

## NRSP-8 National Animal Genome Program Annual Report 2023 (Reporting 2022 Activities)

Submitted by: Benjamin J. Reading, North Carolina State University  
Kent Reed, University of Minnesota  
*--On behalf of the NRSP-8 National Leadership*

**OBJECTIVES:** The NRSP-8 project was renewed as of 10/01/18, with the following objectives:

- 1. Advance the quality of reference genomes for all agri-animal species by providing high contiguity assemblies, deep functional annotations of these assemblies, and comparison across species to understand structure and function of animal genomes;*
  - 2. Advance genome-to-phenome prediction by implementing strategies and tools to identify and validate genes and allelic variants predictive of biologically and economically important phenotypes and traits; and*
  - 3. Advance analysis, curation, storage, application, and reuse of heterogeneous big data to facilitate genome-to-phenome research in animal species of agricultural interest.*
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### NRSP-8 Executive Summary 2023

The Animal QTLdb, CorrDB, Bioinformatics Tools, and the National Animal Genome Research Program (NAGRP) data repository have actively supported research activities for multiple agricultural animal species. The previously implemented ontology hierarchy display tool has facilitated our efforts at expanding and exploring the use of Vertebrate Trait (VT) Ontology, Livestock Product Trait (LPT) Ontology, Clinical Measurement Ontology (CMO), and other ontology hierarchies. This past year we focused on integration of the Animal Trait Ontology into the Vertebrate Trait Ontology (<http://bioportal.bioontology.org/ontologies/VT>). Ten (10) dataset updates were released to the public throughout 2022 and traits specific to livestock products continue to be incorporated into a Livestock Product Trait Ontology (LPT) portal. While databases support multiple genome builds for all livestock species, we adopted a mechanism to designate one “default genome build” per species (in alignment with NCBI/Ensembl). All curated association data continue to be automatically ported to NCBI, Ensembl, UCSC genome browser, and Reuters Data Citation Index in a timely fashion. We made significant efforts to improve the curator tools in order to facilitate trait-variant related data curations and we continue to strengthen the data quality control procedures to help improve data quality. The Data Repository for the aquaculture, cattle, chicken, horse, pig, and sheep communities have proven to be very useful in facilitating research (<https://www.animalgenome.org/repository>). The data downloads from the repository generated over 290 GB of data traffic in 2022. Additionally, the AquaMine RefSeq Database for aquatic species was created that includes information from 21 vertebrate finfish and 4 invertebrate mollusks, and 3 invertebrate crustaceans (28 total species). NRSP-8 continues to host mailing lists/websites for various research groups in the NAGRP

community (<https://www.animalgenome.org/community/>). This includes groups like AnGenMap (with about 3,000 subscribers from 67 countries/regions of the world), FAANG international consortium working groups (with 8 working group mailing lists and websites), and CRI-MAP users (670+ subscribers), and user bulletin boards to facilitate meetings, among other user forums. We have worked to transition to a faster and more secure network at our data center. This was accomplished by better use of the resources for shared workloads, better data and network security, and improved protocols for data backup, management, and inventories.

In 2022, over 7,000 bovine animals were genotyped and the application of omics resources in breeding has been impactful in the beef and dairy industries, especially in regard to carbon footprint reduction. Continued pangenome work is also underway, sequencing additional genomes telomere-to-telomere and coordinating with cattle trait databases. Four new hog genome assemblies are slated to be sequenced, including telomere-to-telomere assembly. Genome editing in the pig is expanding, including in the field of biomedicine. Functional annotations, sgRNA libraries, muscle cell lines, and spatial transcriptomes, among other completed refinement of tools and resources are now available to poultry researchers. A pangenome for chicken and telomere-to-telomere sequence assembly is underway. Aquaculture members contributed to draft genomes that were completed for 11 species, including 8 finfish and 3 shellfish (channel catfish, blue catfish, 2 subspecies of rainbow trout, North American Atlantic salmon, Nile tilapia, striped bass, white bass, eastern oyster, Pacific geoduck, and Pacific Olympia oyster and genome sequencing projects are underway for 7 finfish subspecies of rainbow trout and cutthroat trout and 1 shellfish species, North American Pacific oyster. Genomic selection has been initiated in eastern oyster and other species have domestication and selective breeding programs that interface with industry and are in commercial production including striped bass, white bass, rainbow trout, and channel catfish. Priority commercial aquaculture species identified by USDA & NOAA Marine Aquaculture Initiative include potential future targets for genome sequencing and genomic tool development (about 14 additional species total). These are species that already have commercial production or are deemed commercially viable for US production, however they completely lack genome resources.

There were numerous attendees at the NRSP-8 Species Workshops hosted in 2023 by each of the respective groups. Collectively, over 450 persons from at least 2 dozen different countries were represented with attendees from academic, private sector, and government institutions. The NRSP-8 National Workshop and Business Meeting were attended by at least 150 persons and 72 persons provided contact information for the AnGenMap listserv. Additionally, a pangenome training session was offered by the bovine group with about 40 attendees and a multi-day horse genome workshop event was hosted by the equine group with over 100 attendees, including representatives from industry. Collectively, over 25 conference travel awards were made to students, postdocs, and early career faculty to attend NRSP-8 events and activities. The importance of NRSP-8 funding to providing leverageable and matching funds to support grants and activities relevant to the 3 mission objectives across species groups cannot be overstated.

Lastly, there were 88 publications/products generated from NRSP-8 community members directly relevant to the 3 objectives. A letter attesting to the request for comments from the OSTP/FDA regarding the modernization of biotechnology (i.e., genetic editing of animals in the USA) was produced as commentary from the NRSP-8 community. The group also contributed to the US Department of Homeland Security report (2021) on Threats to Food and Agricultural Resources, which is related to National Security Memorandum-16 (NSM-16) to *Strengthen the Security and Resilience of United States Food and Agriculture* released in 2022. The NRSP-8 has a very important mission in this regard as purveyors and stewards of genomic data critical to the safety and resilience of the US domestic food supply (food security is national security).

## NRSP-8 General Report 2023

### Bioinformatics

*Jim Reecy*

The Animal QTLdb, CorrDB, NAGRP Bioinformatics Tools, and the NAGRP data repository have been actively supporting the research activities for multiple agricultural animal species. The QTLdb has been accommodating active curation of QTL/association data for seven species (cattle, catfish, chicken, horse, pig, rainbow trout, and sheep). In 2022, a total of 22,320 new QTL/association data were curated into the database, bringing the total number of curated data to 258,290 QTL/associations. Currently, there are 36,725 curated porcine QTL, 193,641 curated bovine QTL, 18,313 curated chicken QTL, 129 curated goat QTL, 2,649 curated horse QTL, 4,504 curated sheep QTL, and 2,329 curated rainbow trout QTL in the database (<https://www.animalgenome.org/QTLdb/>).

An additional 2,735 correlations (increase by species: cattle: 640; chicken: 380; pig: 1,321; sheep: 394) and 459 heritability data (increase by species: cattle: 134; chicken: 58; goat: 3; horse: 1; pig: 160; sheep: 103) were curated into the Animal CorrDB in 2022. Currently there are a total of 26,839 correlation data on 806 traits and 4,778 heritability data on 950 traits in 6 livestock animal species.

