Report of the Committee on Biologics and Biotechnology
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The Committee met on October 27th, 2015 at the Rhode Island Convention Center in Providence, Rhode Island from 1:00 PM to 5:00 PM. There were 9 members and 15 guests present. After attendees introduced themselves, the final APHIS responses to resolutions from 2014 were shared.

Presentations & Reports

Title: What's New in the Serum Industry!
Dr. Rosemary Versteegen
CEO, International Serum Industry Association

ISIA has been working hard to upgrade the business practices of the serum industry. This presentation reviewed the major programs being undertaken by the International Serum Industry Association in support of their customers.

The ISIA mission is focused on Ethics, Safety and Safe use of serum and animal derived materials and education of customers and stakeholders. The key programs at this time include 1) Standardization of QC testing methods and test reporting 2) The current state of the ISIA traceability program and recent upgrades to the program 3) The development of testing methods to determine the geographic origin of serum and the tantalizing results obtained to date 4) An update on the progress towards a detailed fact based document being prepared by a consortium of customers, manufacturers, irradiator facilities, and key scientists which will outline the requirements for validated gamma irradiation and results obtained.

Title: Dual Jurisdiction (CVB & CDC) of Facilities Manufacturing Products Using Select Agents
Dr. Kent McClure
General Counsel for the Animal Health Institute

Select Agent (SA) use in the US is overseen by APHIS and the CDC. APHIS deals with animal agents; CDC deals with human agents, and there are overlap agents (see lists at www.selectagents.gov).

The overlap list includes both animal and human pathogens and has both the CDC and APHIS have jurisdiction. Some strains may be excluded (e.g., vaccine strains). The list is currently under review and some organisms have been proposed for removal from the list. There are regulatory exclusions in the regulations, and you can make requests for exemptions (attenuated strains).

Problems are associated with the overlapping jurisdiction. If a facility works with both human and animal SAs, both agencies have oversight. This presents the opportunity for conflicting requirements. For example, CDC say might require a sink in a particular room, and then an APHIS inspector says it has to come out. CDC fairly uniformly wants positive pressure in the rooms being used, and APHIS wants negative pressure. These conflicting requirements create difficulties for companies working under dual jurisdiction.

In 2012, CDC and APHIS entered into a joint memorandum of understanding to try to harmonize their approaches. Subsequently, GAO did a report in 2013 and reviewed the situation, looked at multiple entities and determined that many entities (university labs, commercial labs, etc.) were being inspected

by multiple government agencies. It resulted in recommendations, including joint inspections with one set of findings. They also recommended that one agency should accept another agency's reports.

The situation could still be improved. A resolution will be presented during the business session of this committee meeting.

Title: Center for Veterinary Biologics Activities and Initiatives
Mr. Steve Karli
CVB Director of Inspection & Compliance

Dr. Larry Ludemann
CVB/PEL Section Leader for Bacteriology

Budget: Operating under a continuing resolution. President's budget had a slight increase for 2016. Difficulties in filling vacancies due to budget constraints.

CVB has 91 total FTEs in the program positions, 38 positions in CVB that support NCAH. Safety and Security, and Information Management are shared services.

There are 17 vacant program positions. Some positions have been filled, but others remain vacant. There are recruitment efforts underway for several positions including the PEL Director position.

HPAI was a high priority, even for CVB this year. A number of personnel from CVB were deployed to the field for HPAI activities. In addition, other positions were virtually deployed, although they were able to remain at their duty stations.

Business Process Improvement (BPI) Plans: CVB has been involved in these projects for several years. Electronic submissions processes are moving forward and right now about 72% of submissions are coming in electronically (except for Outlines and Labels). Currently forming an internal working group to expand to Outlines and Labels.

Another project is notification of market release (part of the serial release process). Most were previously sent by overnight carrier, others by regular mail. Now there is an electronic notification for market release, which has resulted in a significant time and money savings for the industry (up to $100K/day in cost savings).

Single tier labeling was also a BPI project, and is in the implementation phase (see below).

