

## REPORT OF THE COMMITTEE ON BIOLOGICS AND BIOTECHNOLOGY

Chair: James Wolfram, FL  
Vice Chair: Joseph Huff, CO

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The Committee met on October 22, 2013 at the Town and Country Hotel, San Diego, California, from 7:00-10:00 p.m. There were seven members and 12 guests present. The meeting was opened by J.H. Wolfram and Vice Chair Joe Huff was introduced. Due to retirement last year, Wolfram is stepping down as Chair and asked for a replacement. Dr. Donna Gatewood has volunteered to do so, pending appointment by the President. Additionally, the chairs have requested an afternoon time slot for 2014.

### **Vaccination of Wild Prairie Dogs against Plague Using an Orally-delivered, Virally-vectored Recombinant Vaccine**

Tonie E. Roche, Ph.D., USGS National Wildlife Health Center

Sylvatic plague, caused by the bacterium *Yersinia pestis* which was introduced into North America about 100 years ago, is a devastating disease of prairie dogs (*Cynomys* spp.) and the highly endangered black-footed ferret (*Mustela nigripes*) which depends on them for prey. We have developed a novel, virally-vectored sylvatic plague vaccine (SPV), deliverable via oral baits to wild prairie dogs. Laboratory studies have demonstrated that consumption of SPV-laden baits effectively protects prairie dogs against plague infection. Field studies to assess the use of SPV as a preemptive management tool against plague began in selected prairie dog populations in 2012. If successful, an oral vaccination program could be initiated in key locations to decrease the occurrence of plague epizootics in prairie dogs, reducing the source of bacteria while avoiding the indiscriminate environmental effects of dusting. Control of plague in prairie dogs, and possibly other wild rodents through the application of SPV, could help stabilize grassland ecosystems, significantly enhance black-footed ferret recovery, and achieve additional economic, environmental, and public health benefits.

### **Reshaping Antibody Diversity in Cows - Implications for New Diagnostics and Therapeutics**

Vaughn Smider, Scripps Institute

Cows have limited genome encoded combinatorial diversity potential, yet mount a robust antibody response. Cows have few V-regions but exceptionally long complementarity determining regions (CDR) H3 loops, however the mechanism for creating diversity is not understood. Crystal structures of two cow antibodies reveal that these CDR H3s form a very unusual architecture composed of a  $\phi$ -strand "stalk" that supports a structurally diverse, disulfide-bonded, "knob" domain. Deep sequencing revealed that ultralong CDR H3s contain a remarkable complexity of cysteines, suggesting that these disulfide-bonded mini-domains may arise during repertoire development. Sequence analysis indicates that diversity arises from somatic hypermutation of an ultralong DH with a severe codon bias towards mutation to cysteine. These unusual antibodies can be engineered to recognize ion channels and GPCRs through the knob structure, opening up unique opportunities for the generation of a new class of biologics.

### **Transforming the Animal Health Regulatory System for the 21st Century: The Institute of Computational Comparative Medicine and the Animal Health Regulatory Science Initiative**

Ronette Gehring, Kansas State University

Jim E. Riviere, North Carolina State University

The Institute of Computational Comparative Medicine (ICCM) was recently established at Kansas State University's College of Veterinary Medicine (KSU-CVM) as a direct result of the University's continued commitment to supporting research and service that is directly related to animal health. The ICCM's focus is to apply quantitative mathematical modeling and simulation techniques to problems in animal health and welfare, which includes predicting impacts on human health and food safety. New faculty will be hired to complement existing expertise at KSU-CVM, making the Institute a one-of-a-kind resource for the animal health industry. One of the goals of the ICCM is to spearhead transformation in

the animal health regulatory system through the Animal Health Regulatory Science Innovation Initiative (AHRsII). AHRsII will facilitate incorporating 21st century science into the animal health regulatory system through the application of novel methods of computational comparative medicine and modern biology. This will be achieved with minimal disruption to existing and established procedures through cooperation and collaboration between the ICCM, industry and the FDA/CVM. An outcome of this initiative will be the training of a cadre of quantitative regulatory scientists capable of improving the underlying scientific basis of the regulatory system in which they will be employed. The long-term deliverables and benefits of this initiative would include development of a vetted, improved and state-of-the-art “animal health product regulatory tool box”. AHRsII is envisioned to be structured as an academic-industrial membership-fee consortium between the ICCM at KSU, and participating animal health companies with contracted consultative input from CVM/FDA. In essence, the AHRsII would serve as an independent translational animal health drug research institute focused on moving modern scientific practices from the bench to the approved drug arena.

