

REPORT OF THE COMMITTEE ON BIOLOGICS AND BIOTECHNOLOGY

Chairman: Bob Pitts, Athens, GA
Vice Chair: Vacant

Gary A. Anderson, KS; Joan M. Arnoldi, WI; Charles A. Baldwin, GA; Yung Fu Chang, NY; James J. England, ID; William H. Fales, MO; Robert W. Fulton, OK; Ted Girshick, CT; Keith N. Haffer, SD; Larry L. Hawkins, MO; Chris S. Hayhow, KS; Ruud G. Hein, DE; Richard E. Hill, IA; Joseph N. Huff, CO; Majon Huff, CO; Terry L. Klick, OH; Hiram N. Lasher, DE; Lloyd H. Lauerman, WA; John C. Lawrence, Me; Randall L. Levings, IA; Robert E. Pitts, WV; Carol L. Rinehart, MO; Deepanker Tewari, PA; Deoki N. Tripathy, IL; Bob Tully, KS.

The Committee met on October 27, 2008 at the Sheraton Greensboro Hotel Greensboro, North Carolina, from 7:00 to 10:15 p.m. There were 10 members and 14 guests present. New Chair Bob Pitts called the meeting to order. He introduced himself as a long time member of the Committee, one involved in vaccine research, production and testing for 33 years, Vice President of Quality Assurance and Regulatory Affairs at Bioniche Animal Health USA, Inc. for 18 years and an individual committed to quality animal health. The Chair asked that everyone introduce themselves. Chair Pitts expressed pleasure at the large turnout and interest. The Vice-Chair position is vacant and applicants were encouraged. The Committee Mission Statement was reviewed and found compatible with the associations new Strategic Operational Plan. The Committee mission statement is as follows:

The purpose of the Biologics and Biotechnology Committee is to monitor 1) new development in veterinary biologics, 2) regulation of the manufacture, distribution and use of veterinary biologics, and 3) needs of the livestock industries for new biological products. The Committee has the responsibility of keeping abreast and advising USAHA of new biotechnology, products and regulations that may have profound economic implications on animal health. Further, the Committee provides a forum to focus on issues and developments in the field of biotechnology that are designed to provide protection to man, animals and the environment.

This Committee meeting conflicts with other Committees and suggestions to alter the time were discussed. Time suggestions were solicited. Due to limits by United States Department of Agriculture (USDA) personnel, the Committee was asked to identify key USDA people that add value to the Committee meeting. Drs. Hill, Rippke and Karli from USDA, Animal and Plant Health Inspection Service (APHIS), Veterinary Services (VS), Center for Veterinary Biologics (CVB) were identified as key participants and presenters for future meetings. There were no resolutions to review and those present were encouraged to sign in and consider joining this Committee.

Center for Veterinary Biologics – Program Activities and Initiatives

Dr. Richard Hill, Center for Veterinary Biologics, VS

Dr. Hill started his comments with recent progress at the 480 acre campus of the National Centers for Animal Health (NCAH), the new combined facility at Ames, Iowa. This is the single largest construction project in the history of the USDA. The APHIS/Agriculture Research Service (ARS) plan for upgrading and modernizing the Ames laboratory facilities brings three animal health institutes together in one site. They are CVB, National Animal Disease Center (NADC) and the National Veterinary Services Laboratory (NVSL). The \$25.1 million, Laboratory/Administrative Phase I, was completed August 2004. Phase 2, containing Biosecurity level 3 (BSL-3) laboratories and administrative offices, at a cost of \$279.5 million, is scheduled for completion in December 2008. The High Containment Large Animal Facility (HCLAF) was completed in February 2007 at a cost of \$104.6 million. It contains 21 animal rooms in a BSL 3 Ag standard. This building made the national news as the building was constructed in a bubble. The Low Containment Animal Facility (LCLAF) construction is scheduled for completion in November 2008 at a cost of \$257 million. Additional investments in laboratory equipment, equipment monitoring, roads, etc., are delayed due to money shortages. Essential equipment such as freezers are currently monitored by hand.

According to Dr Hill the USDA continues to explore ways to meet the total budget. They reduced scope and costs of new construction and continue to use some existing buildings. Equipment and operational expenses are not in construction budget and paying for this in the 2009 budget appears to be

a major challenge. Concern was expressed by Committee member Joe Huff that funds for the operational expenses of the new buildings will not be available in all future budgets.

Dr Hill then discussed some of the current and emerging issues at USDA-APHIS-VS. Bluetongue preparedness was discussed. The gaps in existing plans were evaluated that includes research, surveillance, diagnostics, vaccination policy, collaborations, etc. Another issue, the future of the U.S. Animal Health Laboratory Infrastructure was also examined and it was decided to have a National Forum in the future to address the issues. Effective October 1, 2008 there was a reorganization of APHIS-VS CVB now reports directly to Dr. Jose Diez, Associate Deputy Administrator. The U.S. is challenged by many emerging diseases. The scope includes such animals as reptiles and many new diagnostic tools. The USDA needs to modify their approaches to combating some diseases. Brucellosis was given as an example where a new regional approach for eradication can replace the old national approach due to persistence in the Western Region around Yellowstone National Park.

