

## **Report of the Committee on Biologics and Biotechnology**

**Chair: Mr. Bob Tully, Lenexa, KS**

Gary A. Anderson, KS; Joan M. Arnoldi, WI; Charles A. Baldwin, GA; Karen E. Burns-Grogan, 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 Hein, DE; Richard E. Hill, IA; Joseph N. Huff, CO; Majon Huff, CO; Robert F. Kahrs, FL; Terry L. Klick, OH; Hiram N. Lasher, DE; Lloyd H. Lauerman, WA; John C. Lawrence, ME; Randall L. Levings, IA; Richard E. Pacer, MD; Robert E. Pitts, GA; Carol L. Rinehart, MO; Deepanker Tewari, PA; Deoki N. Tripathy, IL; Jeff T. Trunnell, IA; Mary Anne Williams, CA.

The Committee met on Monday, October 22, 2007 at 7:00pm at the John Ascuaga's Nugget Hotel in Reno, Nevada. Seven members, twelve new members and sixteen attendees were present. The Chairman welcomed the participants to Reno and the Committee meeting. Last year's Committee Report and the agenda for the meeting were reviewed and attendees introduced themselves.

Bob Tully called the Committee to order: The Chair announced that the Vice Chair position was vacant. Bob Pitts volunteered to take minutes for the record. The meeting this year is on Monday evening and the Chairman expressed pleasure with the large interest and turnout.

Following introductions, the Chair read the mission statement and reiterated the reason for our Committee and the responsibility to the industry. The Chair explained the committee action process of resolution formation and the ways that our Committee takes action by submitting resolutions to the Committee on Nominations and Resolutions.

The roster for attendance was passed and all encouraged to list their membership status and encouraged all to join and become involved. The Committee mission statement is as follows.

### **BIOLOGICS**

The purpose of the Committee on Biologics is to monitor 1) new developments 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. Committee action may be in the form of recommendations, or in the case of major issues, resolutions to be considered by the General Membership.

### **BIOTECHNOLOGY**

The purpose of the Committee on Biotechnology is to provide a forum as directed for State, Federal, University, private industry, and citizens-at-large to focus on issues and developments in the field of biotechnology as related to animals. The Committee reviews and discusses regulations and guidelines that are in preparation or have been issued at the national, state or international level in an attempt to regulate developments in the field which are designed to provide protection to man, animals, and the environment. Biotechnology has profound economic implications, brought about by developments of totally new products or processes. The Committee has the responsibility to keep abreast of these changes and advise USAHA relative to impact on the U.S. livestock industry.

Richard Hill, Director, Center for Veterinary Biologics (CVB), Veterinary Services (VS), Animal and Plant Health Inspection Service (APHIS), United States Department of Agriculture (USDA), reviewed and highlighted a number of activities that have occurred at CVB over the last year.

Dr. Hill discussed the recent progress at the National Centers for Animal Health (NCAH), the new combined facility at Ames, Iowa. 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 the Center for Veterinary Biologics: biologics, National Animal Disease Center which is part of ARS and the National Veterinary Services Laboratories, diagnostics. The plan calls for the modernization and consolidation of facilities for existing (2002 level) programs. The Combined Services Plan announced September 2005 calls for 286 support positions assigned to APHIS/ARS.

The USDA has received all \$460,770,000 of the construction budget, The Consolidated Laboratory/Administration Facilities is funded and Phase 1 was complete August 2004. Phase 2 completion is due 2009. Infrastructure pieces are also phased in The High Containment Large Animal Facility (HCLAF) was

completed on February 2007. The Low Containment Animal Facility construction is underway and the completion date is 2008.

According to Dr. Hill, the USDA continues to explore ways to meet the total budget. They are reducing scope and costs of new construction and continuing the use of some existing buildings. The mycobacteria laboratory was completed in July 2004. The digester building was completed September 2004. The training barn was completed in 2004. However, equipment and operational expenses are not in construction budget. Concern was expressed that funds for the operational expenses of the new buildings will not be available in next year's budget.

