REPORT OF THE COMMITTEE ON BIOLOGICS AND BIOTECHNOLOGY

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The Committee met on October 22, 2012 at 7:00 p.m. at the Greensboro Sheraton Hotel in Greensboro, North Carolina. There were 10 committee members present and 12 guests. Three of the five speakers were first time USAHA meeting attendees. No old business was opened for discussion.

Presentations

Converging Science, Medicine, and Agriculture: An Update on Executing the NADC's 'One Health Mission'
Kurt A. Zuelke, Crystal Loving
USDA-ARS National Animal Disease Center (NADC)

The NADC was established in 1961 to conduct basic and applied research on the livestock and poultry diseases of major economic importance to US agriculture. Now 50 years later, the NADC is the largest US federal animal health research facility focused on high-impact endemic diseases of livestock and wildlife. In 2009, we moved into new $470M state-of-the-art laboratory and animal facilities that now enable us to conduct high-level bio-containment research in a wide range of large animal livestock and wildlife species. To coincide with our transition into these new facilities, the NADC leadership team developed an ambitious five-year business plan that leveraged our new facilities with ongoing scientific advances in genomics and the life sciences to address the nation's most pressing animal health problems. The NADC's business focuses around four strategic research themes that include ruminant diseases and immunology; emerging diseases (most notably viral and prion diseases); zoonotic diseases in wildlife and livestock species; and, microbial ecology in food safety and animal health. NADC researchers across all four of these strategic themes are pioneering early development and integration of high-throughput genomics and systems biology platforms to yield new and exciting breakthroughs in potential molecular-based diagnostic and therapeutic technologies. For example, NADC scientists have sequenced and analyzed the genomes and expressed proteins from several strains of the causative bacteria for Johne's disease. Using this knowledge, these scientists recently identified highly specific protein markers that show promise in detecting early stage pre-clinical infected animals so they can be isolated and culled before shedding the organism or developing clinical disease. Johne's disease costs the US dairy industry over $1 billion annually, and having a reliable pre-clinical diagnostic test would be a major breakthrough for better controlling and minimizing the impact of this disease. In another example, NADC researchers are investigating the impact of gut microbial ecology to enable better management of animal and food-borne pathogens, decrease the prevalence of antibiotic resistance, discover and develop new antimicrobial agents, and optimize nutrient utilization and immune system function in livestock and poultry. Another area where NADC is seeking biotechnology partners is in the development and validation of new genomics and bioinformatics based methods to diagnose and analyze newly emerging strains of influenza virus. Since 2009, NADC's influenza research team has conducted successful proof-of-principle research demonstrating the potential power and validity of a comparative genome sequencing-based approach to early diagnosis and analysis of newly emergent strains of influenza virus. A key challenge (and opportunity) is to now develop and validate the bioinformatics analyses that would enable rapid assembly and analysis of multiple genomes in an actual disease-response time frame. The presentation will describe these and other recent findings of NADC research addressing contemporary animal health and food safety problems in livestock, wildlife and poultry.

Selection of Broilers with Enhanced Innate Immune Responsiveness: Functional Genomic Profiling to Improve Resistance Against Food-borne Pathogens
Christina L. Swaggerty[1], Igal Y. Pevzner[2], and Michael H. Kogut[1]
[1]USDA, Agricultural Research Service (ARS); [2]Cobb-Vantress, Inc.

Economic pressure on the poultry industry has directed selection towards fast-growing broilers that have a reduced feed conversion ratio. Selection based heavily on growth could adversely affect immune competence leaving chickens more susceptible to disease. Since the innate immune response directs acquired immunity, efforts to select poultry with an efficient innate response would be beneficial. We have been evaluating the innate immune system of two broiler lines to assess their capacity to protect against multiple infections. We have shown increased *in vitro* heterophil function corresponds with increased *in vivo* resistance to Gram-positive and -negative bacteria and protozoan parasites. Additionally, there is increased mRNA expression of pro-inflammatory cytokines/chemokines in heterophils isolated from the resistant line compared to the susceptible line. The data indicate differences in innate responsiveness are under