### **Veterinary Services Reorganization**

Elizabeth Lautner, National Veterinary Services Laboratories (NVSL), USDA-APHIS-VS

Five years ago, the Veterinary Services (VS) leadership started a review of the organization's strategic direction. After reports from many working groups and development of the *VS: New Perspective* document, the Deputy Administrator in June 2012 announced the intent to reorganize VS and provided a draft business structure based on four units. Additional working groups and leadership interactions developed the final organizational structure. The VS reorganization has received the necessary approvals and is scheduled to take place in November 2013.

The four business units are:

- 1) **Surveillance, Preparedness and Response Services (SPRS)** – The SPRS unit will provide planning, policy, program, regulatory oversight and implementation for VS surveillance, preparedness and response activities. It consists of the functional areas of Commodity Health, Field Services, National Preparedness and Incident Coordination, National Veterinary Stockpile, and One Health Coordination.
- 2) **Science, Technology and Analysis Services (STAS)** – The STAS unit brings together the VS science centers to provide the solid scientific, technical, and analytical foundation needed to support VS in meeting its mission responsibilities. It includes the Center for Veterinary Biologics, the National Veterinary Services Laboratories, the Center for Epidemiology and Animal Health and the Office of STAS Interagency Coordination. The scientific functions include diagnostic capability and capacity; regulatory activities related to the approval and monitoring of veterinary biologics (vaccines and commercial diagnostic test kits); surveillance design, planning and analysis; economic analysis; risk assessments, and predictive modeling in economics and epidemiology.
- 3) **National Import and Export Services (NIES)** – The NIES unit provides policy direction, international collaboration and regulatory oversight activities associated with import, export and interstate movement of animal and animal products. It consists of the functional areas of Policy, Permitting, and Regulatory Services; Service Centers, Animal Import Center Services; Port Services; Agricultural Select Agent Services; and International Animal Health Standards Services.
- 4) **Program Support Services (PSS)** – The PSS unit oversees the budget, information management and technology, administrative services, training and recruitment activities, writing services and strategic planning.

### **Desert Bighorn Pneumonia Outbreak and Response: Old Dad Peak and Marble Mountains**

Ben Gonzales, California Department of Fish and Wildlife

A pneumonia outbreak has been identified in desert bighorn sheep in Mojave National Preserve. The disease has been identified in the Old Dad system (Old Dad Peak and vicinity including Kerr, Vermin, Main Old Dad, and Kelso water sources). Clinically ill animals have also been identified in the Marble Mountains which are in a separate metapopulation; diagnostic tests are pending. A recent helicopter survey (July 16-18, 2013) indicated there were significantly fewer sheep than have previously been surveyed in the Old Dad system, suggesting a large mortality event has occurred.

To date approximately 30 sheep carcasses have been identified. Samples from many of these carcasses have been submitted for necropsy and/or veterinary diagnostic tests. Confirmed respiratory pathogens include *Mycoplasma ovipneumoniae* and *Bibersteinia trehalosi*. Both are bacteria which have been linked to other pneumonia outbreaks in bighorn sheep. Both are pathogens associated with domestic livestock including sheep, goats, and cattle. The inciting cause of the outbreak has not been identified; however, interaction with domestic livestock is suspected.

An interagency working group has been formed to monitor the outbreak, suggest best practices for limiting effects of the disease, and provide recommendations for management actions. Members of the working group represent the California Department of Fish and Wildlife, National Park Service, Oregon State University, and affiliated researchers. Funding and staff for this work is provided by the Wild Sheep Foundation, Society for the Conservation of Bighorn Sheep, California Department of Fish and Wildlife, and the National Park Service.