Specific CVB issues include budget limitations, extraneous agent developments, Pharmacovigilance set back, *E. coli*, Strain O157 coalition, and electronic Freedom of Information (FOIA), swine influenza project and cancellation of the 2009 CVB Public Meeting. Budget shortages continue to cause serious personnel shortages. The CVB staff shows roughly 30 percent vacancies. There are five staff reviewer shortages out of a total of 17. The number of new licensed products has decreased from 76 in 2006, to 63 in 2007 and 59 in the fiscal year 2008. Inspections of firms is now well above the old yearly rate. Some equipment and operational activities are not in the budget. Reagent availability will probably be severely affected. There is likely a re-design of CVB to meet the mission critical programs. User fees charged to vaccine manufactures are a real and imminent option to supply needed funds. Both the Association of Veterinary Biologics Companies (AVBC) and Animal Health Institute (AHI) declined invitations to help set up proposed fee schedules. Extraneous Agent testing will continue to grow in importance as new technologies and research identify contaminants in master seeds and cell lines used in vaccine manufacture. The example of the Retrovirus, Strain RD 114 extraneous viral element in feline cell lines was discussed. Pharmacovigilance activities were not funded by Congress and will be dropped. Dr. Ripcke expressed concern about the possible negative ramifications on exported products by some foreign countries and by concerns from the American Veterinary Medical Association (AVMA). CVB has participated in an *E. Coli*, Strain O157 coalition with various other organizations. The purpose is to apply reasonable efficacy expectations and testing methods for licensing these new food safety related products. New Freedom of Information Act (FOIA) implementations are still on the near horizon. CVB has a template and an example for review available upon request that show the use of efficacy data in the FOIA disseminations. Swine and equine influenza isolate collections are part of a collaboration with the Centers for Disease Control and Prevention (CDC) to monitor genomic changes and to improve vaccines. Recent canine influenza challenge observations did not impress CVB and therefore no licenses were approved to date. They will continue to review license applications for canine Influenza. The new U.S. Animal Health Report is available at www.aphis.usda.gov/publications. Lastly, but unfortunately, the CVB Public Meeting scheduled for 2009 has been postponed to March 29, 2010.

	FY06	FY07	FY 08
Submissions	6646 (-347)	6656 (+10)	5563 (-993)
Product Licenses & permits Issued	76 (-21)	63 (-13)	58 (-4)
New Antigen Combinations	11 (-5)	18 (+7)	7 (-11)
Serials Released Eligible (%Tested)	15945 11,634 (8.46%)	16021 11,938 (6.51%)	15254 11,502 (7.74%)
Inspections	85	85	85
Investigations/Regulatory Actions	53/113	30/113	38/139

National Animal Disease Center (NADC) News and Research Update from the Virus and Prion Diseases of Livestock Research Unit

Dr. Marcus Kehrli, Research Leader, Virus and Prion Diseases of Livestock Research Unit, National Animal Disease Center (NADC), ARS- USDA

NADC is one of three centers in the National Centers for Animal Health. As part of the USDA-ARS, NADC is a national resource where roughly half of the ARS animal health research program is conducted. NADC staff conduct cutting-edge research with a goal to provide solutions to control the most economically important infectious diseases of livestock. Successful completion of our mission enables the livestock industry to provide a safe, healthy, economical and stable food supply to our Nation and the World. Research programs in ARS are Congressionally-mandated, mission oriented and are directed through the ARS Office of National Programs. Individual research projects undergo a rigorous external scientific review process once every five years through the Office of Scientific Quality Review. The research programs and objectives are selected on the basis of multiple external and internal stakeholder inputs regarding the needs of the Nation's economically critical livestock health issues. This list of stakeholders includes numerous veterinary and producer groups, and several other Federal agencies (e.g., Food Safety Inspection Service, APHIS, Environmental Protection Agency, Food and Drug Administration). The projected base funding for FY09 at NADC is \$28 million with extramural funding in excess of \$2.2 million. The extramural funding is at an all-time high and has become critical to our successful operation in the current budget environment. The NADC is made up of five research management units and an essential operational support staff that maintains business operations for a research facility that conducts animal and laboratory research in a range of biocontainment level facilities (BSL1-3 labs and BL1-BL3Ag animal facilities). The research program consists of 18 separate research projects directly supported by 43 PhD-level scientists that currently includes only twelve DVM, PhD scientists. A highly skilled and trained technical and animal care support staff ensures research is conducted to the highest possible standards for animal care and biocontainment necessary for ensuring experimental integrity.