Fourth project was for preparing the inspection reports. Historically, there were delays in getting the reports back to the firms. Now they're using a streamlined method of preparing the reports (46% increased efficiency). An analysis determined that the new process continues to indicate the same types of violations, so it appears that the reports are still effectively capturing the report findings.

Other activities: antigen overages, proposed rule on mandatory adverse event reporting (out for public comment), APHIS's plan to move all licensing systems to CARPOL—CVB is included in this initiative,

Single Tier Labeling: previously a 4-tier system in place, which was a significant resource drain on the firms as well as on CVB in evaluating data to qualify for the 4 different tiers. This is intended for all vaccines, bacterins, but not diagnostic test kits, allergenic extracts, antibody products, or autogenous. They're working to update 9CFR part 112.
The website will have generic information about efficacy and safety studies and there will be a user guide for the end user.

Final rule effective on September 4th, and there will be a 4-year implementation process. Extenuating circumstances will be considered.

The first phase will be aquaculture, feline, immunomodulators this fall. Other species will fall on subsequent schedules.

In vitro assay for rabies to replace the NIH test: they're working with MAbs from ATCC, also working on developing in house MAbs.

Title: Anti-Rabies Monoclonal Antibody PEP for Veterinary Use

Dr. Eric Tsao
Chief Executive Officer
Synermore Biologics Co., Ltd.

We propose to use SYN023, a mixture of two anti-rabies monoclonal antibodies, for the post-exposure prophylaxis of rabies virus infection in unvaccinated domestic animals. The two monoclonal antibodies bind to distinct and non-overlapping antigenic sites on the rabies virus glycoprotein. SYN023 has been shown to neutralize more than 25 contemporary wildlife rabies isolates. Protection against virus challenges was demonstrated in three animal models. The development of the product as well as results from in vitro and in vivo studies will be presented.

Table 1. Broad spectrum neutralization against the North American strains

Rabies Virus Isolate	CTB011	CTB012	Cocktail	HRIG
E Pipistrelle	+	+	++++	++++
Eptesicus Fuscus	+	+++	++++	+
Tadarida	+/-	+	++	++++
Lasiurus Borealis	+	++++	+++	+
Lasiurus Cinerus	+	++++	++	++++
SW Eptesicus Fuscus	+/-	+++	++++	++
NC Skunk	++++	+++	++++	+
SC Skunk	++	+	++++	+
Texas Grey Fox	+	++++	++	+
Florida Raccoon	+/-	++++	+++	+
CVS-11	++++	+	++++	+

Table 2. Broad spectrum neutralization against the Chinese Strains

Rabies Virus Isolate	CTB011	CTB012	Cocktail	HRIG
HN10, Human	+++	++	+++	+++
HuBei, Dog	++	++	+++	+++
ZJ-QZ, Dog	++	++	+++	+++
SX-HZ-6, Dog	+	+	+++	+++
BD06, Dog	+	+	+++	+++
JX13-189, Ferret Badger	+	+	+++	+++
JX08-45, Ferret Badger	+	+	++	+++
JX13-235, Ferret Badger	+++	++	++	+++
JX12-234, Ferret Badger	+++	+++	+++	+++
JX09-17, Ferret Badger	+++	+	+++	+++
JX13-417, Ferret Badger	+	++	+++	+++
JX10-37, Ferret Badger	+++	++	++	++
JX13-228, Ferret Badger	+++	++	+++	+++
ZJ12-03, Ferret Badger	+++	+++	+++	+++
ZJ13-431, Ferret Badger	+++	+++	+++	++

