REPORT OF THE COMMITTEE ON BIOLOGICS AND BIOTECHNOLOGY

Chair: Bob Tully, Lenexa KS
Vice-Chair: vacant

Mr. J. Bruce Addison, MO; Dr. Joan M. Arnoldi, WI; Dr. Charles A. Baldwin, GA; Dr. Karen E. Burns Grogan, GA; Dr. Yung Fu Chang, NY; Ms. Mary Lou Chapek, NE; Dr. James J. England, ID; Dr. William H. Fales, MO; Dr. Patricia L. Foley, IA; Dr. Robert W. Fulton, OK; Dr. Joe S. Gloyd, DE; Dr. Keith N. Haffer, SD; Dr. Larry L. Hawkins, MO; Dr. Robert A. Heckert, MD; Dr. Rudolf G. Hein, DE; Dr. Richard E. Hill, IA; Mr. Joe N. Huff, CO; Mr. Majon Huff, CO; Dr. Robert F. Kahrs, FL; Dr. Terry Klick, OH; Dr. Hiram N. Lasher, DE; Dr. Lloyd H. Lauerman, WA; Mr. John C.. Lawrence, Me; Dr. Randall L. Levings, IA; Dr. Charles A. Mihaliak, In; Mr. Bob E. Pitts, GA; Dr. Anette Rink, NV; Dr. Roy A. Schultz, IA; Mr. Donald A. Shane, WI; Dr. Deepanker Tewari, PA; Dr. Deoki N. Tripathy, IL; Mr. Lawrence Williamson, IN.

The Committee met on Monday, November 7th at 6:30pm. Ten members, ten new members and fourteen other attendees were present. The chair welcomed the participants to Hershey and the Committee meeting. Last year's Committee report and the agenda for the meeting were reviewed and attendees introduced themselves. A special welcome was offered to Majon Huff from Colorado Serum Company for his long standing participation in this Committee. All in attendance were asked to record their attendance on the roster, including indicating membership status. The chair encouraged those interested to become involved members of the Committee. The chair announced that vice-chair Eric Newmann had resigned due to relocating out of the country. Attendance at the Committee meeting last year was lessened as a result of the meeting being held on the last day of the Annual Meeting. It was hoped that attendance would be better this year by holding the meeting on Monday evening.

The Committee mission statement was reviewed and discussed. The Committee's responsibility to the industry was emphasized. The 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."

Finally, the Resolution and recommendation processes were reviewed.

Dr. Richard Hill, Director of the United States Department of Agriculture (USDA), Animal and Plant Health Inspection Service (APHIS), Veterinary Services (VS), Center for Veterinary Biologics (CVB) gave an update on CVB activities. He reviewed a number of activities that had occurred at CVB over the last year. They include: a report on Safeguarding Review implementation activities; the preparation of the first U.S. Animal Health Report; and an update on the National Centers for Animal Health (NCAH), the combined laboratory facilities of USDA-APHIS, National Veterinary Services, USDA-APHIS-VS-CVB, and USDA, Agriculture Research Service. Hill explained that the NCAH modernized and consolidated facilities for existing (2002 level) programs, with no funding for equipment or operational expenses. The Combined Services Plan announced in September 2005 included 286 support positions assigned to USDA-APHIS and USDA-ARS. USDA has received all but $58.8 M of $460.77 M budgeted for the project. The Consolidated Laboratory/Administration Facility - Phase 1, was completed in August 2004. Phase 2 started September 2005 with completion expected in 2009. The Infrastructure Phase 1 completion date is December 2006. The high Containment Large Animal Facility will be completed March 2006. The low containment animal facility had yet to be funded. It is expected to be completed in 2007. USDA continues to explore ways to meet the total budget including reducing costs of new construction and continuing the use of some existing buildings. Other completed projects include the Mycobacteria Laboratory-July 2004, the Digester Building-September 2004, and the Training Barn-2004. Hill showed pictures of the NCAH projects. He demonstrated the time lines for each of the laboratories being built. Dr. Marcus Keahrli was introduced during Hill's presentation. Keahrli is new to the board of the NCAH.