genetic control. Recently, a small-scale selection trial was begun. We identified sires within a broiler population with higher and/or lower-than-average pro-inflammatory cytokine/chemokine mRNA expression and subsequently utilized small numbers of high expressing and low expressing sires to produce progeny with increased or decreased, respectively, pro-inflammatory cytokine/chemokine profiles. This novel approach should allow us to improve breeding stock by improving the overall immunological responsiveness, and will produce a line of chickens with an effective innate immune response, which should improve resistance against diverse pathogens, improve responses to vaccines, and increase livability. Ongoing work from this project is providing fundamental information for the development of poultry lines that will be inherently resistant to colonization by pathogenic and food-poisoning microorganisms. Utilization of pathogen-resistant birds by the poultry industry would significantly enhance the microbiological safety of poultry products reaching the consumer.

Center for Veterinary Biologics Activities and Current/Emerging Issues

Richard Hill
Center for Veterinary Biologics (CVB), Veterinary Services (VS), USDA-APHIS

Dr. Hill discussed the recent modernization efforts in the Veterinary Services, as well as those currently underway in APHIS. Recent program activities include emerging animal health issues, particularly in the area of West Nile Virus (WNV) and Epizootic Hemorrhagic Disease (EHD) in white tail deer during 2012. A new management approach is being proposed for bovine tuberculosis and brucellosis and a proposed rule and program standards are expected to be published soon.

The Veterinary Services modernization, "Vision and Science" will be implemented using a five prong approach: Transform the culture, build new collaborations, optimize animal health competencies, support readiness and response, and invest in technical infrastructure. Hill stressed in this modernization the new priorities of VS, and the CVB, will be regulatory framework, import and export, emergency management, surveillance, one health and wildlife.

In summary, Hill showed the proposed CVB budget and then compared it to funding over the last nine years. The 2012 budget is close to 16 million dollars, and in 2004 the appropriated budget was just over 15 million. A table representing the efforts of the CVB during 2010-2012 showed that there were increases in almost all categories of activities, including 6,000 submissions and 40 product licenses and permits, despite shrinking budgets.

Special mention was given to the new FMD vaccines that have been permitted or licensed; one is a foreign-manufactured killed vaccine, and the other is a domestically-produced adenovirus vector in which the capsid gene is incorporated into the virus vector genetic material. He also mentioned the in vitro test development initiative for all rabies vaccines and the international collaboration in the effort to design and implement a test which reduces animal use. Another area that was mentioned is that of labeling standards, both for organically produced products, as well as the simplified one-tier label claim being proposed for all licensed products. Hill highlighted a few key meetings that presented alternate methods to test the efficacy of a product versus using animal tests.

Hill stressed that it has been 100 years since the Virus- Serum -Toxin Act was signed in 1813. His organization is requesting anyone who may have old photographs or materials to send a copy to the CVB for use in a presentation they are putting together to celebrate the centennial and illustrate the impact of biologics on animal health.

Applying New Science and Technology to Improve Regulatory Testing: Recent Interagency Progress and Future Opportunities

William S. Stokes
Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM), National Institute of Environmental Health Sciences (NIEHS), National Institute of Health (NIH), Department of Health and Human Services (DHHS)

Recent and continuing advances in science and technology are providing new opportunities to improve the efficiency and accuracy of regulatory safety and efficacy testing for drugs, vaccines, and other products. The ICCVAM is a Federal interagency committee composed of 15 Federal research and regulatory agencies that carries out activities to promote the development, validation, and regulatory acceptance of new, revised and alternative test methods applicable to Federal agency needs. ICCVAM, together with its supporting National Toxicology Program Interagency Center for the Evaluation of Alternative Methods (NICEATM) at the National Institute of Environmental Health Sciences (NIEHS) recently released a new draft Five-Year Plan that emphasizes the role that ICCVAM and NICEATM will serve in transforming regulatory testing by promoting the application of innovative science and technology. New methods for potency and safety testing of human and veterinary vaccines are one of the four highest priorities. Recent NICEATM-ICCVAM workshops have focused on identifying promising technologies that can be used to improve the testing efficiency and accuracy for several vaccines. The regulatory acceptance and use of scientifically valid new methods is expected to provide for continued and improved protection of human and animal health while also contributing to more humane and reduced animal use.