Figure 1. PEP in Syrian Hamsters challenged with U.S. Tadarida bat strain

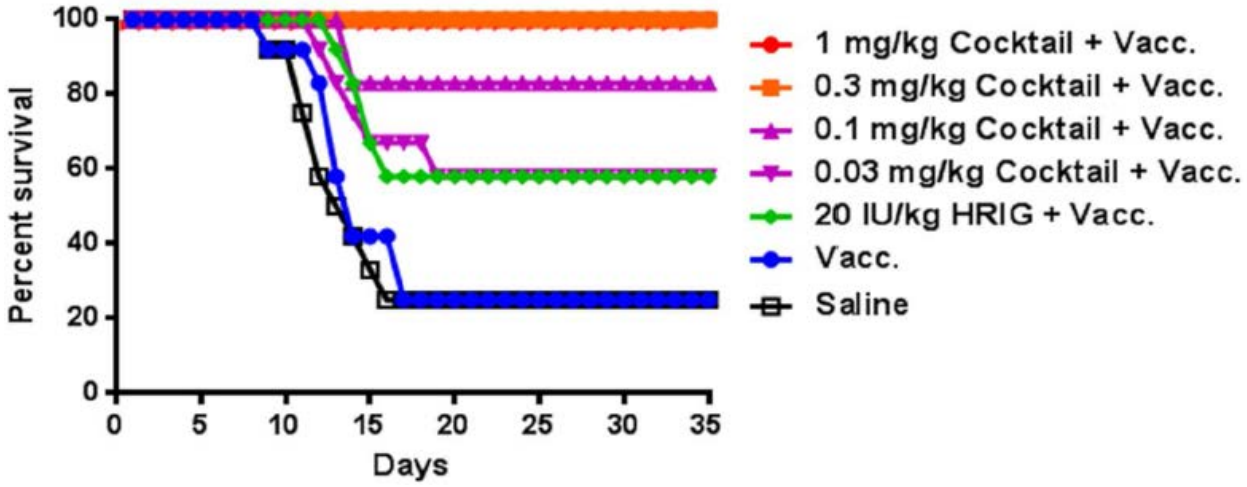
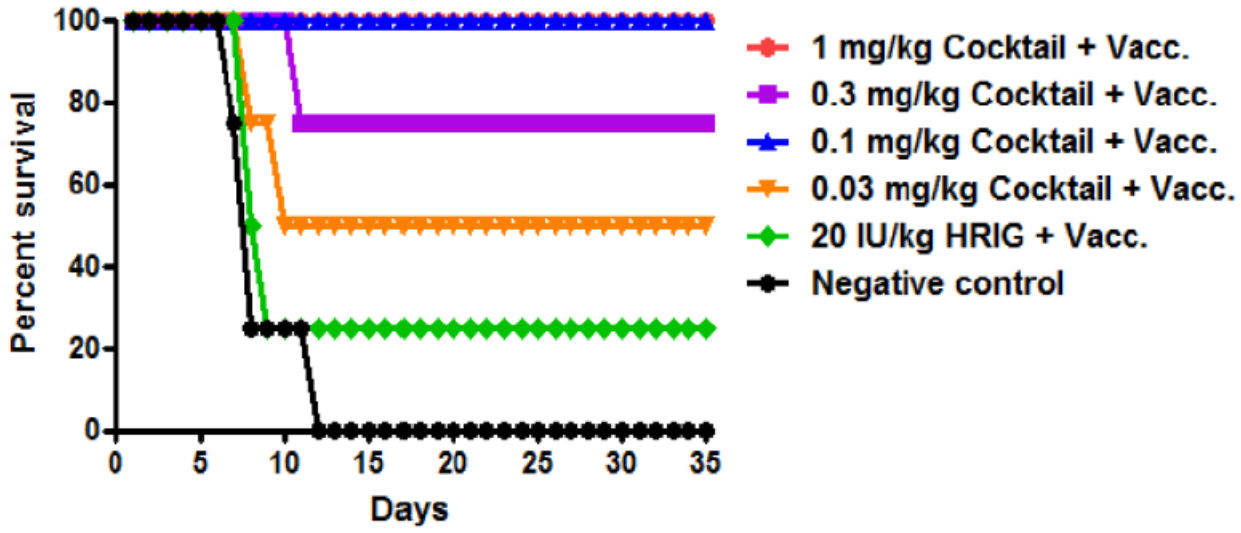


Figure 2. PEP in Beagle dogs challenged with Chinese BD06 dog strain



Title: Panel on Vaccines for Use in Wildlife

Topic Introduction:
Dr. Michael Miller
Senior Wildlife Veterinarian
Colorado Division of Parks and Wildlife