The question was asked about the biosafety level 3 space donated to CVB. Hill explained that the need for large animal space will be small. The whole facility will be shared by all with a requirement to coordinate scheduling of the facility. Existing space will be effectively designed for longer-term projects. The new facility will allow for more effective use of the large animal species that are being housed there.

Hill then spoke about USDA-APHIS-VS' current and emerging disease issues. Included in those are: select agents, Bovine Spongiform Encephalopathy (BSE) surveillance, animal identification, the National Surveillance Unit, Emergency Management, the National Veterinary Stockpile, scrapie, chronic wasting disease, vesicular stomatitis virus, tuberculosis, Johnes disease, avian and canine influenza.

Hill then spoke about the Compendium of Vaccines for Transboundary Diseases. It is intended to be an international resource for government authorities and veterinary vaccine manufacturers. It is a follow-up to the 2002 document published in *Developments in Biologicals,* Vol. 114, 2003. The Compendium is supported with funding from the USDA-APHIS-VS.

Finally, Hill talked about key CVB program activities and staffing, and then reviewed several completed and planned meetings related to veterinary biologics including: the 14th Veterinary Biologics Public Meeting to be held April 3-7, 2006; New Diagnostic Technology: Applications in Animal Health & Biologics Controls (applications in disease surveillance, molecular epidemiology and quality control tests of ingredients of animal origin) held October 3-5, 2005; Biological Crisis Management in Human and Veterinary Medicines, scheduled for November 5-8, 2006 in Lyon, France, and Ploufragen II that will be held in Spring 2007.

Byron Rippke, Director of Policy, Evaluation and Licensing for USDA-APHIS-VS-CVB shared information with the Committee about activities of his section. They are summarized in the following table:

Confirmatory and Investigatory Testing - Testing Numbers for Fiscal Year 2005

Serials Eligible	11,685	
Serials (%) Tested	1,583	(7.30%)
Serials (%) Unsatisfactory	14	(0.89%)
Master Cells Tested	12	
Bacterial Master Seeds Tested	33	
Viral Master Seeds Tested	34	
Recombinant/ GM MS	45	
Post-license testing	2,808	
Reagents shipped (vials)		
Domestic	2,895	
Foreign	130	
Kit panels/slides	154	
Supplied internal (vials)	29,775	
New reagents developed	5	
New lots produced	88	

Ripke discussed CVB involvement with BSE and the enhanced surveillance plan. He explained that with the completion of the testing of high risk animals and the drafting of the enhanced surveillance report to be released yet this year, no further regulatory action was planned. The results of the testing and the report would dictate any regulatory actions in the future. Also of interest to the Committee was the proposed rule on enhancing the feed ban for products of animal origin. It was explained that the rule would not exclude the use of blood and blood products, plate waste, and the banning of poultry litter as feed.

The following list of proposed and pending regulations were discussed:

§113. 119 revision – SR for *Erysipelothrix rhusiopathiae* bacterin - comments on proposed rule under review with a projected publication date of August 2006;

§113.217 new section – SR for equine influenza vaccine - comments on proposed rule under review. May not be finalized as originally proposed; §105/115 revision – Stop sale notification - comments on proposed rule under review with a projected publication date of August 2006;

§101/116 revision – Pharmacovigilance reports - re-proposed rule published August 2005;

§113.215/216 revision – IBR/BVD Potency test(s) - proposed rule withdrawn; no further action at this time;

§114.12/13 revision. – Expiration dating - proposed rule published April 2005; comments on proposed rule under review;

§112 revision – Labeling regulations - drafting a proposed rule; projected publication date August 2006; and

§113.31 revision – Detection of lymphoid leucosis - drafting a proposed rule; projected publication date August 2006.

Ripke discussed an issue involving the use of autogenous vaccines. The two areas of concern were the limitations of adjacent flock/herd use and the utilization of isolates past 24 months. These issues are of great concern with the poultry industry. The answer given by Ripke was that there is adequate flexibility of the current regulations to allow any company or interested party to overcome both of these two issues. The need for regulatory change on these issues would be unnecessary given the flexibility in the current regulations.

