Challenges and opportunities for regulatory harmonization in animal biotechnology: Regulatory approaches in different countries

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The advent of animal biotechnology

- Transgenic animals were first developed as a model of gene expression (Gordon et al. 1980)…
- but the demonstration by Palmiter et al. (1982) that GH-transgenic mice grow to large size led to interest in altering production traits in agricultural animals…
- Subsequent demonstration of plant transformation → huge investment and rapid development of plant biotechnology…
- Mid-1980's → expression of need for regulatory oversight…

Establishment of regulatory oversight

Different countries took *different* regulatory approaches:

- *New* gene technology laws *vs.* extending scope of *existing* laws
- Oversight by different authorities:
- Ministry of Agriculture (or Fisheries)
- Ministry of Environment
- Ministry of Science
- Multiple ministries
- Differences often a function of existing regulatory structures and legal enabling authorities, as well as different philosophies
- Some countries are members of Cartagena Protocol, some not

Regulatory approach has affected the development of animal biotechnology

- Let's consider some case studies…

United States

- Regulatory authority over products from biotechnology was *not* established by an act of Congress.
- In the mid-1980s, the White House Office of Science and Technology Policy promulgated the *Coordinated Framework for the Regulation of Biotechnology*, extending the scope of existing laws to establish oversight of laboratory production, field testing, and marketing
- Agencies with authority under those laws then began rulemaking to implement the Coordinated Framework…

Office of Science & Technology Policy
Executive Office of the President

United States

Under the Coordinated Framework:

- For genetically engineered animals, the scope of the federal Food, Drug, and Cosmetics Act (FDCA) was extended, leading to oversight by the U.S. Food and Drug Administration
- The FDA considers the recombinant DNA construct to be a “new animal drug” under section 512 of the FDCA because it is “an article intended to alter the structure or function” of the animal
- New animal drugs must be licensed based on a showing that the product is “safe” and “effective” for the intended use…

United States

FDA's Guidance for Industry 187 laid out a seven-step evaluation of "safe and effective":

- Molecular characterization of the rDNA construct
- Molecular characterization of the GE animal lineage
- Phenotypic characterization
- Durability assessment
- Food safety assessment
- Environmental assessment
- Claims assessment
- Only with successful passage through all seven steps would the FDA license commercial production of a GE animal.
- Approval can be limited or revoked should adverse outcomes be observed.

China

- Regulatory oversight from laboratory to commercial use is within the Ministry of Agriculture (MoA)
- To seek approval for a GEO, a research institute or company sends a proposal to the National Committee on Biosafety in Agriculture within the MoA
- The NCBA is *both* risk assessor and decision maker for GE plants and animals; an expert group within the NCBA (e.g., the Livestock Animal Expert Group, the Aquatic Organism Expert Group) includes scientists and agency officials with relevant expertise, who will make a recommendation to the NCBA for a vote to approve laboratory use, field testing, or commercial production
- (Ministry of Science and Technology *not* directly involved)

Brazil

- Authority established by 2005 Law No 11.105 that regulates Article 225 of the Federal Constitution to provide mechanisms for activities that involve GEOs, implements the National Biosafety Council (CNBS), and restructures the National Biosafety Technical Commission (CTNBio, part of the Ministry of Science, Technology and Innovation)
- In 2009 CTNBio issued Normative Resolution No. 7 regulating the development, commercial use, and import of GE animals and their release into the environment
- Most GE animal work done by public universities and government institutions (e.g., EMBRAPA, part of Ministry of Agriculture) using imported lines

European Union

Background:

- Public perceptions, commercial use, research, and regulatory approaches vary among the European Union's (EU) 28 member countries
- The EU approval system for GE crops is politicized and operates more slowly than regulatory processes in GE-producing countries
- Animal biotechnology - in several member states, genetic engineering is not used in animals. In others, genetic engineering is used for medical or pharmaceutical applications. GM animal development for food purposes is limited to U.K. (avian influenza-resistant chickens)