Dr Hill then discussed some of the current and emerging issues at APHIS and Veterinary Services (VS). In the leadership area Cindy Smith is the new APHIS Administrator. Kevin Shea is the only Associate Administrator. The Select Agent and Toxin list was republished and is a Proposed Rule out for comment. There is a discussion draft for the Animal Disease Traceability. The APHIS Strategic Plan was briefly discussed and Dr. Hill gave this website for further details, [http://www.aphis.usda.gov/about\\_aphis/strategic\\_plan.shtml](http://www.aphis.usda.gov/about_aphis/strategic_plan.shtml).

The 2007 U.S. Animal Health Report was recently published and is available at this website at [http://www.aphis.usda.gov/about\\_aphis/strategic\\_plan.shtml](http://www.aphis.usda.gov/about_aphis/strategic_plan.shtml).

In a report to the President about Protecting American Consumers, Dr. Hill warned the Committee that new restrictions may occur due to the troublesome issues with recent imports, i.e., toys with lead paint, Tenrecs – any of 29 species of shrew like and hedgehog like mammals that can carry foot-and-mouth disease (FMD) – and tainted feeds with melamine. Consequently, a Strategic Framework for Import Safety was formed. It will include an International Trade Data System with an Interagency Working Group that is requesting public comments on Import Safety. VS is represented on the APHIS Steering Committee. Further detail can be found at [www.importsafety.gov](http://www.importsafety.gov).

Issues surrounding the discontinuance of biological products following a successful eradication/control programs were discussed. Diseases like pseudorabies and brucellosis were given. Challenges such as timelines for discontinuing domestic production of vaccines for export, emergency preparedness (domestic use), Select Agent status and biosecurity, wildlife reservoirs and vaccine/antigen/seed banks are consideration on how to deal with this issue. The white paper, *Vaccine Use Following Brucellosis and Pseudorabies Eradication*, can be viewed at: [http://www.aphis.usda.gov/vs/cvb/PDFs/10\\_10\\_06\\_VaccineUseWhitePaper.pdf](http://www.aphis.usda.gov/vs/cvb/PDFs/10_10_06_VaccineUseWhitePaper.pdf).

The annual summary of CVB activity is summarized below and compared FY 2007 with 2006 and 2005:

	FY 05	FY 06	FY 07
Submissions	6,993 (+48)	6,646 (-347)	6,656 (+10)
Product Licenses and Permits Issued	97 (27)	76 (-21)	63 (-13)
New Antigen Combinations	16 (-1)	11 (-5)	18 (+7)
Serial Released	16,178	15,945	16,021
Eligible % Tested	11,685 (13.5)	11,634 (8.46)	11,938 (6.51)
Inspections	88	85	85
Investigations / Regulatory Actions	47 / 145	53 / 113	30 / 113

CVB is currently operating under the 2007 budget allocation of \$15,687,000. The President's budget of \$19,867,000 is not authorized. The house mark up is \$17,569,000 and the Senate mark up is \$18,156,000. Dr Hill expressed concerns with the lower funds from the Continuing Resolution, the increased campus costs, increased equipment and operational expenses due to the new facilities. These will impact CVB program activities.

The vacancies in various CVB positions are shown in the chart below. The first number is the vacancies. The second number is the total number of positions.

Reviewers	7/17
Specialists	6/16
Epidemiologists	2/2
Lab VMO/Micro	6/17
Technicians	3/30
Asst./Assoc. Directors	1/2

Support Staff	8/32
Safety & Security Unit	11/23
Information Management Unit	8/42

The organization chart for CVB was discussed and given as a handout.

Dr. Hill reported the results of an International Regulatory Report that reviewed various international animal health programs. The International Federation for Animal Health (IFAH) and regional animal health industry associations conducted an international benchmarking the competitiveness of the animal health industry.

There is a specific United States report, however these results come from documents available on the web. Regulatory programs were scored for Europe, Canada, Australia, Japan, and the United States.