Our previously implemented ontology hierarchy display tool has facilitated our efforts at expanding and exploring the use of the Vertebrate Trait (VT) Ontology, Livestock Product Trait (LPT) Ontology, Clinical Measurement Ontology (CMO), and other ontology hierarchies. This tool has been further integrated with other web portals for Animal QTLdb, VT, LPT, and CMO project websites. This past year we continued to focus on the integration of the Animal Trait Ontology into the Vertebrate Trait Ontology (<http://bioportal.bioontology.org/ontologies/VT>). Ten (10) dataset updates were released to the public throughout 2022. We have continued working with the Rat Genome Database to integrate ATO terms that are not applicable to the Vertebrate Trait Ontology into the Clinical Measurement Ontology (<http://bioportal.bioontology.org/ontologies/CMO>). Traits specific to livestock products continue to be incorporated into a Livestock Product Trait Ontology (LPT) (<http://bioportal.bioontology.org/ontologies/LPT>). Three (3) LPT updates were released during 2022. Fifteen (15) updates of Livestock Breed Ontology (LBO; <https://www.animalgenome.org/bioinfo/projects/lbo/>) were made. We have also continued mapping the cattle, pig, chicken, sheep, and horse QTL traits to the VT, LPT, and Clinical Measurement Ontology (CMO) to help standardize the trait nomenclature used in both QTLdb and CorrDB. We have worked with the developer of AgroPortal (<http://agroportal.lirmm.fr/>) to streamline the new updates of VT, LPT, and LBO data into AgroPortal. The ontology data for the VT, LPT, and LBO are also available through Github (<https://github.com/AnimalGenome/vertebrate-trait-ontology>, <https://github.com/AnimalGenome/livestock-product-trait-ontology>, and <https://github.com/AnimalGenome/livestock-breed-ontology>, respectively) where users can automate their data updates. The VT/LPT/CMO cross-mapping has been well employed by the

Animal QTLdb, CorrDB, and VCMMap tools. Annotation to the VT is also available for rat QTL data in the Rat Genome Database and for mouse strain measurements in the Mouse Phenome Database. We have also continued to integrate information from multiple resources, e.g. FAO - International Domestic Livestock Resources Information, Oklahoma State University - Breeds of Livestock web site, and Wikipedia, as well as requests from community members.

While the database supports multiple genome builds for all livestock species, we have adopted a mechanism to designate one “default genome build” per species (in alignment with NCBI/Ensembl). All curated QTL/association data continue to be automatically ported to NCBI, Ensembl, UCSC genome browser, and Reuters Data Citation Index in a timely fashion. Users can fully utilize the browser and data mining tools at NCBI, Ensembl, and UCSC to explore animal QTL/association data. Efforts were continually made, working with our counterparts at these institutions, to eliminate any glitches that arose during the automated or semi-automated data porting process. In addition, we have continued to improve existing and add new QTLdb curation tools and user portal tools. We have made significant efforts to improve the curator tools in order to facilitate trait-variant related data curations. This involved more than 15 web portal scripts serving 47+ curator views/functions.

Our efforts to overhaul and redevelop functionality to improve the usability of CorrDB have continued. The web portal has been updated with additions and/or modifications of its correlation network visualization options with the use of Graphviz dot graph and Cytoscape web tools, and newly added correlation and heritability data batch downloads provide more user-friendly access to the curated data. We continued to strengthen the data quality control procedures to help improve data quality.

The Data Repository for the aquaculture, cattle, chicken, horse, pig, and sheep communities to share their genome analysis data has been proven to be very useful in facilitating research (<https://www.animalgenome.org/repository>). While new data is continually being curated, we have gradually scaled down the support for hosting supplementary files for publications for more sensible use of the NRSP8 bioinformatics funds. As of April 5, 2022, all valid data (a total of 796 data files, 84.25 GB in size, for 92 manuscripts published in 27 scientific journals) have been transferred to Open Science Framework (OSF; <https://osf.io>) for better long-term data security. Appropriate web visit redirections for each data set have been set up on the current site to forward the incoming traffic to the new URL at OSF.

The data downloads from the repository generated over 290 GB of data traffic in 2022. Throughout the year, there were over 110 communication records on our helpdesk AnimalGenome.ORG to handle users’ inquiries/requests for services affecting community research activities and the use of our services. Provided assistance ranged from data transfer and hosting, data deposition, data curation, web presentation, and data analysis, to software applications, code development, advice for tool developments, etc.

In 2022, we actively worked with external working groups and consortia to facilitate bioinformatics support to the community. One such effort was to work with the AgBioData group on recommendations for extending the GFF3 specification for improved interoperability of genomic data (<https://doi.org/10.48550/arXiv.2202.07782>). Another example is to work with scientists from University of Colorado, University of Sydney, and Lawrence Berkeley National Laboratory on development of the Vertebrate Breed Ontology (VBO; <https://github.com/monarch-initiative/vertebrate-breed-ontology>). We believe these efforts will directly or indirectly benefit the livestock genome research community.

We have been maintaining and actively updating the NRSP-8 species web pages for each of the six NRSP-8 species. We continue to host mailing lists/websites for various research groups in the NAGRP community (<https://www.animalgenome.org/community/>). This includes groups like AnGenMap (with about 3,000 subscribers from 67 countries/regions of the world), FAANG international consortium working groups (with 8 working group mailing lists and websites), and CRI-MAP users (670+ subscribers), new meetings, and user bulletin boards to facilitate these meetings, among other user forums.

The Functional Annotation of ANimal Genomes (FAANG) website (<https://www.faang.org/>) has been re-developed in 2022 to support a transition of earlier working groups to new “task forces” for more focused FAANG activities. The FAANG site serves not only as a FAANG-related information hub, but also as a platform for this international consortium’s communication, collaboration, organization, and interaction. It serves over 660 members and 8 working groups and sub-groups, with 10 listserv mailing lists, bulletin board, database, and tools for membership and working group management. The actively hosted materials include meeting minutes, tools/protocols for FAANG activities, incorporation and use of data portal hosted at EBI, presentation slides, and video records of scientific meetings and related events, all interactively available to members through the web portal.

We have worked with Iowa State University IT in a transition to a faster and more secure network at our data center. We have consequently adopted new protocols and procedures to work with collaborators on data transfer and collaborative works involved in getting through the new firewall. Efforts were made to improve data backup, security, and availability. This was accomplished by better use of the resources for shared workloads, better data security and network security, and improved protocols for data backup, management, and inventories.

We have been sending periodic updates to more than 3,000 users worldwide (<https://www.animalgenome.org/community/angenmap/>) to inform the animal genomics research community of the news and updates regarding AnimalGenome.org. “What’s New on AnimalGenome.ORG web site” emails were sent out 3 times in 2022, consistent with the pace/pattern of the past 18 years (<https://www.animalgenome.org/bioinfo/updates/>).

Efforts are underway to move data off of animalgenome.org to preserve these data (external resources, to the “cloud”). James Koltes and others are looking into other funding opportunities to keep these resources and personnel around.