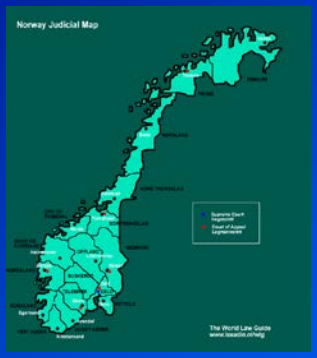
European Union

Regulation:

- In 2012, the European Food Safety Authority (EFSA) published *Guidance on the risk assessment of food and feed from genetically modified animals and on animal health and welfare aspects*, which provides guidance under the framework of Regulation (EC) No 1829/2003 on GE food and feed.
- EFSA is still working on a similar guidance document on risk assessment relating to the safety of releasing GE animals bred for food and feed purposes into the environment.
- (At least until 2012,) EFSA has not received any applications on GE animals.

Norway

- Norwegian Gene Technology Act: Section 1: “The purpose of this Act is to ensure that the production and use of genetically modified organisms and the production of cloned animals take place in an *ethically justifiable* and *socially acceptable* manner, in accordance with the principle of sustainable development and without adverse effects on health and the environment”.
- Responsible authority - Directorate for Nature Management (advisory, executive agency under Ministry of the Environment).
- Section 26 of the Act establishes the Norwegian Biotechnology Advisory Board (NBAB).
- Sustainability assessments are performed not only for domestic cultivation, but also for products imported for food and feed.
- Norway has prohibited release of some GEOs approved in the EU. (Feed manufacturers have complained that this affects their competitive position.)

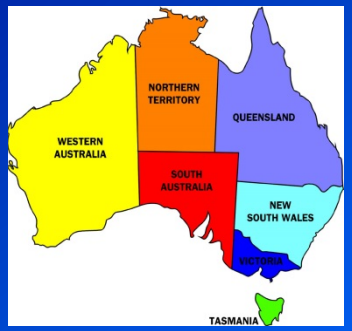


Canada

- GE animal products regulated under Canadian Environmental Protection Act – administered by Environment Canada and co-administered by Health Canada in collaboration with Canadian Food Inspection Agency (CFIA)
- Safety of foods from GE animals assessed by Health Canada under Novel Foods Regulations promulgated under the Food and Drugs Act
- The Animal Biotechnology Unit (ABU) of the Animal Health and Production Division of CFIA is responsible for establishing animal health standards and augmenting regulatory controls for development of GE animals

Australia

- National regulatory scheme enacted by the Gene Technology Act (2000)
- Office of the Gene Technology Regulator (OGTR), an independent body, oversees science-based risk assessment
- The OGTR evaluates applications regarding the release of GEOs into the environment on a case-by-case basis
- The public has the opportunity to comment on the application, risk assessment, and risk management proposals
- If application approved, OGTR may impose conditions and has power to investigate and prosecute any breaches
- Foods derived from transgenic animals are subject to pre-market and safety assessment by the co-national Food Standards Australia New Zealand (FSANZ).
- Applicable Food Standards Code is 1.5.2. – Food produced using gene technology.



New Zealand

- Two main legislations: Hazardous Substances and New Organisms (HSNO) Act (1996) and the Biosecurity Act (1993)

- The HSNO Act seeks to protect the environment and the health and safety of people and communities by preventing adverse effects of hazardous substances and new organisms (including GEOs). Act allows interested parties to make submissions prior to assessment and decision-making process outlined in the Act.
- The Environmental Risk Management Authority (ERMA) responsible for approving release of GE animals, following detailed criteria set down in a formal Methodology, considering risks, costs and benefits case-by-case.
- Some decisions for low-risk GEOs delegated to Institutional Biological Safety Committees (IBSC) in scientific institutions, which also have to follow the Act and the Methodology.

