USAHA COMMITTEE ON BIOLOGICS AND BIOTECHNOLOGY
Chair: Keith Haffer, SD
Vice Chair: Alan Young, SD

Gary Anderson, KS; Chris Ashworth, AR; Randall Berrier, CO; Duane Chappell, KY; Maria Cooper, IN; Barbara Determan, IA; James England, ID; James Evermann, WA; William Fales, IA; Allison Flinn, MD; Patricia Foley, IA; K. Fred Gingrich II, OH; Gail Golab, IL; Keith Haffer, SD; Joseph Huff, CO; Elizabeth Lautner, IA; John Lawrence, ME; Randall Levings, IA; Joanne Maki, GA; David Marshall, NC; Will McCauley, DC; Scott McVey, NE; Leela Noronha, KS; Steve Parker, GA; Allison Phibbs, DC; Kathryn Simmons, DC; Caleb Smith, MN; Jessica Watson, MI; Dennis Wilson, CA; Josh Winegarner, TX; Mark Wood, GA; Alan Young, SD.

The Committee met on October 9, 2020 virtually, from 2:30-4:30 p.m. Eastern Standard Time (EST). There were 11 members and 48 guests present.

Presentations & Reports

Center for Veterinary Biologics (CVB) Update 2020
Byron Rippke, CVB

- COVID -19 response
  - With the exception of on-site inspections, CVB has maintained operations at “normal” levels.
- Budget & Staffing
  - Currently under a continuing resolution. Will maintain spending at FY2020 levels.
  - Brought on seven new positions with increase of $800K received.
- Decision Tracker – New system for knowledge management related to policy development
  - Captures contextual information as well as versions of policy
  - Helps with succession planning
- Pharmacovigilance implementation
  - Final rule in 2018, implementation in February 2021
  - Requires mandatory reporting
- Revised Inspection Memo (800.91)
  - Puts U.S. more in line with other global inspection systems
  - Provides a U.S. Good Manufacturing Practices (GMP) Inspection Certificate
- Virtual Inspections – limited to currently licensed, new or remodeled facilities
- Potency Specification Policy – data driven overages
- Policy on cancer immunotherapies – provides guidance to industry of what’s required for this class of products
- Autogenous vaccine policy revision
  - Extension of isolates

    - International movement of isolates and product
    - Third party stockpiling/distribution of product
- Ingredients of Animal origin – looking at tightening requirements
- Reference monitoring – extend the "life span" of references if possible
- Updating diagnostic policy – evaluating current diagnostic kit policy

Perspectives, Priorities, and Updates from the Veterinary Biologics Industry

Will McCauley, Animal Health Institute (AHI*)*

Ingredients of Animal Origin

The animal health industry and the USDA continue to discuss potential new requirements for the testing and sourcing of ingredients of animal origin (IAO) used in the manufacture of veterinary biologics. The pertinent regulation/guidance on this topic is Title 9 of the Code of Federal Regulations Sec. 113.53 and Draft Veterinary Services Memorandum 590 - *Ingredients of Animal Origin Testing*. There are multiple points of contention between manufacturers and the USDA, but a major disagreement is on the "workability" of a proposed requirement for the use of a particular reagent in the manufacture of master seed and cell stocks for veterinary biologics. The reagent in question, a particular type of fetal bovine sera, is not available in sufficient amounts to meet the needs of the veterinary biologics industry, even if global sources are included.

Potency Specifications of Veterinary Biologics

The animal health industry and the USDA have reached an agreement on the overage levels of antigens that must be present in US-produced veterinary biologics, as well as appropriate testing/evaluation methods to confirm potency. This information will be included in a pending version of VSM 440 - *Guidelines for Potency Specifications of Biological Products Administered to Animals*. Focus has now shifted to discussion of the stability of biologics; manufacturers and USDA continue to actively pursue an agreement on appropriate requirements/measurements of product stability and look forward to completion of Draft VSM 155 - *Guidelines for Conducting Product Stability Studies*.

USDA GMP Inspection Certificate

USDA plans to finalize creation of its GMP Inspection Certificate soon and will begin issuing this document for manufacturers who export product to countries that require/desire GMP language on their import documentation. The hope is that this will help address the (unfounded and incorrect) perception that U.S. veterinary biologics manufacturing facilities are sub-standard as compared to some international manufacturers. The certificate will include:

- All addresses the USDA-CVB Specialist(s) visits
- The start/end date of the inspection
- A 5-year expiration date, which starts with the inspection date
- CVB authority signature

Diagnostics-focused industry meeting held by Animal Health Institute (AHI) on September 30

The Animal Health Institute held its Fall Veterinary Biologics Section meeting on September 30,2020; the meeting's General Session focused on conversations around needed changes to diagnostics regulation and the plans on how to address these changes. AHI will be establishing a Diagnostics Working Group to begin the task of determining what USDA-CVB should and should not be expected to regulate within the realm of diagnostics, with other topics/issues to follow as determined.

