Virtual Breakout Group Session in Animal Biotechnology
Developers and Researchers

Attending: Justin Bredlau (USDA, USA), Luiz Sergio Camargo (EMBRAPA, Brazil), Ana Granados (EU, Brussels), Eric Hallerman (Virginia Tech, USA), Joan Lunney (USDA, USA), Alan Mileham (STS Genetics and Genetic Visions, USA), Ana Maria Perez (Accilegen, Colombia), Tad Sonstegard (Accilegen, USA), Alison Van Eenennaam (UC-Davis, USA), Mark Walton (AquaBounty, USA), Matthew Wheto (university, Nigeria), Diane Wray-Cahen (USDA, USA)

Overarching Questions:

1. *Challenges* –What are the main challenges in your countries facing the development and application of animal biotechnology (technical, regulatory, funding, communication, …)
   - What are recommendations to help overcome these challenges?

   The challenges clearly vary by country. These differences among countries may affect future competition.

   In Brazil, for example, funding and technical challenges of applying the technology are at the fore, while regulatory issues are not.

   In the United States, the regulatory process is problematic in several senses. First, oversight is triggered by process, but how relevant is that to gene editing if you cannot distinguish the products of gene-editing from that of conventional breeding? And the regulatory costs are extraordinary. If a developer works to edit a gene such that no foreign DNA is added, couldn't that animal and its products be subject to regulatory discretion? Could oversight of animals intended for use as food not be passed to the Department of Agriculture while FDA retains authority of pharmaceutical applications? Further, for companies with over $20M working capital, FDA has an Investigational New Animal Drug fee of $450,000, which is a lot of money.

   In Canada, the modified or edited animal is regulated separately from its products; hence, a developer may have to go through regulation twice, e.g., once for fish fillets and once for head-on gutted fish.

   In Europe, regulatory costs are sufficiently high that no one has tried to go through the regulatory pipeline. Further, the European Court recently rendered a decision that gene-edited animals and products would be regulated as are genetically modified animals and products. Because of this ruling, the public perceives gene-edited products as they do GMOs. Further still, in Europe, an EU Directorate General will promulgate a directive, which is then implemented in national laws, which may differ. Consultation is ongoing on the issue of how to implement a method of detection directive; how to implement this directive for gene-edited animals when the product is indistinguishable from that from conventional breeding? Many developers just disregard Europe as a market for genome editing. How will precluding this technology affect the farmers in Europe in the future? Europe does not care about productivity or efficiency, and see

genome editing as a solution to problems that have been created by intensive production systems. Lots of discussion about ethical problems about genome editing. Brexit also poses a challenge, inasmuch as there may be different regulation between the UK and Europe. From the breeder's point of view, the trait at issue matters; productivity traits are not of interest to any but producers, while welfare-related traits such as disease resistance may prove acceptable to the European public. Results of a social benefits survey could be useful for an EU audience.

Public perception being important, communication is important. Distinguishing gene editing and genetic engineering is difficult for some, but needed. Breed associations may be savvy, but ranchers not. Trade and retail associations do not understand the distinction or accept the products. The point was made that "the public won't accept" is just a trope, that if the product is good, people will buy it. Some NGOs, e.g., Greenpeace, purposefully conflate gene-editing and genetic engineering. The example of the AquaBounty salmon was cited, that marketing focuses on small environmental footprint and boost of rural employment; this messaging is critical to public acceptance. There was disagreement as to whether gene editing might better be referred to as "new breeding technologies", with some saying that new branding was helpful, but others saying that it seemed like industry-speak.

Regulators should ask for data only if these data support testing of a relevant hypothesis. Do not ask for meat or milk composition data if it is not relevant, If the animal is not intended for use as a drug.

2. <u>*Regulatory Cooperation, Alignment and Compatibility*</u> – How do you envision regulatory cooperation in animal biotechnology oversight being helpful?
   - What types of cooperation or potential regional approaches would be most helpful?
     - mutual recognition?
     - joint reviews?