Controlling Wild Pig Populations: A Novel Approach to Species-Specific Immunocontraception

Frank F. Bartol[1,4], Anna M. Chochran[3], Alexandre M. Samoylov[3], Valery A. Petrenko[2,4], Timothy D. Braden[1,4], Nancy R. Cox[2,3,4], Stephen S. Ditchkoff[5], Tatiana I. Samoylova[2,3,4]

[1]Department of Anatomy, Physiology and Pharmacology; [2]Department of Pathobiology; [3]Scott-Ritchey Research Center; [4]College of Veterinary Medicine and [5]School of Forestry and Wildlife Sciences, Auburn University

Wild pigs (*Sus scrofa*) pose a real and growing problem on a global scale. In the US alone, the wild pig population is estimated in excess of 4 million animals. Wild pigs are omnivorous, eating plants including cultivated crops, as well as invertebrates, smaller vertebrates, eggs and even carrion. Beyond the threat posed by these animals to fragile ecosystems, damage to property and related agribusiness losses due to wild pigs in the US are estimated to approach two billion dollars annually. Additionally, wild pigs carry and can transmit diseases such as swine brucellosis and pseudorabies to domestic pigs, other domestic animals and humans. Thus, the growing wild pig population poses a risk to both animal agriculture and public health. Controlling wild pig populations is both essential and challenging. Traditional approaches, such as hunting and trapping, while part of the solution, are insufficient to deal with a problem of this magnitude. Technologies aimed at control of wild pig populations via regulation of reproduction have great potential. However, given the highly conserved nature of mechanisms regulating mammalian reproduction, any such technology must be species-specific in order to avoid suppression or ablation of reproduction in mammalian species other than the pig. At Auburn University, phage-display technology is being employed to develop pig-specific immunocontraceptive vaccines. A filamentous phage is used as a delivery vector for immunogenic peptides. The phage vector itself contributes to vaccine antigenicity. Using this approach, one strategy is aimed at induction of immunogens that will interfere with sperm-egg interactions and block fertilization.

To this end, multiple phage-peptide constructs were generated to mimic zona pellucida (ZP)-binding peptides expressed normally on porcine sperm cell surfaces. Phage constructs were selected from a phage display library based on their ability to bind the ZP with species specificity. Domestic swine vaccinated with these phage-peptide constructs produced anti-sperm antibodies. Species specificity of anti-sperm antibody binding was evaluated using spermatozoa from pigs, dogs, bulls, cats and mice. Phage-peptide constructs were identified that induced antibodies in vaccinated swine displaying differing degrees of species specificity. Reproductive tracts obtained from immunized sows displayed no gross pathology as a result of immunization with phage-constructs. Species-specific immunocontraception, developed using phage display technology, may provide an environmentally safe and effective method for suppression of reproduction in wild pigs through interference with sperm transport and/or inhibition of fertilization.

Committee Business

In summary the meeting went very well with some 20 plus attendees. A few additional points from the speakers are noted. In Dr. Loving's presentation it was noted that by 2050 the earth's population will be approximately 9 billion people and that will require doubling the food supply. Animal health and one health will become increasing important. Loving showed the budgetary increases per federal government agency over the last decade or so. The NIH budget doubled since the 1990s while the USDA budget only increased a few percent. USDA will require additional funding levels to sustain the One Health initiative.

Dr. Swaggerty showed that in the US there are still three-five million cases of food poisonings per year costing an estimate of $5 to $15 billion with 30,000 hospitalizations and causing 500 fatalities.

Dr. Bartol indicated even though the research results show great promise as a means of controlling the wild pig population, no hurdles have been jumped as yet with the regulatory agencies dealing with a number of issues that will be required to use this technique in the field.

No other business was discussed and the meeting was adjourned.