## Bovine

*Alison Van Eenennaam*

Some 7,000 animals have been genotyped and the application of omics resources in breeding has been very impactful. Continued pangenome work is also underway, sequencing additional genomes telomere-to-telomere and coordinating with the cattle trait databases. Carbon footprint reduction has been a major highlight greatly influenced by genomic resources.

The sequencing of the bovine genome unleashed a number of opportunities to accelerate the rate of genetic improvement in cattle using DNA-based information. First, it revealed the presence of millions of SNPs and indels between individuals of the same species, which when informed by a suitable genotyped and phenotyped reference population, could be harnessed to enable genomic selection. This allows breeders to identify genetically superior young animals from DNA testing based on the fact that information from a large number of markers distributed across the genome can be used to estimate the genetic merit, or breeding value, of that animal. Since the implementation of genomic selection, almost seven million US dairy animals have been genotyped and the rate of genetic gain has more than doubled. Additionally, a large proportion of the US dairy herd is now sexed using female semen in combination with genomic-tested elite heifers to produce female replacements and inseminating the remaining dairy cows with beef-breed semen to produce beef-on-dairy F1 calves, or embryo transferring beef embryos, to produce calves that are better suited to the beef industry. This development has many sustainability advantages as it replaces less desirable dairy male calves with beef calves to enter the beef supply. Beef-on-dairy calves show greater feed efficiency (compared to purebred dairy calves), which lowers the environmental footprint associated with their production, and the increased feed efficiency significantly reduces greenhouse gas (GHG) emissions. Beef-on-dairy also delivers increased volumes of higher-grading beef carcasses, providing feed yard operators more access to value-based marketing opportunities as well as providing dairy producers income as beef-on-dairy calves are more valuable in the marketplace for dairies than purebred dairy calves. It is estimated that there are about three million head of beef-on-dairy cattle that are part of today’s beef supply. Sequence data also enabled the identification of the causative mutations of Mendelian traits, and this information can and is being used to avoid carrier matings that could result in affected calves. And more recently, genome editing offers an approach to introduce targeted genetic variation into the germline of elite parents such that genetic improvements are inherited by the next generation. Such variation may include the repair of genetic defects, inactivation of undesired genes, and the moving of useful alleles and haplotypes between breeds in the absence of linkage drag that normally accompanies crossbreeding. Introducing desirable characteristics like disease resistance and heat tolerance offers an opportunity to not only protect livestock from environmental challenges, but also reduce animal death and suffering, and the need to use chemicals to control disease; goals that

align with the values of many consumers. Many undergraduate and graduate students as well as post-doctoral fellows are being trained within the project.

Four students were funded to present in 2022 (prior to cancellation) and four in 2023 that did present at PAG. The PAG 2023 Cattle-Pig workshop had 175 attendees from 24 countries, 20 different experiment stations and 20 different companies (commercial/private sector breeding companies, biotech, etc.) were represented at the workshop as well. The Cattle-Sheep-Goat workshop estimated 120 attendees, 20 countries, 23 companies. Funding for a postdoc was also awarded. A pangenome training session was held with 38 attendees, and this training will also be offered at the next PAG meeting (2024).

A letter to the request for comments from the OSTP/FDA regarding the modernization of biotechnology (i.e., editing of animals in the USA puts them into the “drug” category) due on 3 February 2023. Specifically addressing the requirements for the disposal of edited animals and the process of commercialization of these animals. Plants are regulated through USDA APHIS and other countries have a much more risk-based approach. A motion was made to have the NRSP-8 genome community develop a position statement to be submitted by 3 February 2023 regarding their stance on this issue (animals regulated as food not drugs). Motion was seconded and not met with opposition. The plan is to send the draft letter to the listserv and have people sign virtually. Industry/companies can sign as well. A copy of this letter is provided in Appendix I.

#### Equine

*Samantha Brooks*

PAG 2023 workshop attendees was in excess of 70 persons. A successful conference grant was awarded for a multi-day horse genome workshop held at Cornell over the summer of 2022 (>100 attendees including industry representatives). Participants include breed registries, sports regulatory representatives, and biotechnology companies. A new website was developed in collaboration with the FAANG group and hosts horse pangenome among other data. A multi-state project was put together for the horse group and experiment stations. The horse group averages 10-12 student and early career awards a year (over 200 travel awards in equine have been awarded throughout this NRSP-8 program).

#### Porcine

*Chris Tuggle*

Four new assemblies are slated to be sequenced in the next several months including telomere-to-telomere assembly. Additional linkage with the FAANG project through genome sequencing of the FAANG founder animals and scRNAseq analysis of the adult tissues for which epigenetics data has already been completed. Genome editing in the pig is expanding, including in the field of biomedicine. Five speakers were funded at the 2023 workshop including 3 travel award winners; the workshop included 18 presentations with 50 attendees from 6 countries.

#### Sheep & Small Ruminants

*Noelle Cockett*

General highlights if NRSP-8 impacts across the species were provided, including the importance of having leverageable and matching funds for grants.

## Poultry

*Haijun Zhou*

General highlights include functional annotations, RNA library, muscle cell lines, spatial transcriptome, among other completed refinement of tools and resources available to poultry researchers. Pangenome for chicken and telomere-to-telomere sequence assembly are underway. Numerous students have been supported for travel to NRSP-8 activities.

## Aquaculture

*Benjamin Reading*

From 2018-2023, NRSP-8 Aquaculture members contributed to draft genomes that were completed for 11 species, including 8 finfish species and 3 shellfish species (Channel Catfish, Blue Catfish, 2 subspecies of Rainbow Trout, North American Atlantic Salmon, Nile Tilapia, Striped Bass, White Bass (not annotated by NCBI), Eastern Oyster, Pacific Geoduck, and Pacific Olympia Oyster.

In 2022 a new customized 50K SNP array was designed and made available for Atlantic salmon and genome sequencing projects are underway for 7 finfish subspecies of Rainbow Trout and Cutthroat Trout and 1 shellfish species, North American Pacific Oyster.

AquaMine RefSeq Database for aquatic species was created that includes information from 21 vertebrate finfish and 4 invertebrate mollusks, and 3 invertebrate crustaceans (28 total species). This database includes information for NRSP-8 priority species.

Genomic selection initiated in an eastern oyster breeding program and other species have domestication and selective breeding programs including striped bass, white bass, rainbow trout, and channel catfish in place that interface with industry and are in commercial production.

The 2023 aquaculture workshop had 65 attendees (an average of 35-45 Participants usually at each presentation) with 33 institutions represented (6 government, 15 university/academic, 12 private sector companies) from 12 countries (including USA). There were 3 student travel awards for attendance/presentations.

It is noted that genomic information of most aquatic species is still generally lagging behind that of terrestrial species. Priority Species Identified by USDA & NOAA Marine Aquaculture Initiative include candidate commercial aquaculture species as are potential future targets for genome sequencing and genomic tool development (about 14 additional species total). These are species that already have commercial production or are deemed commercially viable for production in the United States, however they completely lack genome resources.

## General

*Benjamin Reading*

There were 88 publications from NRSP-8 community members directly relevant to the 3 objectives in 2022 (see Appendix II. Products generated by NRSP-8 members in 2022).