The regulatory framework is the biggest single obstacle for maintaining/extending licenses and/or competitiveness is the regulatory framework in some other regions and the U.S. Specifically, APHIS had some very low scores: Safety, quality and efficacy guidelines are applied on the basis of practical and rigorous assessment of risks and benefits – 29 percent. Overall scientific assessment of risk and benefits is clear and respected by other regulators internationally – 25 percent. Dr. Hill expressed disappointment but it was noted from the audience that all other international regulatory agencies scored lower.

Additional issues and activities include pharmacovigilance agreements with the International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products (VICH), epizootic hemorrhagic disease incidences, *In vitro* policies and guidance documents, member of an *E. coli* Coalition with National Cattlemen's Beef Association (NCBA), Food Safety Inspection Service (FSIS), Centers for Disease Control and Prevention (CDC), and Food and Drug Administration (FDA), dealing with *E. coli*, O157 pre-harvest interventions, and the recent certification of the lab to ISO 9001:2000 standards.

Dr. Hill noted the submission response times have decreased over the years and now are a respectable 40+/- days. This is the average of all submissions but is fearful the budget constraints and vacancies will increase these times in the future. CVB tracks individual categories such as biometrics that are much longer.

His presentation ended with an announcement about future meetings of interest. The 14th Veterinary Biologics Public Meeting will be held in Ames, Iowa on April 7 to 11, 2008, Global Animal Health Conference, November 15 to 16, 2007 in London and Ploufragen II, a follow-up to the first Harmonization meeting in 1992, sometime in 2008.

Donna Gatewood, Policy, Evaluation and Licensing (PEL), CVB-VS-APHIS-USDA, shared the following information with the committee in regards to the agencies activities.

The current PEL organizational chart was made available. Gatewood highlighted the PEL 2008 priority activities, including: staffing, application review, laboratory testing, program documentation (policy) and Program Quality Assurance. She shared documents that the program had published in 2007, which comprised by 15 CVB notices, four VS Memorandums and 25 documents posted to web site for comment.

Gatewood discussed the 2007 Establishments and Permittees from PEL. There were three establishment licenses issued and no permittees. On the contrary, four Establishment Licenses were terminated, as well as three permittees. Total numbers for 2007 were 83 Licensees and 18 Permittees

For 2007 products, 57 product licenses (includes three unique products) were issued while 216 licenses were terminated. In all for 2007, there were 2,063 active product licenses

Gatewood presented summary graphs of the following PEL licensing data (contact PEL office for copies):

- Number of biotech products licensed over time (1987 to 2007)
- Number of biotech products licensed by category (1, 2 and 3) – 1993 to 2007
- Number of diagnostic products licensed over time (1987 to 2007)
- Number of licensed establishments vs products licensed over time (1987 to 2007)
- Number of FFM products licensed over time (1987 to 2007)
- Number of unique products over time (1993 to 2007)
- Number of biologic permits issued in 2007 – also shown on graph from 1991 to 2007
- Number of research and evaluation permits – 265
- Number of transit shipment permits – 1
- Number of doses produced and destroyed 1986 to 2006
- Number of total submissions compared by category from 1995 to 2007
- Number of aquaculture products licensed over time (1987 to 2007)
- Number of permittees, 2007, as listed below:

	<u>Vac/Bact</u>	<u>Antibody</u>	<u>Diagnostic</u>	<u>Immunomodulat</u>
Canada	12	2	1	0
Austral/NZ	18	1	8	1
Europe	0	0	11	1
Mexico	0	0	3	0

Mr. Steven Karli, Director, Inspection and Compliance (IC), CVB-VS-APHIS-USDA, reported CVB-IC fiscal year 2007 activities. CVB-IC monitors over 135 active licensees and permittees at nearly 175 sites globally. CVB conducted 38 in-depth inspections, three follow-up inspections and 44 special inspections. The majority of special inspections were conducted for product or facilities inspections and also to conduct inspections for the VS-National Center for Import and Export (NCIE) for compliance to the Select Agent regulations as part of the registration process under the Agriculture Bioterrorism and Preparedness Act of 2002.