Domestic testing option for swine biologics exported to China

AHI continues to advocate for domestic testing options for biologics manufacturers seeking to abide by Announcement #172 from the Chinese Ministry of Agriculture and Rural Affairs. Announcement #172 requires that any foreign biologic (or component) imported into China for use in swine must be tested for the presence of the African Swine Fever (ASF) virus by polymerase chain reaction (PCR) methods. While there are U.S. companies who are willing and able to provide this testing within the United States, APHIS recommends that this testing be performed at overseas laboratories at this time. AHI will continue to work with APHIS and various diagnostic entities to find an appropriate way to offer this testing stateside until Announcement #172 can be dealt with in trade negotiations, as it represents a non-tariff trade barrier that is not allowed by current World Trade Organization (WTO) guidelines.

ARS Veterinary Biologics Industry Training Program

The USDA's Agricultural Research Service is seeking contact from veterinary biologics manufacturers who are interested in hosting ARS employees at their facilities to learn "hands on/real world" knowledge of the vaccine manufacturing process. ARS's goal is for their staff to gain valuable information on:

- Quality Assurance/Quality Control
- Assay development
- Master seed and cell production
- Clinical development
- Technology transfer
- Etc.

SARS-CoV-2 RealPCR Test: development and commercial release of a veterinary test

M. Alexis Seguin, IDEXX Reference Laboratories

Early in the course of the COVID-19 pandemic, there were questions about the role of companion animals in the transmission of SARS-CoV-2 infection. Due to these concerns, IDEXX Reference Laboratories quickly developed and analytically and clinically validated a novel real-time polymerase chain reaction (PCR) test to detect SARS-CoV-2 (COVID-19) for use in veterinary species. The IDEXX SARS-CoV-2 (COVID-19) RealPCR Test is based on a unique alignment to the published genetic sequences of the virus from the human outbreak and targets the same nucleocapsid gene as used in CDC assays. This target was based on sequence analysis showing high conservation and adapted to meet the melting temperature and analytical requirements of our standardized platform.

Analytic validation of the test first involved sequence blast analysis against more than 300 publicly available genetic sequences. Second, a synthetic positive control was used to functionally validate the assay for performance, which met requirements for robust signal-to-noise ratio, amplification efficiency, intra-run and inter-run reproducibility, and correlation. In addition, IDEXX implemented three CDC assays to run in parallel with the IDEXX assay for confirmatory purposes. Specificity studies showed no cross-reactivity with the new PCR test against common veterinary coronaviruses affecting companion animals. Likewise, currently available RealPCR tests for these veterinary coronaviruses were demonstrated to not detect synthetic COVID-19 nucleic acid.

Clinical validation was performed using characterized clinical isolates from humans. Forty-eight clinically characterized human isolates (32 SARS-CoV-2 positive and 16 negative) were tested and compared to results from an approved human diagnostic laboratory. All characterized SARS-CoV-2 positive specimens tested positive and all characterized negative specimens tested negative with the IDEXX SARS-CoV-2 (COVID-19) RealPCR Test. IDEXX Reference Laboratories was also invited to participate in two rounds of proficiency testing, resulting in external quality-control assurance certification through the European group, INSTAND e.V. This proficiency testing involved testing of characterized clinical specimens, including heat-inactivated specimens positive for SARS-CoV-2 in varying concentrations, and specimens positive for seasonal human CoV and MERS-CoV in varying concentrations. IDEXX achieved certification after demonstrating 100% sensitivity and specificity in detection of SARS-CoV-2 virus in these specimens.

In April 2020, the IDEXX SARS-CoV-2 RealPCR veterinary test was released for ordering by veterinarians in 23 countries across the Americas, Europe and Asia-Pacific. Due to the internationally reportable nature of this disease, consultation with regulatory authorities in each country was critical to navigate the complex and varied requirements. Clear diagnostic guidance is provided that testing of animals is recommended only in specific exceptional cases where there is a strong reason to suspect infection including known exposure, consistent clinical signs, after more common veterinary causes have been ruled out, and following consultation with relevant public health authorities.

Since the global release, testing has been appropriately low, in accordance with diagnostic guidance. Species tested include dogs (53%), cats (42%) and other species (5%) including exotic felids (lions, tigers, clouded leopards) and small mammals (e.g., ferrets, rats, chinchillas and otters). Only seven positives (five cats and two dogs) have been detected to date by IDEXX Reference Laboratories. All positives were in the United States and were confirmed by the National Services Laboratory (NVSL-USDA).

Committee Business:

A quorum of the committee was present and voted on a resolution brought forth by Joseph Huff. The resolution, *Reaffirmation of commitment of CVB to continue risk-based policy development*, was voted on, passed by unanimous vote and forwarded to the Committee on Nominations.

The meeting was adjourned at 4:36 p.m.