The group also contributed to the report on Threats to Food and Agricultural Resources to the US Department of Homeland Security and the US Office of the Director of National Intelligence *Analytic Exchange Program* in 2021 (“TFAR report”). Homeland Security Presidential Directive 9 (HSPD-9) directs Homeland Security to coordinate the overall national effort to protect the *Food and Agriculture Sector*. National Security Memorandum-16 (NSM-16) to *Strengthen the Security and Resilience of United States Food and Agriculture* was based in part on the Threats to Food and Agricultural Resources report and released by the National Security Council in 2022; NSM-16 supersedes HSPD-9. From the Threats to Food and Agricultural Resources report and relevant to USDA NRSP-8:

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*“Among the top threats and vulnerabilities to the United States it is indicated that the **country needs to promote domestic seafood production and that this can be carried out through aquaculture**. Thus, the importance of aquaculture for future food production has been thrust to the forefront. **Further, the importance of genomics and other genome-based or -enabled information and technologies** including convergent biotechnology and transformative or disruptive technologies such as artificial intelligence, synthetic biology, quantum biology, and predictive phenomics is realized. **These will be the tools of 21st Century biology** and that they pose great strengths as well as inherent risks.”*

*“Innovation is a crucial aspect of the Food and Agricultural Sector. **The U.S. public-private R&D sector is developing plant varieties and new terrestrial and aquatic animal breeds, biomanufacturing processes, and omics profiles...that provide competitive commercial advantages with national security relevance**. However, R&D within U.S. organizations are the target of foreign cyber espionage, trade secret, and intellectual property theft [and other threats]...As genomic data become linkable to other data sources, individuals, animal, or plant breeds become identifiable and potentially a target of malicious activities....*

*...Much of this [genomic] data and the algorithms to mine this information reside in private repositories that state and non-state actors can target to steal, destroy, modify, and therefore disrupt years of costly research. At the same time, these attacks can modify genomic information to decrease the bioforensic and attribution capabilities of the U.S...”*

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From US White House/National Security Council and US Department of Homeland Security Fact Sheet on NSM-16:

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*The food and agriculture sector is extensive, interconnected, diverse, and complex. Designated as critical infrastructure and primarily owned and operated by private sector and non-Federal entities, food and agriculture systems and supply chains are vulnerable*

*to disruption and damage from domestic and global threats. The evolving threat environment requires the sector and its essential workforce to better prepare for and respond to incidents with broad impacts on our national and economic security.*

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Proposed deliverables and activities include enhanced protection of food and agriculture critical infrastructure and associated supply chains; defense against the introduction of high consequence pests and diseases; Improved intelligence gathering, data analysis, and information sharing; workforce training in food and agriculture defense.

The NRSP-8 has a very important mission in this regard as purveyors and stewards of genomic data critical to the safety and resilience of the US domestic food supply.

**Food security = national security.**

## **PAG 30 NRSP-8 Morning Meeting and Business Meeting Notes updated: 16 February 2023**

### **PAG 30 NRSP-8 Morning Meeting Minutes**

**15 January 2023**

#### **NRSP – 8 Leaders Meeting**

*7:00 – 8:00 a.m. SkyView Meeting Room 1 Town & Country Hotel, San Diego, CA*

#### **AGENDA**

1. Welcome and introductions – Kent Reed, NRSP8 Chair; Benjamin Reading NRSP8 Chair-Elect
2. Recap submission of NRSP8 Capacity Proposal and timeline for review – Archie Clutter, NRSP8 Administrative Advisor (by phone); Fiona McCarthy and Stephanie McKay, Writing Committee Chairs
3. Administrative Advisor transition – Archie Clutter
4. Updates on plans for AGBT-ag, and efforts to secure additional (non-NRSP) funding – Jack Dekkers
5. Project Chairs and Coordinators comments (focus on plans, new issues or concerns)
  - a. Kent Reed, Chair
  - b. Jack Dekkers, Past-Chair
  - c. Coordinators
    - i. Aquaculture – Ben Reading
    - ii. Cattle - Alison Van Eenennaam
    - iii. Equine - Ernie Bailey
    - iv. Swine – Chris Tuggle
    - v. Poultry - Huaijun Zhou
    - vi. Sheep/Goat – Noelle Cockett
    - vii. Bioinformatics - James Reecy
6. Select Chair-elect from Equine group for 2024-2025 term
7. Additional Administrative Advisor comments; Other items Additional Information:

#### **Guidance for Annual Reports**

- a. Include at least one impact statement from the project’s work since Oct 1, 2021.
- b. Include any grants awarded since Oct 1, 2021 (granting agency and amount) that contributed to the objectives of NRSP 8.
- c. Include workshops’ attendance numbers and institutions represented (if possible).
- d. Need to get annual reports to Kent and the incoming chair (Ben Reading) by mid-February.

## Chair Rotation (changes after annual meeting at PAG)

Sheep/Small Ruminants – 2020-21  
Swine – 2021-22  
Poultry – 2022-23  
Aquaculture – 2023-24  
Equine – 2024-25  
Cattle – 2025-2026

## Meeting Overview

- Elements of new “renewal” proposal have come together (**referred to here as “NRSPx”**)
- This proposal has responded to points raised by external reviewers and been resubmitted to Station Directors to review/approve; Western Region Ag Experiment Station was the leading approver/manager for NRSP
- This is a capacity track proposal and leadership structure will change from NRSP-8
- Look at nominations for new leadership positions...decisions should be made in the business meeting later today
- The five regions of Ag Experiment Station Directors will receive proposal with comments and provide additional feedback in June-July. Final recommendations will be made in summer and the vote in final approval will occur in the fall (by October)
- Funding runs October 2023 - October 2024 (federal fiscal year)
  - o Best approach is likely to plan for approval by making decisions on leadership prior to funding announcement (October); contacting stakeholders, collaborators, & Ag Experiment Station Directors; planning for a meeting similar to the existing NRSP-8 format; and then moving forward with new structuring, etc. in regard to planning the 2024 workshop.

## New Proposal Details (NRSPx)

- Proposal Aims:
  1. Extending genomics capacity to a broader range of animal genomics stakeholders
  2. Supporting capacity to integrate genomic and biological data
  3. Education, training, and outreach
- Budget is ~ \$100k per year (request is just over the \$500,000 stipulated)
- No species-specific coordination. The objective of no species groups is to take what NRSP-8 has done and sharing it for USE generally with stakeholders and external collaborators

- New NRSP Leadership Structure:

<u>Position</u>	<u>Number of People</u>
Chair/Co-Chair	2
Chair & Co-chair for each Aim	6 (1 per aim)
Stakeholder Rep for Aims	3 (1 per aim)
Executive Advisory Board (EAB)	11
-One industry representative per commodity group <sup>1</sup>	
-One Extension professional	
-One informatician	
-One biological/agricultural engineer	

<sup>1</sup> Current NRSP-8 commodity groups are: aquaculture, cattle, poultry, horse, swine, sheep/goat, bioinformatics. The EAB will consist of industry professionals engaged with agricultural animal species (aquaculture, beef cattle, dairy cattle, equine, swine, poultry, sheep and goats), as well as an Extension professional, an informatician who is directly involved in analyzing large datasets of phenotypes (data scientist), and an agricultural engineer who is developing new approaches to measuring animal phenotypes (phenomics).

