

State of Knowledge and Research Needs Regarding Heritable Genomic Modification in Food Animals

Session 2. Horizon scan – A view from Argentina

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Development and regulation of animal ag-biotech in Argentina

- 2003: first FT of a transgenic animal (molecular pharming).
- 2011: First International Workshop on the Food and Environmental Safety Assessment of Genetically Modified Animals.
- 2012: GM milking cow for “humanized” milk.
- 2017: Regulatory criteria for gene-edited animals and first regulatory applications.
- 2018: First locally developed GEd animals were born.
- 2019: Full pathway for the commercial approval of GM animals.



Gene Editing: Do not forget about Animal Agriculture

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Horizon scanning

Representative examples of current local projects in Uruguay, Brazil and Argentina

(primarily) Non-food animals

Sportive animals:

- “Natural” ↓myostatin (increased strength) in polo horses (SDN2)
- Sex change (to female) in polo horses.
- (↓myostatin) in race camels (for UAE).



Human-healthcare related:

- Xenografts: kidney/heart xenograft (GMO: 3 KO + 5Kin); Pancreatic b-cell xenograft (GEd: 4 KO)
- Sheep otoferlin KO (human deafness model)
- Molecular pharming in cattle milk: HGh, lysosomal enzyme.



Food animals

Transgenic:

- Cattle expressing human lactoferrin and human lysozyme (“humanized” milk)
- Sheep expressing cellulase in saliva
- Cattle expressing llama nanoantibodies against rotavirus (functional foods, dairy products).



Gene-edited:

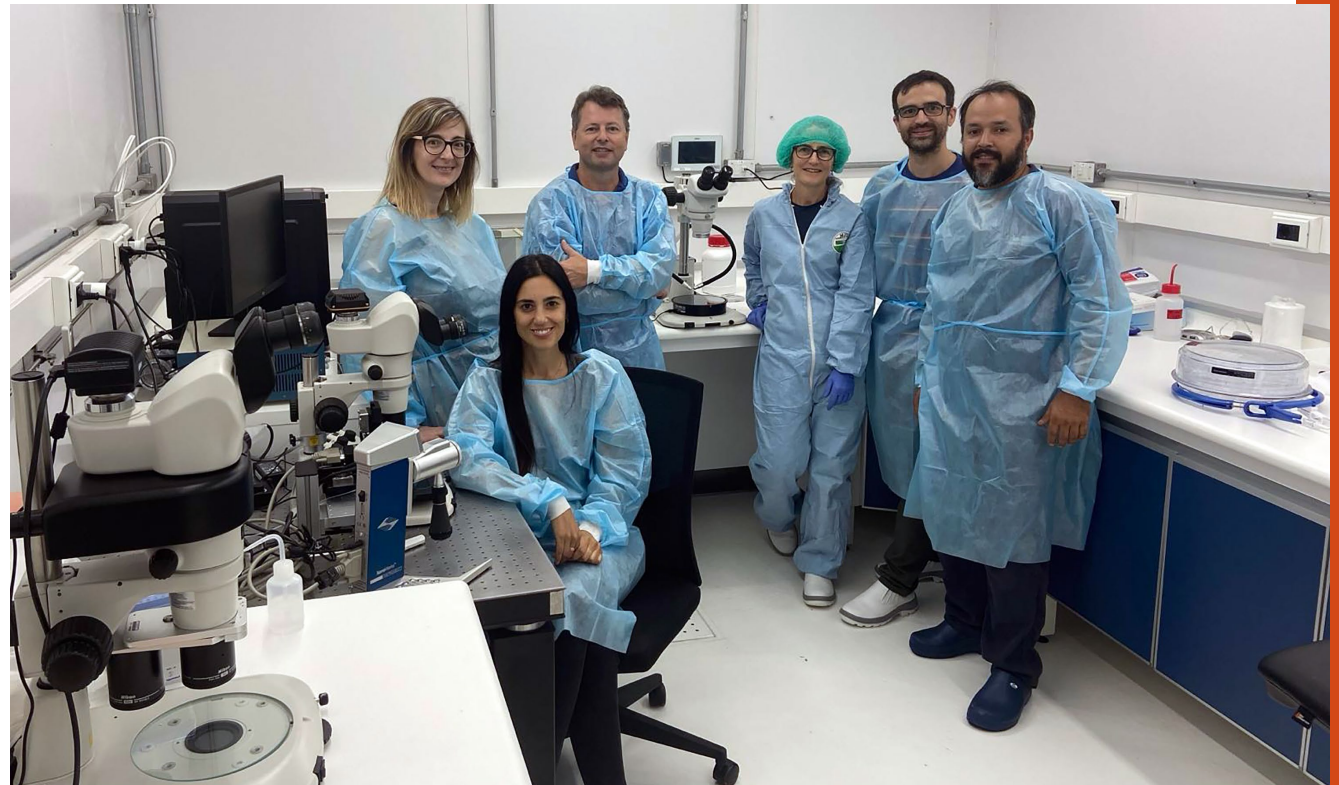
- B-lactoglobulin KO (hypoallergenic milk) in cattle.
- ↓myostatin sheep for meat production.
- Silverside for increased growth rate
- Prion KO in cattle (BSE prevention).