Dr. Michael Miller, Colorado Division of Parks and Wildlife, opened our session on vaccines for use in wildlife. The broad needs and applications for wildlife vaccines include health and human safety, agricultural commodity protection, conservation, and national security. Dr. Miller emphasized the tremendous value in having more readily-available "hands-off" disease prevention and control tools for wildlife medicine and health management. (Specific examples of such tools in plague, Lyme disease, and rabies control were the topics of the presentations that followed.) Despite a growing need, wildlife vaccine development has lagged. This appears to be largely because such vaccines are "niche" products, with use (and thus markets) restricted to state and federal agencies and further limited by available funding and logistics. It follows that the cost-return imbalance for developing wildlife vaccines to the same regulatory standards as more traditional commercial vaccine products makes the former largely unattractive for private manufacturers. More flexible standards and expectations for efficacy and delivery form, perhaps modeled after those used in conditional licensing of conventional products, could expedite progress toward the field evaluation and use of wildlife vaccines without compromising established purity and safety standards. Dr. Miller expressed hope that this session would bring more attention to this important aspect of biologics development & regulation, and encouraged further consideration of clear and achievable regulatory paths for wildlife products.

Sylvatic Plague Vaccine in Prairie Dogs
Dr. Tonie Rocke
Research Epizootiologist
National Wildlife Health Center
US Geological Survey

Sylvatic plague, caused by the bacterium *Yersinia pestis* is a zoonotic disease that causes frequent outbreaks in prairie dogs (*Cynomys* spp.) and other wild rodents. Scientists at USGS and UW Wisconsin developed a virally-vectored sylvatic plague vaccine (SPV), deliverable via oral baits to wild prairie dogs that has been shown to protect animals from plague in laboratory studies. Field safety and efficacy studies to assess the use of SPV as a preemptive management tool against plague began in 2012 and will continue through 2016 with the cooperation of numerous state and federal partners. If successful, these resource agencies are interested in using SPV to decrease the occurrence of plague epizootics in selected prairie dog populations as a means to stabilize grassland ecosystems, enhance black-footed

ferret recovery, and achieve additional economic, environmental, and public health benefits. Regulatory challenges in developing baits for use in wildlife, testing the product in the field, and finding manufacturing partners were discussed.

Lyme Disease Vaccine for White-footed Mice
Dr. Linden Hu
Professor of Microbiology
Tufts University

The incidence and geographic distribution of Lyme disease in the U.S. has increased steadily since its first description in 1977. Efforts to stem the spread of the disease through controlling the population of its tick vector and/or the mouse reservoirs of the disease have met with only limited success. The only approved human vaccine to protect against Lyme disease was removed from the market by its manufacturer further highlighting the need for new approaches to controlling the disease.

Tufts has developed an orally-available vaccine targeted towards the mouse and tick reservoirs of the disease. This vaccine is patterned after the successful Raboral vaccine for rabies and utilizes a vaccinia virus vector. They have shown that vaccination of mice with the vaccinia virus encoding the outer surface protein A of *B. burgdorferi* protects them against infection with *B. burgdorferi* by feeding ticks as well as protects uninfected ticks from acquiring infection from vaccinated but infected mice giving the vaccine two potential mechanisms for decreasing environmental persistence of *B. burgdorferi*. They have performed testing in simulated environments but have had a long path to approval for field testing of the vaccine. Important issues that will need to be resolved during a field trial include optimization of the vaccine and doses to match animal feeding behaviors, accounting for the effects of prior infections with other agents and the effects of the release on the environment and non-target animals.

Overview of 35 Years of Use of an Oral Rabies Vaccine for Wildlife
Dr. Joanne Maki
Director, Global Veterinary Public Health for Rabies
Global Commercial Development
Merial, a Sanofi Company

