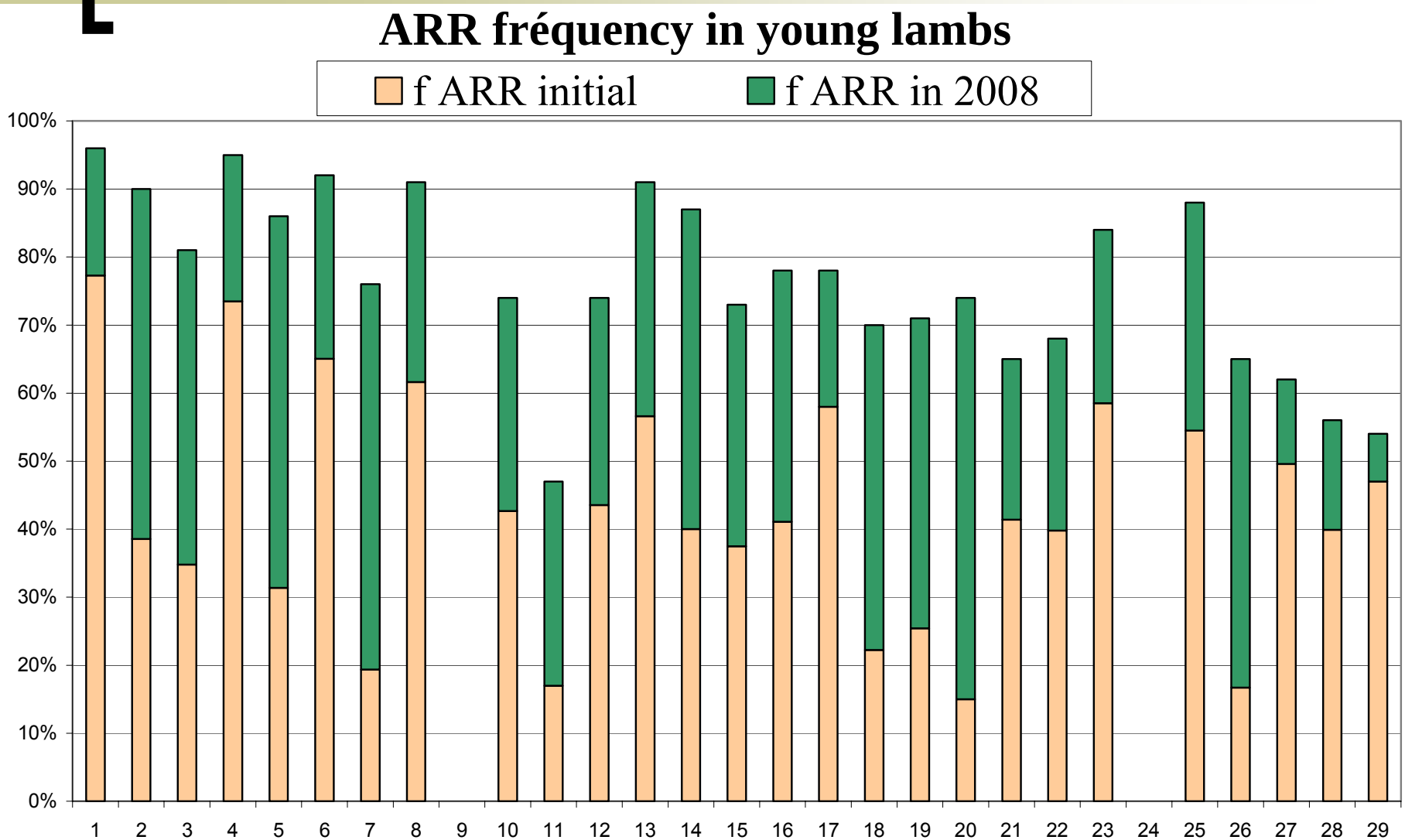
Organisation and circulation for genetic information in France (since 2004)