### Annual Meeting

- Will need another annual meeting location:
  - o This could be PAG or another conference. Benefits of PAG are that we already have the structure and system in place and NRSP-8 folks are already slated to attend. Timing of PAG is also beneficial for faculty that teach. Con of PAG is less genomics-oriented collaborators would not otherwise be attending (most likely).
  - o Careful considerations regarding hosting the meeting at rotating universities. (1) takes more coordination (i.e., no standard system), (2) it may be more difficult for collaborators and stakeholders to have funding available to go to workshops held at [insert whichever university] compared to a conference such as PAG or other
  - o Applying for a **conference grant** to support the annual meeting was proposed. Angelica Von Goor (USDA NIFA) mentioned in her afternoon talk that the deadline to submit a letter of intent and apply for a conference grant *that would be awarded in time for PAG 2024* through USDA NIFA is Sunday **1 July 2023 (LOI)** with the proposal submitted by **15 August 2023**.

TO DO's:

- \* Proposal is in NIMSS, review and look at stakeholder letters.
- \* Benjamin Reading: Send email to group as reminder to contact agriculture experiment station director to discuss the upcoming NRSP project and sunset of NRSP-8 with the intention of expressing positive support of the proposal/future of NRSP-work and inclusive effort; Noelle Cockett to provide a statement regarding this communication that will be forwarded to members.
  - Fiona McCarthy will compile executive summary and stakeholder letters to be provided to others (Ag Experiment Station Directors, potential collaborators, etc.)
- \* Recruit colleagues (non-genomics people that may want to incorporate genomics) and continue to recruit stakeholder involvement (interdisciplinary!)
  - Colleagues and stakeholders recruited for both involvement and word-of-mouth power to recruit others and connect with their Ag Experiment Directors
  - Steve Lommel said LKA can send him materials and he would distribute to solicit interest via NCSU University listserv
- \* Compile a member list (Appendix E) – this will be available in the months ahead

**NRSP – 8 Workshop and Business Meeting**

**PAG30**

**Sunday, January 15, 2023 1:30 – 6:15 p.m.**

**Town & Country Resort, San Diego, CA**

**NRSP-8 workshop**

**1:30 Welcome and introduction**

**1:40 Zhiping Weng** *ENCODE Registry of candidate Cis-Regulatory Elements (cCREs) for Annotating the Human Genome*

**2:30 Daniela Lorenc** *Large-scale genomic predictions with sequence data*

**3:30 Break**

**3:45 Chris Tuggle** *Visualizing the Road to Genome to Phenome in Agriculture*

**4:15 Angelica Van Goor** *Perspectives on the Future of Animal Breeding, Genetics, and Genomics: Fit of Genome to Phenome and the Blueprint within the USDA priorities*

**Business meeting**

- **2022 meeting review (Dekkers)**
- **“Renewal” Writing teams**
- **USDA rep report**
- **Species reports**
  - **Aquaculture: Benjamin Reading/Steven Roberts**
  - **Bioinformatics: Jim Reecy/Fiona McCarthy**
  - **Bovine: Alison Van Eenennaam/Robert Schnabel**
  - **Equine: Samantha Brooks/Ernie Bailey**
  - **Porcine: Chris Tuggle/Cathy Ernst**
  - **Poultry: Huaijun Zhou/Hans Cheng**
  - **Ovine and Small Ruminants: Noelle Cockett/Stephen White**
- **Going forward (Archie Clutter)**
- **6:15 adjourn**

***Attendees at the 2023 NRSP-8 Workshop in 2023 are provided in Appendix III (72 persons signed in and 150 persons were counted in attendance in the room).***

## 2022 NRSP-8 Meeting Review

*Jack Dekkers*

- 2022 PAG meeting was cancelled including NRSP-8 business meeting; rescheduled to coincide with the AGBT Ag meeting
- Made request to USDA NIFA for Conservation Innovation Grants (CIN)
- Conference grant written for AGBTAg24 students & networking (denied→exclusivity)
- Survey to NRSP-8 to hold 2023 meeting (at PAG)
- AG2PI Farm Day will be held June 15-16, 2023 in Kansas City, MO

## NRSPx Renewal Writing Team (Capacity Grant)

*Fiona McCarthy*

- Grant writing team: Fiona McCarthy, Stephanie McKay, Benjamin Reading, Noelle Cockett, James Koltes, Bob Schnabel, Ted Kalbfleisch, Darren Hagen.
- Focus is developing capacity. Elements about bioinformatics are tabled for the sake of the capacity proposal.
- Aims:
  1. Extending genomics capacity to a broader range of animal genomics stakeholders (i.e., what we should be doing is getting the genomics out there as a tool for biologists broadly, such as physiologists)
  2. Supporting capacity to integrate genomic and biological data (i.e., moving on from straight bioinformatics and genomics and moving into data integration, sitting down with people developing phenotype collection devices and other with scientists and stakeholders in the same room...beyond the genomics community)
  3. Education, training, and outreach (i.e., continue training for [our] own students, students in other related fields, and working with industry to consider their workforce needs. Develop educational resources so they can be utilized by whomever needs them to link students→internships→early career professionals). This is *not* to only include academic, but development of educational and training resources with industry stakeholders.
  4. A summary of the capacity building proposal is provided in Appendix IV.

## USDA Rep Report

*Angelica Van Goor*

Angelica Van Goor expressed being impressed with the renewal capacity grant, specifically the 23 letters of support from industry and the linkage to the goals of USDA, etc. Angelica provided a handout with links/QR codes to useful resources for grants and awards. Mention of the conference grant (*see*: above highlighted text from morning minutes) as a viable option for PAG 2024 and/or species groups.

## Species Reports

### Aquaculture

*Benjamin Reading*

PAG 2023 Workshop: 65 attendees, 33 institutions, 12 countries, 3 student travel awards, 18 presentations. Leveraged funds = \$2,000,000 (\$15 million the aquaculture group has brought in over the last 5 years, which is 45:1 ROI for every dollar spent). 42 publications in 2022 (180 in

the last 5 years). NRSP-8 Aquaculture has put out genomes for 11 species (8 finfish & 3 shellfish); data for 28 aquatic species have been published, 14 priority species identified by NOAA with no genomic resources have been identified (priorities moving forward). US DHS activities / food security priorities and tool development. Yniv Palti is the incumbent workshop chair, Neil Thompson is the chair-elect.

### Bioinformatics

*Jim Reecy*

Data movement off of animalgenome.org to preserve these data (external resources, to the “cloud”). James Koltjes et al. are looking into other funding opportunities to keep these resources and personnel around.