Ripke concluded by encouraging everyone wishing to seek more information to access the CVB website as seen below.

Mr. Steven Karli, Director of Inspection and Compliance, CVB reported on his section's activities for fiscal year 2005 that have resulted in continued compliance with the regulations and standards promulgated under the authorities in the Virus-Serum-Toxin Act (VSTA). His section monitors over 120 active licensees and permittees at nearly 175 sites globally. They conducted 36 in-depth inspections, 5 follow-up inspections and 54 special inspections. The majority of special inspections were conducted for prelicensing product or new facilities and to inspect licensed manufacturers for compliance to the Select Agent regulations as part of the registration process under the Agriculture Bioterrorism and Preparedness Act of 2002.

In Fiscal Year 2005, CVB processed 363 requests for Export Certificates (serial) and in excess of 2,400 Certificates of Licensing and Inspection. Export activities by serial were reduced by nearly 50% and export activities by product were reduced by approximately 9% from FY 2004 levels. The reduction in product exports was still recognized due mainly to the report of Bovine Spongiform Encephalopathy in the United States. Serials reviewed and processed by CVB were reported and summarized as 16,721 with 16,178 serials released for marketing. A pilot study for Administrative Inspection Review conducted in FY 2004 led to full implementation for all licensees in FY2005. To date, CVB has processed 61 reviews of licensees. This new inspection process has provided CVB with a means to work with licensed manufacturers outside of the normal inspection process to assure CVB files are current as well as providing manufacturers with the opportunity to schedule their resource utilization to make sure their regulatory files are kept current. In FY 2006, CVB will continue reviews of all licensees, and expand the process to include permittees.

Quality Management activities were reported as well. CVB continues to affirm its Quality Vision Statement by the CVB Directors on an annual basis. Changes have been made to reflect updates in the CVB Quality Management system. In FY 2005, CVB initiated process audits to further improve internal processes for both CVB Inspection and Compliance, and the Policy, Evaluation and Licensing units. In addition, ISO 17025:2005 and ISO 9001:2000 training has been contracted for all CVB employees to be delivered beginning early calendar year 2006. Inspection and Compliance personnel continue to function as quality management specialists assigned to the CVB laboratory activities to help improve internal processes as well.

Compliance activities reported included updates on investigation numbers for CVB (47 opened, 11 closed). Investigations opened included false and misleading advertising, promotions and/or product labeling. In addition, information was provided on compliance concerns related to animal owner exemptions and autogenous products under 9 CFR Part 107, advertising issues, and products prepared as planned exposure. An update on pharmacovigilance activities was also provided and progress within VICH continues. In addition, a new proposed rule for adverse event reporting was published and the comments received are being reviewed for next steps by CVB. Voluntary reports of adverse events continue to be received by the CVB and a summary of the types of reports may be found on the web at www.aphis.usda.gov/vs/cvb.

Progress continues toward development of the Licensing, Serial Release and Testing Information System (LSRTIS). This is the CVB portion of the VS Ames Automated Information Management System. Phase I was completed in 2003 and progress continues on Phase II. Release 1 is scheduled for production in Spring of 2007. Release 2 is not currently scheduled.

USDA-APHIS-VS signature verification guidelines for electronic serial release of products (Level 3 Application) continues to be unresolved.

A time specific paper entitled “Use of Bovine Single Nucleotide Polymorphism Markers for Confirmation of Identity and Perentage”, was presented by W.W. Laegreid, U.S. Meat Animal Research Center, USDA, ARS. The paper is included elsewhere in these proceedings.

Dr. Robert Simer, Perryton, TX, gave a scheduled scientific paper entitled “New Method of PRRSV Surveillance Using Oral Fluids.” The paper reports on a study on an alternative to traditional restraint and venipuncture for serum collection. Animals were allowed to voluntarily chew upon a cotton rope and oral fluids were collected instead of serum for Porcine Reproductive and Respiratory Syndrome Virus testing. The complete paper is included at the end of this Committee Report.