In August, the consolidation of Information Management Unit was initiated as a support services for the National Center's for Animal Health. This unit reports to the Director of Inspection and Compliance and includes information technology, library and visual services for the National Veterinary Services Laboratories (NVSL), National Animal Disease Center and CVB. Full implementation of the unit is targeted to be completed by February 2007. On September 1, 2007, the Information Management Resource Services unit came under CVB supervision and direction. This unit, previously reporting to the Director of NVSL, included all of the APHIS information technology support for the Ames campus.

In addition, budget resources for fiscal year 2007 continue to be limited. As a result, CVB is implementing a plan to shift resources (human and financial) to priority areas identified by the Center Directors. Inspections and quality assurance continue to be priorities for the unit.

In Fiscal Year 2007, CVB processed 456 requests for Export Certificates and in excess of 2834 Certificates of Licensing and Inspection. Export activities by serial increased by nearly 25 percent this year and export activities by product increased by approximately 5 percent from FY 2005 levels. These numbers still represent overall reductions in product exports primarily due to the report of bovine spongiform encephalopathy (BSE) in the United States. Serials reviewed and processed by CVB were reported and summarized as 16,655; 15,945 serials were released for marketing – representing nearly stable numbers since FY 2003. Administrative Inspection Reviews continued in FY 2006 and was expanded to include permittees as well. CVB sent out 65 reviews and processed 49 of those reviews. 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.

The CVB Directors have continued their commitment to a Quality Management System. In FY 2007, all employees received training specific to the International Standards Organization (ISO) 9001 and ISO 17025 standards. In addition, CVB Inspectors also received specific training for auditing guidelines (ISO 19011) in March 2006. CVB continued its commitment to process improvement by conducting process audits to further improve internal processes for both CVB Inspection and Compliance, and the Policy, Evaluation and Licensing units. CVB has also contracted with an ISO Registrar for ISO 9001 Registration to be completed in fiscal year 2008.

Compliance activities reported included updates on investigation numbers for CVB (50 opened, 17 closed). Investigations opened included false and misleading advertising, promotions and/or product labeling. Additional compliance issues facing CVB in 2008 are continuing to look at our regulations to determine changes as a result of lessons learned from previous investigations/cases. Also, CVB is working collaboratively with the California Department of Food and Agriculture to take a comprehensive look at those firms that operate under the California exempted program. An update on pharmacovigilance activities was also provided and progress within the International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) continues. The expert working group met two times this fiscal year and has been able to make progress on documents. See the VICH website for specific documents and their status. Voluntary reports of adverse events continue to be received by the CVB and a summary of the types of reports was published in the October 1, 2006, issue of the Journal of the American Veterinary Medical Association.

Issues from the floor included a status report on the 2004 Resolution 13 regarding publication of rule-making authorizing the use of gamma irradiation for the importation of commercial shipments of fetal bovine serum from countries and/or regions that are free of BSE, but having restrictions because of other pathogens that can be eliminated by gamma irradiation. In 2005 the Committee made further recommendations on two measures for the agency to consider in the re-proposal. Representatives from NCIE were present at the 2006

committee meeting and stated there was no change as the proposal was in progress and the risk analysis and regulatory work plan have been drafted. No NCIE representative was present at the Committee meeting. The Chair reported he had discussed the matter with Dr. Michael David who was present at the meeting in an acting capacity due to Dr. Lee Ann Thomas' recent transfer. David attempted to contact today staff members that are close to this matter however, he advised the Chair he was unable to make contact. Dr. David will source a response and contact the chairman upon his return to Washington.

A question was raised to CVB staff regarding the current requirements for conditional license requirements. An ensuing discussion resulted. Dr. Richard Hill stated that the basic requirements for conditional license approval are 9 Code of Federal Regulations (CFR) compliance with purity and safety standards along with supportive data demonstrating a reasonable expectation of efficacy.