### Bovine

*Alison Van Eenennaam*

Some 7,000 animals have been genotyped and the application of omics resources in breeding has been very impactful. Carbon footprint reduction has been a major highlight greatly influenced by genomic resources. Four students were funded to present in 2022 (prior to cancellation) and four in 2023 that did present at PAG. The PAG 2023 Cattle-Pig workshop had 175 attendees from 24 countries, 20 different experiment stations and 20 different companies (breeding companies, biotech, etc.) were represented at the workshop as well. The Cattle-Sheep-Goat workshop estimated 120 attendees, 20 countries, 23 companies. Andrew Hess is the incumbent workshop chair. Pangenome work is also underway, sequencing additional genomes, coordinating the cattle T-to-T data. Funding for a postdoc was also awarded. A pangenome training session was held with 38 attendees, and this training will also be offered at the next PAG meeting. Publications and grants will be reported in the 2022 report (not yet compiled).

A letter to the request for comments from the OSTP/FDA regarding the modernization of biotechnology (i.e., editing of animals in the USA puts them into the “drug” category) due on 3 February 2023. Specifically addressing the requirements for the disposal of edited animals and the process of commercialization of these animals. Plants are regulated through USDA APHIS and other countries have a much more risk-based approach. Motion made by Allison to have the NRSP-8 genome community to develop a position statement submitted by 3 February 2023 at 5:00 PM EST regarding their stance on this issue (animals regulated as food not drugs). Motion was seconded and not met with opposition. Alison’s plan is to send the draft to the listserv and have people sign virtually. Industry/companies can sign as well.

### Equine

*Samantha Brooks*

PAG 2023 workshop attendees was in excess of 70. Successful conference grant awarded for a multi-day horse genome workshop held at Cornell over the summer of 2022 (>100 attendees including industry representatives and more folks wanted to attend). Participants include breed registries, sports regulatory representative, biotechnology companies, etc. A new website was developed with collaboration with FAANG group and hosts pangenome data, among other data. A multi-state was put together for the horse group and experiment stations. The horse group averages 10-12 student and early career awards a year (over 200 travel awards in equine have

been awarded throughout this NRSP-8 program). The incumbent workshop (?) chair is Elain Norton ([elainenorton@arizona.edu](mailto:elainenorton@arizona.edu)) and Co-Chair is Ann Staiger ([elizabeth.staiger@tamuk.edu](mailto:elizabeth.staiger@tamuk.edu)).

### Porcine

*Chris Tuggle*

Four new breed/species are slated to be sequenced in the next several months for pan-genome projects, including T-to-T assembly of Hampshire/Landrace in collaboration with Emily Clark at Roslin Institute. Five speakers were funded at the 2023 workshop, including two for the Joint Swine/Bovine Workshop in the morning as well as three Jorgenson Travel award winners in the afternoon session, which included 18 presentations with 50 attendees from 6 countries. There was further discussion and planning made for using the current year NRSP-8 funding; these included travel funding to attend the Ruminant Pangenome meeting in Nebraska in February to discuss a broader effort in artiodactyls. Additional linkage with the FAANG project through genome sequencing of the FAANG founder animals and scRNAseq analysis of the adult tissues for which epigenetics data has already been completed. Juan Stiebel is the incumbent workshop chair for 2024.

### Sheep & Small Ruminants

*Noelle Cockett*

General highlights across the species were provided, including the importance of having leverageable and matching funds for grants.

### Poultry

*Huijun Zhou*

General highlights include functional annotations, RNA library, muscle cell lines, spatial transcriptome, among other completed refinement of tools and resources. Pangenome for chicken, T-to-T assembly, etc. are underway. Numerous students have been supported. Brian Boyd is the incumbent chair. Yvonne Doechsler is the chair-elect.

### Going Forward (NRSPx)

*Archie Clutter*

*\*Noelle Cockett comments provided after USDA rep and before species reports integrated here\**

Noelle asked for a round of applause to Fiona McCarthy and Stephanie McKay for leading the grant writing team effort.

The NRSPx capacity proposal broadly focuses on the enormous potential of continuing animal genomics work. Also see aims and expanded notes provided by Fiona McCarthy in section above “NRSPx Renewal Writing Team (Capacity Grant)”.

### Submission and Review

The proposal will be submitted this week through NIMSS, then will go to the Western Experiment Director (Bret Haas, currently administering NRSP), Bret will distribute the proposal, budget, 23 stakeholder letters, and response to review to the other four regional Experiment Directors (listed below) to further distribute to their constituents. These five regional directors will have regional meetings in the spring and later provide feedback to NRSP about the proposal in June-July. Final decision made in fall 2023 for October 2023 start.

### *Regional Ag Experiment Stations:*

Western Region (WAAESD) <http://www.waaesd.org/>  
Southern Region (SAAESD) <https://saaesd.org/>  
North Central Region (NCRA) <http://ncra-saes.org>  
Northeastern Region (NERA) <http://www.nerasaes.org/>  
1890Land-Grant Universities (ARD) <http://www.umes.edu/ard/>

Archie Clutter made note that Joe Cassidy is taking over the lead academic advisory role and the North Central advisory role.

### Action Items for NRSPx Members

- Noelle encouraged all to make an appointment with their Ag Experiment Station Director and express your current involvement in the present NRSP-8 and your future support of the new NRSP (“NRSPx”) and desire to be included. Archie reinforced the initiative to meet with regional Ag Experiment Director (possibly through respective Department Heads).
  - o On timeline for meeting with Ag Experiment Station Directors: The NRSP group will meet in spring (May-June). The proposal will be voted on in the fall of 2023 for October start (if awarded).
  - o On what to communicate: Reiterate proposal structure (focused on aims, not species), enthusiasm, and benefits. Noelle will write an executive summary describing what the proposal is for, how folks will benefit (within and outside of the genomics/existing NRSP-8 community), and the industry letters of support will also be included.
    - Noelle will send the summary and letters to Benjamin Reading and Kent Reed, they will distribute to current NRSP-8 members
  - o Suggested to “find a buddy” from industry, Extension, or academia who would benefit or is interested in the use of genomics, but is at present unfamiliar with the methods and applications. This will be towards meeting the NRSPx aim of facilitating “Extending genomics capacity...”
- For NRSPx participation: your name needs to be added to the Appendix E (member list) for official inclusion. Archie will confirm whether this can begin, being compiled soon.

### New Leadership

Benjamin Reading is NRSP-8 Chair. Annette McCoy is NRSP-8 Chair-Elect (*See*: “Chair-Elect” information below for information about role). Stephanie McKay and Fiona McCarthy will serve as the Chair and Chair-Elect for the NRSPx, and will help coordinate the nomination and voting process for this new leadership structure along with Ben Reading, Noelle Cockett, and Annette McCoy.

Ben Reading and Kent Reed are presently writing the Year 4 report due mid-February 2023.

Votes will be solicited for new NRSPx leadership via email.

### Chair

*Gathering annual reporting from the Coordinators and compiling the Annual Report. Report should be assembled for submission by beginning of March if possible.*

*Coordinating planning for the 2024 meeting. We will be awaiting approval of a capacity-track proposal that includes a new leadership structure and we will not have confirmation of approval until later in the year. The group can decide how to structure the workshops/programs for 2024, but this will need to be prepared to move to the new leadership structure (assuming the proposal is approved). The transition process is currently written into the capacity building proposal as follows:*

*“In preparation for an approved Capacity proposal, the Co-Chairs for the Capacity Proposal Writing Committee will work with the current leadership for NRSP8 (Chair, Past-Chair and Coordinators) to solicit nominations for the Leadership positions in the new structure for the Capacity project and organize the January 2024 meeting at which election for Leadership positions will be completed and terms of the new Leadership Team members will begin.”*

Benjamin Reading named final NRSP-8 Chair by aquaculture group.