A recommendation was passed to forward the comments by Dr. Percy Hawkes back to USDA-APHIS-VS regarding their unsatisfactory response to the Committee’s 2004 Resolution regarding irradiation of fetal bovine serum (FBS) from countries free of Foot and Mouth Disease with vaccination. The proposal from the FBS industry proposed the importation of irradiated FBS from countries free of FMD with vaccination. The VS response to the 2004 USAHA resolution 13 did not reflect this. The VS response stated *“USDA has received a proposal from private industry to irradiate FBS sourced from FMD countries.”* The Committee recommends that the new proposed rule reflect the original request from industry; “FBS sourced from FMD countries free of FMD with vaccination”. The proposal submitted by private industry to VS also proposed that VS establish specific measures (which were not part of the 1994 proposed rule) to address the problem of fraud and misrepresentation in the FBS industry. The VS response to the 2004 USAHA resolution does not address this need or problem. The measures suggested by industry would allow APHIS, as well as the FBS industry, to establish long needed standards and guidelines aimed at addressing fraud and misrepresentation. The Committee recommended that standards and guidelines to address the problems of fraud and misrepresentation also be included in the proposed rule, which is being prepared by APHIS on this issue**.**

New Method of PRRSV Surveillance Using Oral Fluids

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Porcine Reproductive and Respiratory Syndrome virus (PRRSV) is an economically damaging disease to the commercial swine industry. Most major herds are working on eradicating this virus from some or all of their pigs. Monitoring and testing for PRRSV especially during eradication process is labor intensive and costly.

This study reports an alternative to traditional restraint and venipuncture for serum collection. We allowed animals to voluntarily chew upon a cotton rope and collected oral fluids instead of serum for PRRSV testing.

This aspect of the project focused on detection (PCR) of PRRSV in pen-based oral fluid samples. Isolation of PRRSV from individual pig oral fluid samples was reported in 1997 (Wills et al. 1997). A field study was done to determine whether observations made under experimental conditions applied to production settings.

Methods: Twelve pens were randomly selected out of 36 pens in a commercial finishing barn. Each pen contained approximately 25 pigs. This barn was chosen because PRRSV was believed to be circulating at the time of collection. Two pen-based oral fluid samples along with two randomly chosen individual serum samples were collected from each pen. Serum and oral fluids were submitted for PCR testing.

Results: 20 of 24 (83%) pen-based oral fluid samples and 17 of 24 (71%) individual pig serum samples were PCR positive.

Conclusions: Polymerase Chain Reaction results on pen-based oral fluid samples collected in the field corroborated earlier experimental data. Oral fluid sampling offers several advantages over serum sampling. Safety to animal and handler is a big benefit of this method of collection. Animals voluntarily participate for the non invasive sample. Pen based sampling allows for more animals to be tested when sampling larger populations. Oral fluid sampling costs less then traditional serum sampling.

Use of Bovine Single Nucleotide Polymorphism Markers for Confirmation of Identity and Perentage

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Development of animal identification systems for use in the event of livestock disease outbreaks and public health investigations has recently become a national priority. While various tagging, implant, and/or other technologies will form a sound basis for an identification system, they remain subject to error or fraud. Thus, a means to audit and verify the performance of identification systems will be required. DNA marker technology represents a promising means for confirming the identity and parentage of an animal because DNA is the only informative identification that 1) is integral to most parts of an animal, 2) remains stable throughout the life of the animal, and 3) provides a “code” unique to the animal. Compared with other types of DNA markers, single nucleotide polymorphisms (SNP’s) are attractive because they are abundant, genetically stable, and amenable to high-throughput automated analysis. In cattle, the challenge has been to identify a minimal set of SNP’s with sufficient power for use in a variety of popular breeds and crossbred populations. We report the development of a set of bovine SNP markers with high informativity in U.S. cattle populations and provide examples of their use in confirmation of identity or parentage in field situations.