- Management actions currently under consideration include:
  - collaring healthy bighorn sheep in areas peripheral to the outbreak to sample for disease surveillance, monitor disease spread, and determine sources of mortality;
  - strategically using water sources to discourage connectivity between sub-herds in an attempt to limit disease spread;
  - and removing clinically ill animals from the population to limit disease spread.
- Exact dates and implementation plans for these considered actions are in development.

### **Veterinary Biologics Program: 2013 Highlights and Current/Emerging Issues**

Rick Hill, Center for Veterinary Biologics

Dr. Hill presented the accomplishments of the Center for the past year and compared those accomplishments with the budgetary constraints that this office has had over the past decade. Hill also described the changes that will be occurring in this Center as a result of the reorganization that is occurring. Dr. Byron Rippke and Mr. Steve Karli, proposed speakers, were not able to make the meeting this year due to government constraints.

Dr. Hill reported CVB-IC fiscal year 2013 activities for Mr. Steven Karli, Center for Veterinary Biologics-Inspection and Compliance (CVB-IC) who was unable to attend the conference. Due to the lapse in appropriated funding, final year end numbers were not available in time for USAHA. The presentation will be amended and posted to the CVB website in November 2013.

An update was provided on the Licensing, Serial Release, Testing Information System (LSRTIS) used by CVB as the primary information system for veterinary biologics review, release and compliance activities. CVB regulates more than 125 licensed veterinary biologics manufacturers and over 2,500 different licensed products. In FY2013, CVB provided market releases of veterinary biologics for over 90 billion doses of products. Status of LSRTIS modules and the ongoing system enhancements was summarized. It was also noted that as a result of USDA Departmental data consolidation, the application will be moving from Ames to the USDA data warehouse located in Kansas City.

CVB has utilized the VS Stakeholder Notification through GovDelivery. Stakeholders are encouraged to register with GovDelivery, through a link on the CVB website. In return, when CVB publishes Notices, Memoranda, or Regulations, stakeholders will receive a bulletin announcing the publication. In February 2013, approximately 8,000 stakeholders had registered. CVB has issued a total of 43 bulletins since March 2012.

A summary of the Business Process Improvement project for Electronic Notification of Serial Release was provided. The project was initiated in March 2013 and fully implemented by September 30, 2013 to provide manufacturers with an email notification of market release for veterinary biologics. This has reduced industry wait times and provides for timelier product delivery to customers.

Pharmacovigilance activities within the CVB were summarized. PVWorks has been fully implemented and is being utilized to track and analyze data related to limited adverse event reports (AER) for veterinary biologics. A proposed rule will be published in FY2014 to move the United States to mandatory reporting of summary report of AER's. It is anticipated that a final rule would not be implemented prior to FY2016 or 2017.

An update on current Compliance initiatives was also provided. Infraction notices for license or permitted manufacturers continues to be a significant area of regulatory activity. Efforts reducing regulatory burden for the manufacturers, while still maintaining compliance was discussed. CVB is

currently participating with two industry organizations to gather input and feedback for consideration of expanding process control deviations procedures.

Dr. Hill discussed the projects and priorities for the Unit in FY 2013 on behalf of Dr. Byron Rippke, Center for Veterinary Biologics-Policy, Evaluation and Licensing shared the Units Business Process Improvement. These process improvements focus on helping the Center position itself to implement and expand its ability to receive licensing submissions electronically. These improvements should help the Center more efficiently utilize its resources relative to processing submissions, and reduce the time it takes to ultimately license new biological products.

Another highlighted project is the One-tier label claim proposed rule. This rule is intended to simplify the review of product applications, and provide enhanced product licensing information to the public.

Additionally, work-measures relative to licensing issues (up through September 15, 2013) were presented.

**Committee Business:**

There was no further business by the Committee. The meeting was adjourned following presentations.