   Mutual recognition of regulatory decisions would be very useful. South American countries are aligning, especially for simple gene-edits that do not involve DNA insertions, which is a hopeful development. If that kind of cooperation would spread around the world, then developers would not have to generate regulatory packages repeatedly. For example, Brazil considers the food safety data package on AquAdvantage from other countries. Note that mutual recognition is different from using data from other applications. For example, Vietnam has a rule that if X number of countries have approved a particular product, then they do not need to do their own studies. There is a trend toward mutual recognition among countries in South America, and other developing countries are looking at this approach. How much influence do developed-world regulators have on developing-world regulators? There is a like-minded group of countries USA/Canada/Australia/several South American countries (e.g. Brazil, Argentina, Paraguay, Uruguay)/South Africa that was originally formed around cloning.

3. <u>*Scope of regulation*</u> – Does the country(ies) you work in exempt any types of genome edited or genetically engineered/modified animals or products thereof?
   - What types of exemptions?

- How do regulatory processes affect what traits/technologies that you work on?
- How are you affected by different determinations in different jurisdictions relative to what is or is not regulated under each country's biotech/GMO laws? (i.e., Trade issue associated with regulatory misalignment)

  For crops in the United States, companies can make their own determination for edits that are like those that could have been priced by conventional breeding, but for animals, all modifications are regulated. There are exemptions in Brazil for SDN-1 – still need to show submit data showing no foreign DNA in the animal. AquaBounty is looking to expand outside of the United States, and they are considering moving to countries with a regulatory process in place that has been shown to work. Policies affect the choice of research topics, e.g., knock-outs are easier to pass through regulatory pathways than knock-ins, so we are effectively using only half the potential power of gene-editing technology. In Canada, proponents have to put an economic value on a trait, which means that only really high-value traits are targeted. Accilegen prefers to do exact conversions of alleles of existing genetic variation. In Australia, food approval is different from the approval for the animal. In several countries, there are several different agencies that need to give approval of a product. In Canada, it was recommended that a food-safety evaluation be done for gene-edited polled cattle, not required, but to "make the public more comfortable".

4. <u>*Preparing for Innovation*</u> - What is your country doing to encourage innovation and support developers in the application process?
   - What steps can be taken to [draft/adapt] regulations able to adapt to the future technologies?
   - How might one make regulations smarter and fairer
     (e.g., to avoid only/mainly big companies controlling products)?
   - What are the costs of meeting regulatory requirements in your country(ies)?

   While funds for traditional gene transfer have dried up in the United States, there are USDA funds for genome-editing work. The regulatory cost of this work is expensive – especially if the investigator ultimately has to incinerate all animals. If the regulatory process became clear in USA, then likely developers would move forward. The uncertainty of approvals and cost is holding everything back, and concern that consumers won't accept a product. The developing world does not have the luxury of the ethical debates that are ongoing the in the developed world. In Nigeria, there are issues around funding to do genome editing in livestock species, as well as lack of facilities to do this work. It is hard to get funding for this work in Brazil. Accilegen just got funding from the Gates Foundation for tropical edits. Does that open the door for additional collaboration without "dictation"?

   The funding problem in the developing world – "lack of freedom" for farmers due to intellectual property issues is more of a problem for plant breeders than for animal breeders – There are no restrictions on working on animals in Nigeria from the government – now Nigeria is trying to iron out the IP in terms of plant breeding. The IP depends on the level of vertical integration in the industry – less freedom in pigs and chickens than in the large ruminants.

5. <u>*Next steps*</u> - Identify potential follow-up activities that would be beneficial within your region.
    - *What types of activities?*
    - *For what target audiences?*
    - *What can be done virtually?*
    - *What are the next steps?*

    We need to have an open discussion about the regulation of simple genome edits for food-animal applications. It will depend a little on audience – the current regulatory paradigm in the United States is a barrier. We need a forum where legislative people hear the issues we are facing – the Coordinated Framework is not working – we need to have a new path forward for the regulatory framework. We need an Executive Order. We need parallel conversations in each country. We also need funders to be aware of limitations in the developing world and help facilitate funds to countries with a more science-based regulatory process.