Kent Reed is Past-Chair

Fiona McCarthy and Stephanie McKay are the Co-Chairs Capacity Proposal Writing Committee

### Chair-Elect

Primary duties are: (1) coordinate the final NRSP-8 report with current chair, Benjamin Reading; (2) to help coordinate the 2024 NRSPx workshop and business meeting; and (3) contribute to the PAG 2024 organizing committee.

Annette McCoy named final NRSP-8 chair-elect by equine group.

### Final NRSP-8 Report

- Due mid-February 2024 for federal fiscal year October 1 2022 – September 30 2023
- Aim to have this completed in fall 2023
- Collect information from NRSP-8 species coordinators below (sunset):
  - o Aquaculture – Benjamin Reading
  - o Cattle – Alison Van Eenennaam
  - o Equine – Earnie Bailey
  - o Swine – Chris Tiggle
  - o Poultry – Huaijun Zhou
  - o Sheep/Goat – Noelle Cockett
  - o Bioinformatics – Jim Reecy

### Meeting Plans 2024

The idea is that species groups workshops are slated to still occur at PAG 2024, as many of these sessions are coordinated with other organizations, and, very importantly, we do not want to lose our meeting times in the PAG agenda. *See above for information on the conference grants (USDA NIFA, Angelica Van Goor)*. Noelle Cockett's suggestion was to include pictures of past NRSP-8 leaders and activities to showcase at PAG 2024 as tribute to the program and success.

*Kent Reed*: Recommendation from leadership was to meet at PAG in 2024. A motion was placed and seconded with no opposition.

### Other Business

*Jim Reecy*: Asked for a round of applause to those who have been involved in NRSP-8 since the beginning.

*ADJOURN*

## Appendix I.

30 January, 2023

Animal and Plant Health Inspection Service

US Department of Agriculture

4700 River Road

Riverdale, MD 20737

Attn: Alan Pearson

Via eRulemaking Portal at <https://www.regulations.gov/>

**SUBJECT:** *Docket No. APHIS-2022-0076 - Request for Information; Identifying Ambiguities, Gaps, Inefficiencies, and Uncertainties in the Coordinated Framework for the Regulation of Biotechnology*

This comment is made on behalf of, and signed by, members of the USDA-funded National Animal Genome Research Support Program (NRSP-8). The membership of the NRSP-8 encompasses academics and research scientists from the dairy and beef cattle, poultry, equine, sheep, goat, swine, and aquaculture sectors, and impacts agriculture in every state and region of the United States. Livestock and poultry are top US agricultural commodities accounting for more than half of the agricultural cash receipts, at least \$100 billion each year. On the other hand, the US imports ~90% of its seafood, at a deficit of more than \$14 billion per year. Therefore, advances in livestock, poultry and aquaculture production capacity and efficiency are essential to advance national and global food security, especially with increasing consumer demand for animal welfare, growing restrictions on antibiotic use, and changing environments. To enable agrifood industries to increase their efficiency and sustainability, we need robust animals with superior health and production traits. A major requirement for increasing production efficiency is **genetically improved strains of animals** with sufficient genetic diversity to allow continued improvements in traits including yield, disease and pest resistance, efficient reproduction, and stress tolerance, while assuring nutritional quality and animal welfare.

Animal breeders have widely adopted the practice of genomic selection as part of their conventional breeding programs over the past decade. This technology allows for the accurate selection of genetically superior and efficient animals based on an economic index which typically includes production and health traits. This process does not trigger regulatory oversight anywhere in the world. There is no “claim verification” required for the economic selection index, nor any testing required to determine the accuracy of the genomic prediction. However, the gradual increase in the rate of genetic improvement over time, and the doubling of the rate of genetic change that occurred with the adoption of genomic selection in the US dairy industry,<sup>1</sup> is validation enough of the veracity of the genetic improvement claims. Such changes have resulted in a dramatic decrease in the greenhouse gas emissions associated with producing a glass of milk. In other words, producers are successfully selecting for more productive, disease-resistant animals using the naturally-occurring genetic variation, also known

as genomic alterations, that exist in the population in the absence of any regulatory oversight by FDA or USDA. It is widely accepted that introduction of new traits into animals via conventional breeding practices is a safe process and the food safety processes in place are sufficient to ensure human, animal and environmental safety. It is also widely accepted that these new traits are the result of naturally-occurring genomic alterations in the genome, also known as the very basis of evolution.

**We write to express our collective disagreement with the Food and Drug Administration’s Center of Veterinary Medicine (FDA-CVM)’s determination that intentional genetic variations introduced into the genome of animals using modern biotechnology meet the definition of a drug.** Heritable genetic information is an integral part of an organism and therefore cannot be considered a drug. Many DNA variants alter the form or function of an animal, they are the basis of all livestock genetic improvement programs. Furthermore, there is no scientific rationale for regulating heritable genetic information differently based solely on whether it is natural, induced, intended, or designed. As a result, in the United States an intentional DNA alteration in an animal’s genome that is produced using modern biotechnology is currently regulated as an unapproved new animal drug. From a genetic perspective, if the modified sequence naturally occurs in existing food animal populations, there is no meaningful difference between these two scenarios, an observation supported by nearly four decades of research. This is a clear example of a policy decision made in the absence of scientific support. US researchers and animal agriculture are at a disadvantage globally, and current regulation makes it more difficult for US farmers and ranchers to rapidly respond to the challenges posed by climate change.

In the 2017 Draft Guidance for Industry, “**Regulation of Intentionally Altered Genomic DNA in Animals**”,<sup>2</sup> the FDA outlined its intent to regulate intentional single base pair changes, deletions, and insertions in animals as new animal drugs. The guidance stated that “A specific DNA alteration is an article that meets the definition of a new animal drug at each site in the genome where the alteration (insertion, substitution or deletion) occurs.” Additionally, it outlined that “each specific genomic alteration is considered to be a separate new animal drug subject to new animal drug-approval requirements.” As a result, animals with the exact same genotype produced using different approaches, e.g. conventional selective breeding versus gene editing face inconsistent and vastly different regulatory burdens, irrespective of actual product risk.

This approach directly contradicts the 1992 Update to the Coordinated Framework which reaffirmed that Federal oversight “**focuses on the characteristics of the biotechnology product and the environment into which it is being introduced, not the process by which the product is created**”. However, when it comes to animals carrying intentional genomic alterations, the regulatory oversight trigger is the modern biotechnology process used to create the product. In essence, rather than the risk assessment itself determining the regulatory action that may or may not need to be taken, the introduction of an intentional alteration into the genome of an

animal using modern biotechnology is what triggers the expensive and time-consuming new animal drug approval pathway, irrespective of any actual product risk(s).