New Zealand

- The Biosecurity Act allows exclusion, eradication and management of pests and other unwanted organisms – including GEOs.
- ERMA can take findings from New Zealand's Bioethics Council into account in decision-making processes.
- HSNO Act requires ERMA to take into account the relationship of the Maori people and their culture and traditions.
- Foods derived from GE animals subject to pre-market and safety assessment by Food Standards Australia New Zealand (FSANZ).
- Guidelines for the Safety Assessment of Genetically Modified Foods' (last updated 2004) base the regulatory approach on substantial equivalence. GE foods are labeled.
- Ministry of Agriculture and Forestry carries out inspections to ensure that work with organisms approved for experimental or conditional release is done according to regulations
- An Animal Ethics Committee must approve all research involving animals under the Animal Welfare Act

Japan

- After ratification of Cartagena Protocol, Japan established Law Concerning the Conservation and Sustainable Use of Biological Diversity through Regulations on the Use of Living Modified Organisms (LMOs):
- Experiments involving rDNA techniques for development of LMOs are regulated by the Ministry of Education, Culture, Science, Sports and Technology (MECSST)
- Applications of LMOs for field use or veterinary purposes are regulated by the Ministry of Agriculture, Forestry and Fisheries (MAFF).
- An application must be made to the MAFF for approval.
- The subgroup on animals in the Committee for Evaluation of Biological Diversity Effects gives an opinion.
- The required risk assessment then is discussed in the Agriculture, Forestry and Fisheries Research Council of the MAFF.

Chile

- National Commission for the Development of Biotechnology → National Policy for the Development of Biotechnology (2003), which set objectives, regulatory and institutional frameworks, public participation, …
- General Law of Fishing and Aquaculture modified (2006) to regulate import and culture of GE aquatic species
- Undersecretary of Fisheries (Ministry of Economy) has case-by-case oversight authority based on animal health and environmental impact assessment.
- Proposals reviewed also by National Fisheries Service (MoE) and Environmental Impact Assessment System within the National Environmental Commission

Cuba

- Two levels of environmental risk assessment:
- Biosafety staff of agency or institution proposing use of biotechnology
- Within the National Center for Biological Safety, an Authorizing Department evaluates proposal and sends review to a group of experts from Ministries of Health, Agriculture and Fisheries, universities and others
- Experts review risk assessment and evaluate proposal and propose risk management
- Risk evaluation norms specify that the assessment be done in transparent and scientific manner (international assistance may be sought).

Thailand

- Ministry of Natural Resources and Environment manages matters relating to Convention of Biodiversity.
- National Biosafety Framework (2001) was developed by secretariat of National Biosafety Committee (representatives of Departments of Agriculture, Livestock Development, and Fisheries, Food and Drug Administration, Ministry of Commerce, private sector, and academia)
- A proposal is first reviewed by proposing institution's biosafety committee. If approved, referred to competent national authority, which will decide in consultation with other departments and ministries

Argentina

- Formal system in place for animal biotechnology, regulations for insects are being drafted
- Regulatory trigger is using of modern biotechnology
- Secretariat of Agriculture, Livestock, and Fisheries is competent authority
- Applications assessed by CONABIA (representatives of the public and private sectors) and Biotechnology Directorate

Costa Rica

- 2006 law establishes Animal Health Service as competent authority; other agencies may be brought in, e.g., Ministry of Environment for wild species, Ministry of Public Health for arthropods
- Scope includes GE animals, GE feeds and medicines
- Regulatory framework considers the quality and safety of GE animal foods for human consumption and safety and welfare of animals.
- No applications under consideration

El Salvador

- Special Regulations for Safe Management of Genetically Modified Organisms apply to all GMOs generally, not animals *per se*
- Competent authority is the Ministry of Environment and Natural Resources, working with the Ministry of Agriculture and the Ministry of Health
- Institutions and policymakers consider social needs, ethics, economics and issues related with intellectual property and patent protection

Ethiopia

- Regulatory system adapted from existing laws/regulations, general for GMOs, not specific for animals
- Proclamation no.655/2009 on biosafety covers importation, use, transit or movement, requires food labelling and traceability
- Environmental Protection Authority is lead agency
- Regulatory guidelines are not yet published
- Regulatory considerations include science, societal needs, ethics, religion and taboos, animal health