In the Virus and Prion Diseases of Livestock Research Unit we focus on the major viral disease pathogens affecting U.S. swine and cattle. Six scientists on the Swine Viral Disease Pathogenesis and Immunology Project are conducting research to identify mechanisms of swine viral pathogenesis that may ultimately lead to the development of improve vaccination strategies to enhance or provide broad cross-protection for circulating subtypes of swine viral pathogens. Viruses we currently are researching include *porcine reproductive and respiratory syndrome virus* (PRRSV), *swine influenza virus* (SIV) and *porcine circovirus type 2* (PCV2). Research includes a combination of molecular biology, immunology and disease pathogenesis studies in pigs to enable development of vaccines with improved efficacy. Using molecular genetic methods we are dissecting the genetic basis for viral virulence in the pathogens as well as the host response to infection. This two-fold attack will enable us to better understand the host-pathogen interaction of these challenging viral diseases so as to reveal the most effective way to intervene with these important swine pathogens.

Currently, only two scientists are focusing on countermeasures to control and support eradication of *bovine viral diarrhea virus* (BVDV). This virus is one of the most economically important viral diseases in cattle throughout the world. Despite its name and association with a diarrheal disease, BVDV is the most frequently isolated virus in pneumonic lungs from cattle reported with bovine respiratory disease; in 21 percent of these cases BVDV was isolated. Our research is focusing on the unique capability of this pestivirus to create a persistent infection in the fetus of pregnant cattle and deer. When these persistently infected calves or fawns are born, they typically appear healthy but will shed large amounts of virus and thus represent significant disease risks to healthy cattle they contact. Effective control of BVDV in wild deer will become paramount to the success of our nation's efforts to better control BVDV in cattle. More basic research will be needed to understand the pathogenesis of fetal infections, how to diagnose an infected fetus in a pregnant animal and finally how to effectively protect the fetus from infection.

Another research project focuses on the transmission, differentiation and pathobiology of transmissible spongiform encephalopathies (TSEs). Four scientists are leading research assessing the cross-species transmissibility of TSEs in livestock and wildlife. Data from a completed series of interspecies TSE transmission studies to cattle reveal it is possible to differentiate Bovine Spongiform Encephalopathy (BSE) in cattle from cattle with experimentally-transmitted scrapie, chronic wasting disease (CWD) or transmissible mink encephalopathy (TME) inoculated intracranially into the brain of

cattle. These studies indicate a species barrier will prevent transmission of scrapie or CWD to cattle. We also discovered a novel prion allele in the 2006 BSE case that is a germline mutation and may represent a genetic form of BSE; research efforts are underway to verify this as a genetic cause of BSE. Research is planned to investigate the pathogenesis of atypical BSE. Preliminary findings of research methods for ante mortem diagnosis of BSE based on retinal accumulation of PrP^{Sc} indicate the possibility of diagnosing BSE in preclinical stages of disease.

Finally, we recently published research on a potentially automated method to detect central nervous system (CNS) tissue contamination on meat and carcasses. Future efforts will also focus on developing methods to inactivate infectious prions in agricultural settings.

Importation and Movement of Genetically Engineered Animals

Dr. Donna Malloy, Biotechnology Regulatory Services (BRS), APHIS

USDA-APHIS published a request on September 19, 2008 for information on genetically engineered (GE) animals. This is part of the process of gathering information about ongoing and future research on GE animals to ensure that these do not pose risks to livestock health. Planning ahead will allow the regulatory agencies to keep pace with the industry and anticipated future needs. APHIS was part of the Coordinated Framework (CF) together with the Food and Drug Administration (FDA) and Environmental Protection Agency (EPA) in 1986 that initially provided some regulations of GE as part of the biotechnology area. APHIS currently uses the Animal Protection Act for regulating importation and movement but new and specific regulations are needed. To date the USDA has received over 500 comments and the FDA has received approximately 35. The FDA will be the lead agency in regulating the GE animals. At this time none have been approved by the FDA for commercial use. Dr. Malloy stressed it was the product and not the process that was to be regulated by this effort.

Committee Business:

The Committee entertained a resolution request from member Joe Huff for USDA to provide more funding for the operation of new facilities at NCAH in Ames, Iowa. There was inadequate funding in the 2009 budget. The committee is concerned that program such as licensing new products, vaccine product releases, monitoring and surveillance of emerging diseases, and other regulatory initiatives will be negatively impacted if funds are shifted to pay for vastly increased utilities and maintenance of the new facilities. The motion was seconded by Dr. William Fales and passed unanimously. The Resolution was forwarded to the Committee on Nominations and Resolutions.

Dr. Jim Evermann discussed the need to safeguard current microbiological collections. With funding decreases affecting locations throughout the U.S. that currently store these vital collections for research, archival and historical purposes, we need to assure future maintenance and availability of these valuable assets. These collections would be of value for studies such as: the changing epidemiologic pathogenesis patterns of microbes, their evolutionary/ phylogenetic profiles; their antimicrobial resistance patterns; their value for diagnostic reagents; their potential for vaccine production; challenge models, etc. A proposal is anticipated during the next meeting to address this issue. It is the intension that this Committee and others will jointly support a resolution on maintenance and availability issue. The Committee was very receptive and will probably support this issue next year.