The US FDA-CVM stands alone globally in regulating intentional DNA alterations as veterinary drugs. In a growing number of countries, gene-edited animals are treated no differently than those produced through conventional breeding, and such edited animals are allowed to enter commerce. There are fast-growing myostatin knockout fish approved for sale in **Japan**, gene-edited hornless dairy cattle have been judged to be no different than naturally occurring hornless cattle in **Argentina**, and heat-tolerant PRLR-SLICK cattle, with a premature stop missense mutation in the prolactin receptor gene, have been judged to not be “GMO” in both **Brazil** and Argentina. In Argentina, the first country that enacted regulatory criteria to exempt gene edited organisms that do not contain novel DNA sequences from GMO regulation, there was an increase in applications from small to medium-sized developers, in addition to an increase in the types of traits and organisms being edited, including applications from livestock developers.<sup>3</sup>

The 2017 Draft Guidance for Industry<sup>2</sup> stated that under the Food, Drug & Cosmetic Act, a new animal drug is “deemed unsafe” unless FDA has approved a new animal drug application (NADA) for its intended use. It is stated that a primary goal during the investigational phase of development of the animal with an intentionally altered genome is to ensure that edible products from these investigational animals do not enter the food supply without prior FDA authorization. This means that research animals and their products (milk, honey, eggs, muscle tissue, as well as other tissues such as liver, kidney, skin, and fat) are not allowed to enter the food supply. Rather, all research animals and their biological products be disposed through incineration, burial, or composting, unless the product conforms to specified exemptions for food use under an Investigational New Animal Drug (INAD) exemption. This means that academic research laboratories working on gene-editing applications in food animals must either incinerate, bury, or compost all of their gene-edited livestock (e.g. cows, sheep and pigs), or apply for an INAD and subsequently provide data to support an Investigational Food Use Authorization (FUA) to introduce gene-edited animals and their products into the food supply. These safeguards were designed for development of actual drugs and are cost prohibitive for most academic laboratories at land-grant universities working on gene-editing in large livestock food animals like cattle.

Moreover, history has shown that regulating bioengineered animals as drugs has stalled the commercialization of useful applications.<sup>4</sup> Genetically engineered livestock were first reported in 1985, and yet in 2023 only a single food animal, the fast-growing AquAdvantage salmon, is available commercially in the United States. Additionally, the GalSafe pig has been approved for food use. The founder lines of both of these examples were produced more than 20 years ago.<sup>5</sup> <sup>6</sup> The costs associated with delayed commercialization of bioengineered livestock, beyond the normative 10-year product evaluation period following the first peer-reviewed publication announcing its development, were modeled using three case studies: mastitis-resistant dairy

cattle,<sup>7</sup> porcine reproductive and respiratory syndrome (PRRS) virus-resistant pigs<sup>8</sup>, and the AquAdvantage fast-growing salmon<sup>4</sup> in a 2021 paper.<sup>9</sup> It was estimated that delays of 5 or 10 years in the commercialization of these livestock harboring intentional genomic alterations were associated with **billions of dollars in opportunity costs**, and reduced global food security. For example, it was estimated that delaying the commercial availability of the gene-edited knock-out PRRS virus-resistant pigs by 10 years in the United States and the European Union would be associated with opportunity costs of **\$14 billion**. Additionally, the new animal drug-approval process can take seven to eight years, sometimes longer, and patent rights may expire before the approval process is even completed. As there is no legal method of enforcing a royalty after a patent expires, this regulatory approach further creates a disincentive for inventors and investors.

The drug-centric regulatory policy for bioengineered animals is not fit-for-purpose,<sup>10</sup> and disadvantages the research, investment and adoption of these technologies by US farmers and ranchers at a time of increasing concern regarding the environmental footprint of animal agriculture. This regulatory approach appears to be based exclusively on legal precedent, rather than on both scientific and legal precedent. As a result, the United States is now lagging behind the rest of the world when it comes to the approval, and ultimately the adoption of biotechnology innovations to allow continued genetic improvement in livestock for traits such as disease and pest resistance, efficient reproduction, heat and stress tolerance, and animal welfare.

**The US FDA and USDA should consider the following specific policy recommendations to reconcile the emerging technical consensus on how to effectively regulate animals and animal cells for food purposes produced using biotechnology.**

- The FDA shall promulgate regulations of animals and animal cells that harbor nonheritable natural, induced, intended, or designed genetic information for the purpose of producing a therapeutic formulation (a drug), and for which an in vivo half-life can be measured.
- The USDA Animal and Plant Health Inspection Service (APHIS) shall promulgate regulations of animals that harbor natural, induced, intended, or designed genetic information in agricultural food animals for the purpose of preventing the introduction and dissemination of diseases and pests.
- The USDA Food Safety Inspection Service (FSIS) shall promulgate regulations of animals that harbor natural, induced, intended, or designed genetic information in agricultural food animals for the purpose of ensuring that products derived from such animals are wholesome and safe, and are not adulterated or misbranded.

The views expressed in this comment are supported by the signatories in a personal capacity only, and do not represent the official position of their employing institution, or of the USDA.

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### Appendix III. NRSP-8 Workshop and Business Meeting Attendees in 2023 (72 persons).

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#### **Appendix IV. Summary of the renewal NRSP capacity building grant.**

We propose a national project that develops capability in using genomics-enabled technologies within diverse animal industries. In this context we define genomics-enabled technologies as any high-throughput platform that relies on genomics-wide data analyses (including transcriptomics, sequencing, proteomics, etc.), global analysis of metabolites, and the microbiome, as well as phenomics and large-scale genetics studies (including GWAS, haplotype analysis, and use of genetic markers, traits, or phenotypes). Developing this very broad capacity requires an infrastructure that supports consistent collection and use of genomics data types, their integration with rich phenotypic (meta) data, and the development of human expertise in bioinformatics and related informatics and engineering techniques. Building both informatics and human capacity will ensure the application of these techniques into predictive biology that supports resilient agricultural systems.

Our overall goal is to develop the infrastructure and expertise required to apply genomics-enabled technologies to US animal industries. This overall goal is supported by three specific objectives:

- (1) Extending genomics capacity to a broader range of Animal Science stakeholders.** New genomic technologies support the collection of expanded “omic” data types and increasing data volume. In fact, for most researchers, it is now easier to generate genomic data than it is to manage and analyze the resulting data. Aim 1 specifically addresses the ways researchers can acquire, analyze, share and re-use genomics data types for their own programs.
  
- (2) Supporting capacity to integrate genomic and biological data.** New engineering technologies are now allowing animal scientists to collect biological data for a wide variety of animal traits and phenotypes. Similar to Aim 1, we now need to develop the ability to manage, analyze and integrate these large and complex biological datasets and then connect them to the genomics information that is also being collected. Aim 2 specifically addresses the need for scientists to integrate diverse data types, both biological measurements and genomics, for a more complete understanding of complex agricultural systems.
  
- (3) Education, training and outreach to develop a data-savvy workforce.** The animal genomics community has been relatively successful at providing bioinformatics training that supports genomics studies. However, there is an acute need to extend this capability to the entire animal science community and to ensure that animal scientists can manage and apply the expanding range of data types which are used in animal industries (e.g., genetic, genomic, epigenetic, GIS, images and audio data types). Aim 3 specifically addresses the need for ensuring that we are developing the 21st century agricultural workforce in the areas of informatics science, which can keep US agriculture globally competitive and resilient.