India

- Regulation of all GMOs is under Environmental Protection Act (1986) and its rules (1989)
- Plan to formulate specific guidelines for transgenic animals
- Lead agencies Ministry of Environment and Forests (administration of law) and Ministry of Science and Technology - Department of Biotechnology (risk assessment and formulation of guidelines for all types of transgenics)
- Food labelling mandatory, but not implemented

Kenya

- Regulatory authority adapted from existing laws/regulations covers all LMOs; within the regulations, sections address animal biotechnologies depending on intended use
- Lead agency is the National Biosafety Authority. Other agencies involved include Bureau of Standards, Department of Veterinary Services, Directorate of Public Health, Pest Control Products Board, Intellectual Property Institute
- In process of developing arthropod containment guidelines
- Labelling mandatory if GE content in the final product is > 1%

Malaysia

- Biosafety Act (2007) covers modern biotechnology, including animals
- National Biosafety Board makes decisions on GMOs – members incl. representatives from ministries of Natural Resources & Environment (chair); Agriculture & Agro-based Industry; Health; Plantation Industries & Commodities; Domestic Trade, Co-operatives & Consumerism; International Trade and Industry; Ministry of Science, Technology & Innovation
- Decision-making based on scientific risk assessment, although socioeconomics may be considered
- Food labelling is mandatory

Panama

- Law No. 48 establishes the National Biosafety Commission comprised of Ministry of Agriculture, Authority of the Environment, Water Resources Authority, Ministry of Health, Ministry of Commerce, Food Safety Authority, Foreign Ministry
- Depending on intended use, there are sectorial committees on agricultural biosafety, health, and environment
- Regulatory system based on science, but socioeconomic factors may be considered
- Food labelling voluntary

Philippines

- The National Biosafety Framework or Executive Order No. 514 s. 2006 covers functions of agencies responsible for administrative functions for biosafety, depending on the GMO
- E.O. 514 can serve as the basis for the formulation of rules and regulations for animal biotechnologies.
- The Department of Agriculture responsible for biosafety decisions concerning fisheries and aquatic resources, domesticated animals and biological products used for animal husbandry or veterinary purposes and biological agents for biocontrol

Indonesia

- Formal statutory /regulatory system is still being developed for feeds
- Regulatory requirements will be set by decree of Ministry of Agriculture
- Considerations include socioeconomics, farmers' rights, safety plans, and environmental risk
- Regulatory trigger is process
- Many agencies involved, led by Agency for Agriculture Research and Development

Mexico

- Law of Biosecurity of GMO; amimal biotechnology is regulated; adapted from existing laws/regulations and Cartagena Protocol
- There are *not* specific norms or rules for animals, as there are for plants, e.g., special protection of maize in Mexico
- Regulatory trigger - all products derived from biotechnology require a regulation
- Regulatory authority depends on the final use of GMO, could be Ministry of Agriculture or Environment of Health; lead agency is CIBIOGEM, a department of Minstry of Science ministry that coordinates all regulation of GMOs

Codex Alimentarius

- Codex Alimentarius Commission – an intergovernmental body with >180 members within framework of the Joint Food Standards Program established by UNFAO and WHO to protect the health of consumers, ensure fair trade practices and promote coordination of food standards.

- Foods Derived from Modern Biotechnology, 2nd ed. (2009) contains Guidelines for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Animals
- Addresses safety and nutritional aspects of foods derived from animals with history of safe use as food and that have been modified by biotechnology.

Guideline for the Conduct of Food Safety Assessment of Foods Derived from Recombinant-DNA Animals

- Describes recommended approach for food safety assessment where a conventional counterpart exists and identifies data applicable to making such assessments:
- The nature of the rDNA construct and its expression product,
- The health status of the rDNA animal, and
- The composition of food products produced, including key nutrients.
- *Useful for standardizing food safety assessments and harmonizing trade in foods derived from rDNA animals*
- Guideline does *not* address animal welfare; ethical, moral and socioeconomic aspects; environmental risks; safety of rDNA animals used as feed, or safety of animals fed with rDNA feedstuffs

There are as many regulatory approaches as there are countries!