RABORAL V-RG®, was first used in Europe during the 1980s to control and eliminate rabies in red fox populations in France, Belgium and Luxembourg. This year marks the 25th anniversary of RABORAL V-RG use in the United States for wildlife rabies control and prevention. The US regulatory path required of this first recombinant vaccine for use in three different rabies outbreaks in raccoon, coyotes, and foxes required a multi-disciplinary collaborative effort between researchers, manufacturer, field program managers and regulatory agencies. After 25 years of experience and data gathering, it is our opinion that wildlife vaccine efficacy is best demonstrated by scientific review of cumulative field data demonstrating uptake and effectiveness of the bait and vaccine in the target species. Product performance on a population level under circumstances which more accurately reflect intended use of the product have benefits that outweigh traditional individual animal cage challenge studies. The current regulatory path for approving veterinary vaccines does not clearly define standards for regulatory consideration of field data for wildlife vaccines which is cumulative over time and does not fit existing regulatory approval pathways. Merial is committed to supporting the evolving US wildlife ORV program as field parameters shift to eliminating raccoon and skunk rabies variants. To meet current challenges and best prepare for other emerging zoonoses, the animal health community must identify suitable methodology and standards for utilizing field data towards product licensing and/or adding species label claims to wildlife vaccines. The unique market niche for the majority of wildlife vaccines, (i.e., products used exclusively by government programs for public health risk mitigation) should be reviewed since unreasonable barriers to adding species claims have repercussions on multi-species disease control programs managed by state and federal agencies. The growing role of wildlife diseases in public health is well accepted globally. Adding label claims to wildlife vaccines used by government agencies include a growing body of products targeting a variety of diseases of public health importance. For these reasons, wildlife vaccines used for public health risk mitigation should have unique regulatory considerations. Thus, finding a rational consensus on how to best assess and regulate these products will broadly benefit the cost and efficiency of wildlife disease control efforts.

Novel Bait Matrices for Oral Vaccines
Mr. Steve Wisdom
President, Foodsource Lures

Over the past ten years, FoodSource Biotech has been developing Incortrix, a patented material that is for the oral delivery of active ingredients to animals in domestic, commercial and wild environments. Using Incortrix as a foundation, FoodSource Biotech creates custom animal drug delivery solutions in solid, liquid, granular, paste, and gel forms. It also provides versatility in incorporating flavors, colors, scents and texture agents creating an end product capable of enticing the target animal with multiple sensory attractions. Incortrix is unique in that it offers a profound capability to incorporate active ingredients utilizing a low temperature process, which eliminates concern for degradation of live organisms or fragile compounds. . Every product we develop is tailored to meet the needs of a specific customer and targeted animal. The Incortrix material is made with food ingredients which are biodegradable, environmentally friendly, and USDA, FDA, EPA friendly.

Our mission is to collaborate with manufacturers, universities, and government agencies to create innovative, environmentally friendly products for delivering beneficial and protective ingredients to animals in domestic, commercial and wild settings. Wildlife vaccine research, veterinary public health, companion animal, domestic aquatics, and commercial aquaculture are just some of the industries we are interested in serving. We are focusing on providing solutions for the oral delivery of vaccines, therapeutics, probiotics, parasiticides, nutritionals, and contraceptives.

Steven Wisdom @ steve@fsbiotech.com or 205-335-8778
Visit our website FoodSourceCorp.com

Committee Business:

1st Resolution: Select Agent Registration

The Resolution was presented by Dr. Kent McClure.

This resolution asks APHIS to implement the findings of the GAO report of 2013 titled: "Overlap and Duplication: Federal Inspections of Entities Registered with the Select Agent Program." Specifically, that APHIS and CDC accept each other's inspection results rather than conducting independent inspections. Further, that where Select Agent Registrants are already regulated and inspected by APHIS that the lead agency be APHIS.

A motion was made to accept as written. The resolution passed with a vote of 9 to zero.

2nd Resolution: Categorical Exclusions

The Resolution was presented by Dr. Kent McClure.

This resolution urges APHIS to expeditiously respond to the Council on Environmental Quality request for information regarding APHIS' implementation of the National Environmental Policy Act, and to propose and finalize a rule to amend 7 CFR 21 § 372.5(c) to allow APHIS the ability to grant categorical exclusions for veterinary biologic products in appropriate cases.

It was noted that the original text referred to the "National Environmental Protection Act" rather than "National Environmental Policy Act". A motion was made to accept with the correction. The resolution passed with a vote of 8 to zero.

There was no additional business. The committee adjourned at approximately 5:00 PM.