Predictions interest for selection : results for meat breeds in 2008



Results after 8 years of selection



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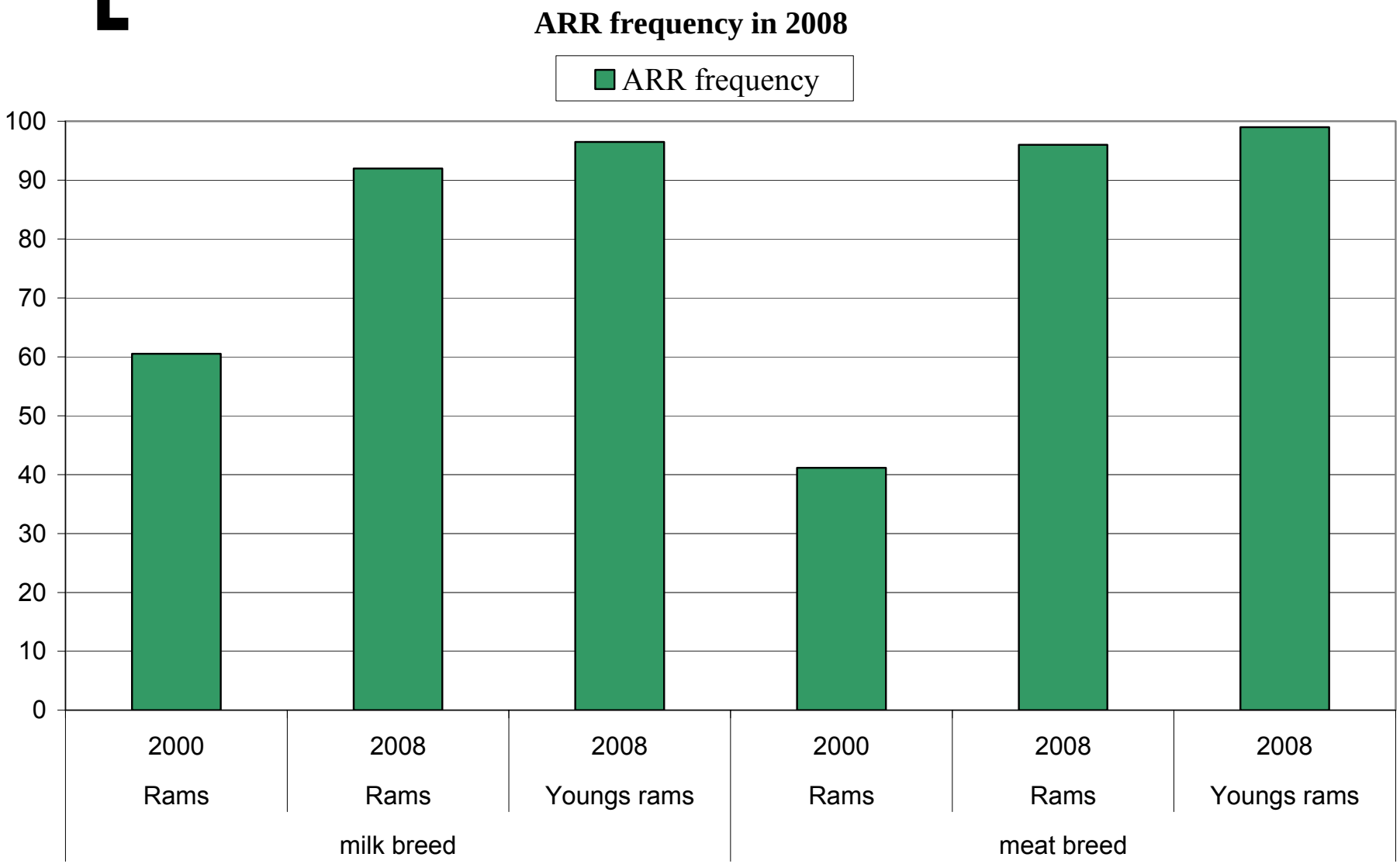
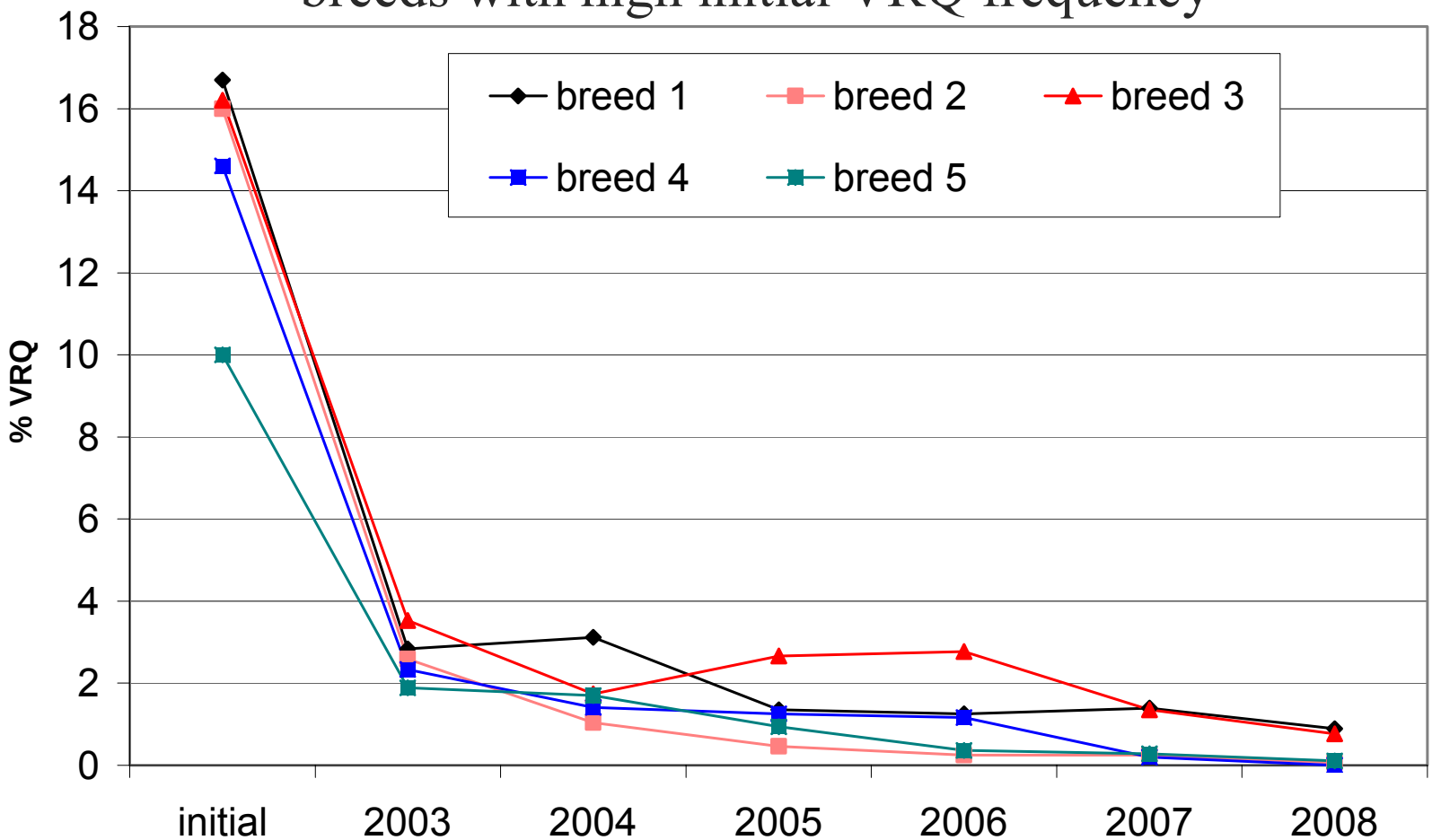


Elimination of VRQ allele

VRQ frequency evolution in ewes by year of birth for 5 meat breeds with high initial VRQ frequency



Resistance diffusion in commercial flocks

- Milk breeds : reproduction mainly by AI
  - In 2008 : 485 000 AI and 96 % by ARR/ARR rams semen
- Meat breeds : reproduction mainly by natural mating.
  - In 2008 : 7800 rams sold to commercial flocks
  - But 10 300 could be produced and 5 300 of them have a genotype known by prediction.(only with terminal sires breeds)

Conclusion

- Good results in selection flocks
- VRQ allele almost eliminated in selection flocks (few ewes carrying VRQ allele)
- A lot of young rams ARR/ARR with good genetic merit available for commercial flocks
- Logistic could be used for other genes