- Little consistency *between* countries
- Much room for interpretation *within* countries
- *Regulatory approach may not matter greatly so long as it is effective:*
- Science-based and defensible
- Transparent
- Expeditious
- Credible to the public – which may be more concerned about non-scientific, values-based issues

International harmonization

What is required?

- Agreement on what comprises relevant information; e.g., food safety criteria in Codex Alimentarius
- Sharing of technically reliable scientific information
- Intergovernmental consultation and information exchange
- Capacity building, especially for developing countries

Harmonization has been limited:

- Differences in regulatory approaches among countries, even among EU member states…
- Food labeling issue can prove divisive
- Regulatory triggers, esp. product vs. process

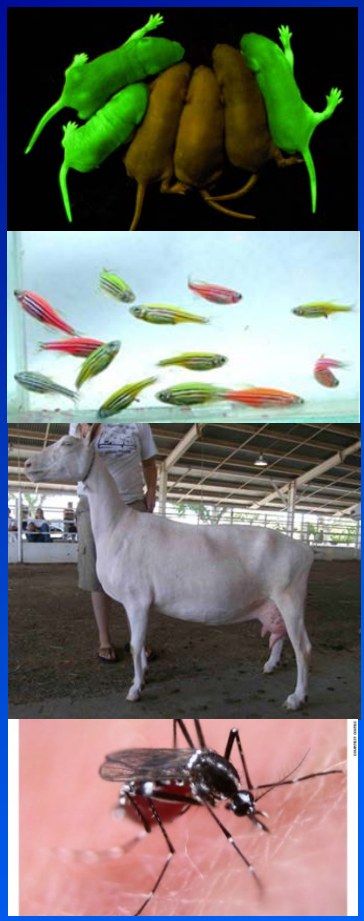
Targets of opportunity for harmonization

What can we do to foster harmonization?

- Adopt *product*-based approach
- Assess risk relative to conventional animal production
- Ask only for information to be *used* in risk assessment or risk management – if it is not relevant, do not ask for it
- With permission of sponsor, share technical information among countries
- Exchange of best practices and experience
- Develop a points-to-consider framework
- Share case-studies (methods and outcomes) of oversight
- Meet as we do here, and have virtual meetings via internet in between
- Have clear, same rules for both domestic and imported products

Commercialization of animal biotechnology

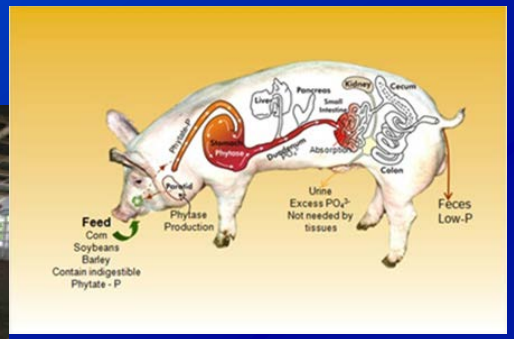
- Transgenic model animals (mice, rats, zebrafish) for biological and biomedical research, are in commercial use
- Of the many lines genetically engineered for non-research applications, only a *few* have moved from the laboratory to commercialization:
- Since 2003, GloFish have been sold as aquarium pets in the United States
- In 2009, the first GE animal producing a pharmaceutical product, a goat synthesizing recombinant human antithrombin III in its milk, was approved by the US-FDA
- In 2014, Brazil announced first commercial release of Oxitec GM mosquito into the wild to fight Dengue fever
- *To date, no GE animal intended for use as food by humans has received regulatory approval*



Acknowledgment

U.S. Dept. of Agriculture Foreign Agriculture Service


HUMAN GROWTH HORMONE GENE
MT PROMOTER
pBR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Colon
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Corn
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