Many proofs of concept without a real commercial intent. Possibly due to the lack of a local partner that could exploit a (relatively) low-added_value/unit trait at a payback scale.

Non-edible animals for agricultural purposes

- Screwworm suppression gene drive
- GM silkworms





Regulatory challenges

Prospective consideration of pending/future issues

Current/future Regulatory issues (in general)

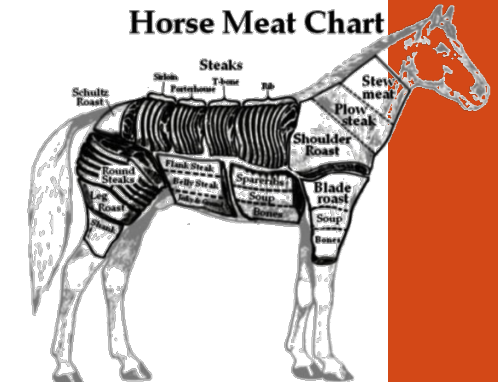
Applicable animal welfare rules:

- Ordinary rules for ag animals vs. special considerations for ad hoc facilities and/or husbandry conditions in case of certain non-food purposes.
- Case-by-case (trait-related) assessment, when necessary (e.g., increased udder): estimating/measuring “unwelfare” and setting ethical boundaries.



Food use of animals developed primarily for non-food uses:

- Coping with different husbandry conditions (e.g., vaccination).
- Ambiguous situations (e.g., GEd sportive animals).
- Perception issues (e.g., “humanized milk vs. humanized meat”).
- Every other aspect to be dealt with as a “for food” animal.
- Industry requests “to test the waters”.



Others:

- Parallel assessments of GM/GEd animal cell lines for cultured meat.

...re gene editing (non transgenic)

State of the art in SDN off-target effects:

- Can it be “accumulated” (e.g. with plant SoA)?
- Moving target

Considerations for ruling out unintended insertion:

- Sources: purposely introduced nucleic acids, DNA from adjuvant material, unintended “cisgenesis”
- Techniques: WGS vs. Southern vs PCR... (esp. for LADs*)
- Thresholds (size, non-coding regions, etc.)
- Intermediate treatment for inconsequential insertions

State-of-the-art in somaclonal variation, large offspring syndrome, etc:

- How comparable to other ARTs in commercial use?
- If quali/quantitative equivalent, no oversight?

*Less-Advantaged Developers



...re transgenic animals

Food safety assessment:

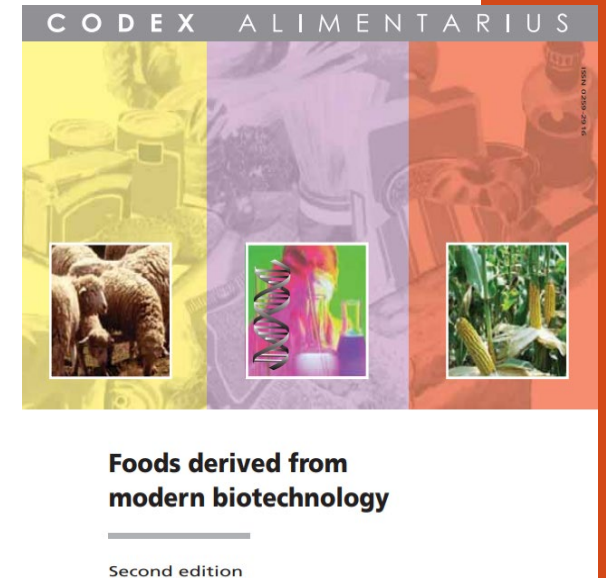
- Codex Guideline CXG 68-2008 for the “Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Animals” suffice (*also for gene-edited animals, when necessary*). But more OECD consensus documents (on food composition and biology) are warranted.

Environmental risk assessment:

- unlikely to be an issue for highly domesticated farm animals.
- Significant for other animals, but preliminary experiences (e.g. Aquadvantage Salmon) suggests it does not require extraordinary guidance or regulatory criteria.

Risk management if segregation is proposed for certain cases (speculative) :

- Expression of foreign, known allergenic proteins
- Altering disease/stress resistance in a way that creates potential counterbalancing weaknesses (re further breeding)
- “non-food” animals’ tracing.



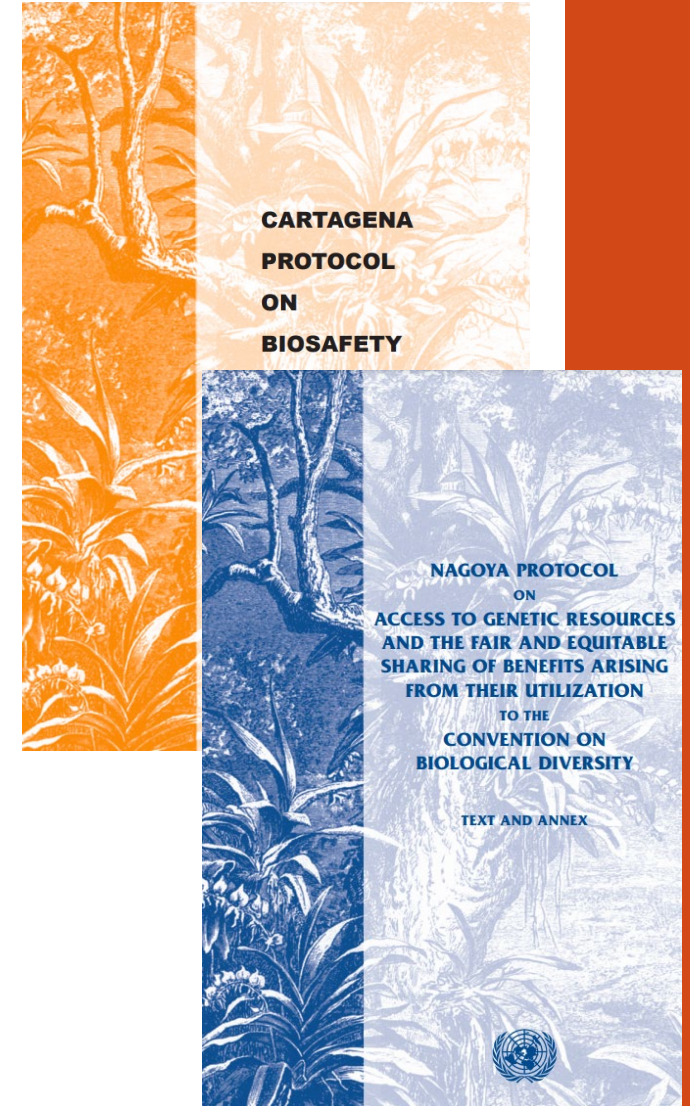
Finally, crosscutting issues

Regulators' measures to avoid trade disruption:

- Trade impact assessments
- Sworn statements (e.g. CPB “may contain”, food labeling, exportation of reproductive material).
- Official and improvised detection methods.

FTO and benefit sharing:

- Intellectual property re the animals themselves.
- Nagoya Protocol.



Truly thanks for your attention

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(online profile including
publications and other
relevant content)