

from the president...



We are pleased to announce the USDA approval of Megan®Egg. Megan®Egg is designed for use in chickens to prevent the colonization of internal organs including oviducts/

ovaries and from the digestive tract including the ceca from Salmonella enteritidis (SE). Megan®Egg is different from other live Salmonella vaccines on the market as it is designed to protect chickens that are older (> 42 days of age). Birds are this age are resistant to vaccination and require a more aggressive vaccine to effectively stimulate the immune response against Salmonella enteritidis. Other live Salmonella vaccines are specifically labeled for use only in "young growing chickens".

Megan®Egg has been extensively researched by Lohmann Animal

Health scientists and outside groups as well. This vaccine is made to fit into your Salmonella enteritidis prevention program. Ask one of our Area Managers or Veterinarians for details. They will show you how to construct an effective and economical Salmonella prevention program using LAHI Salmonella vaccines. Lohmann is the leader in Salmonella research and vaccine selection worldwide.

avian insight

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Autogenous Vaccines: Current Use Patterns and End Users' Needs in the Integrated Broiler Industry

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Extracted from proceedings from the International Association of Biologists, entitled the International Veterinary Meeting on Consideration of Alternative Licensing Procedures for Vaccines for Minor Species, Minor Indications and Autogenous/Autologous Products.

approximately 105,000,000 doses of roughly 100 different autogenous vaccines and bacterins for 78 customers. At least 16 different species of organisms were used, including *Bordetella avium*, *Erysipelothrix rhusiopathiae*, *E. coli*, *Haemophilus paragallinarum*, *Mycoplasma spp.*, *Ornithobacterium rhinotracheale*, *Pasteurella multocida*, *Riemerella anatipestifer*, *Salmonella spp.*, *Staphylococcus aureus*, Adenovirus, Avian Influenza Virus, Infectious Bronchitis Virus, Infectious Bursal Disease Virus, Avian Paramyxovirus 3, and Reovirus. Customers included primary broiler and turkey breeder companies, broiler and turkey integrators, and table egg producers.

Today's vertically integrated poultry business structure has resulted in dense poultry populations that turn over rapidly. Large, changing poultry populations likely contribute to rapid emergence of variant strains of these mutable viruses, driving the need for new vaccines. Widespread use of commercial vaccines applies selection pressure, encouraging the survival of mutants that are different from the commercial vaccine strains. The immense size and wide geographic distribution of the industries create the possibility for geographically localized variants as well.

The need for autogenous vaccines seems to be increasing. There are four main factors driving this need.

1. The pathogens: Many of the major pathogens have a demonstrated ability to mutate and drift antigenically. Infectious Bursal Disease (IBD), Infectious Bronchitis Virus (IBV), and Reovirus are prominent examples.

2. The host: The birds have been selected intensively for productive characteristics, and as a result experience considerable physiological stress associated with rapid growth. Stress reduces innate resistance and adaptive immune responses. Relatively minor antigenic changes in a pathogen, that may have gone undetected years ago, now are resulting in measurable decreases in productivity and even overt disease in these modern, rapidly growing and heavily laying birds.

Only 0.18% of all doses of animal vaccines, bacterins, and vaccine/bacterin combinations produced in U.S. licensed establishments in 2002 were classified as autogenous products. Nevertheless, autogenous vaccines and bacterins are increasingly important adjuncts to health maintenance and food safety in the integrated broiler, turkey, and egg industries in the U.S. A survey was submitted to the three major producers of autogenous poultry vaccines in the U.S. These three producers manufactured in 2002

In this issue of avian insight:

Autogenous Vaccines: Current Use Patterns and End Users' Needs in the Integrated Broiler Industry.....p.1
From the presidentp.4

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continued from page 1

Practitioners working with today's genetics need vaccines that are more closely matched antigenically to the resident pathogens. The increased fragility of the modern bird is especially evident in heavy breeder males, which have been selected most intensively of all. These males poorly tolerate live *P. multocida* vaccines, and so the reliance on killed fowl cholera vaccines has increased. The extreme serotype specificity of killed fowl cholera vaccines has necessitated widespread use of autogenous fowl cholera vaccines for the local serotypes in cockerels.

3. New management priorities: Couple this increased sensitivity of the modern host with efforts to decrease the use of antimicrobials, and the need for rigorous, precise prophylactic strategies is apparent. Food safety and salmonella control are increasingly important. With over 2400 serovars, autogenous salmonella vaccines are critical to advancing salmonella control, especially in primary and multiplier breeders.

4. The vaccine industry: The commercial vaccine industry is becoming concentrated in fewer, larger businesses, and the process for regular (as opposed to autogenous or conditional) licensure of a commercial vaccine is rigorous, as it should be. Unfortunately this structure is not exceedingly nimble. It is difficult to respond quickly to a new pathogen with a regularly licensed product. The poultry vaccine business also is extremely competitive, with narrow profit margins that depend on volume for profitability. It is not economically feasible to respond to a geographically localized pathogen with a regularly licensed product. If either a new or a geographically localized pathogen becomes permanently established and widespread, then a regularly licensed commercial product is feasible and should be required. In the meantime, autogenous vaccines are the best alternative.

The U.S. regulations governing the manufacture of autogenous vaccines in 9 CFR 113.113 are administered by the United States Department of Agriculture, Animal and Plant Health Inspection Service, Veterinary Services, Center for Veterinary Biologics (the agency). While these regulations have served the veterinary profession and the regulatory agency well, they no longer fully meet the needs of the modern commercial poultry industry. Commercial poultry veterinarians who are the end users of these vaccines have approached the agency via the American Association of Avian Pathologists' (AAAP) Biologics Committee with several specific concerns.

The regulations apparently were devised with individual cattle and swine herds and private practitioners in mind. It apparently was assumed that autogenous vaccines would be used primarily to address sudden, severe outbreaks of livestock disease, usually in a single herd or in a localized area. Once the outbreak was quelled, the need for the vaccine should disappear. Autogenous vaccines are no longer used solely to control sudden epornitics. Due to the changes in the industry, in the birds, and in disease prevention priorities, autogenous products are used in a truly prophylactic manner. "Less-than-serotype" changes in mutable and emerging viruses are followed much more closely than in the past, to control diseases as they emerge, not after they are out of hand. Some practitioners use commercial vaccines as the basis of their immunization programs, with additional autogenous vaccines that evolve as the pathogens evolve, literally one step behind the pathogens. We are attempting to provide the most homologous protection possible, to absolutely minimize disease and our reliance on antimicrobials.

It would appear that there has been (and perhaps remains) a need to protect the farmer from unscrupulous veterinarians and vaccine manufacturers, and to prevent unscrupulous manufacturers from using the autogenous regulations to circumvent the process of obtaining full licensure for some products. These safeguards need to remain in place. However, the current structure of the poultry industries (broilers, turkeys, and layers) is such that some of these safeguards are not only no longer needed, but are actually interfering with effective use of autogenous products. The integrated company owns the parent breeder birds and retains ownership of the production progeny. Most of the larger companies have staff veterinarians who are full-time employees of the company. In terms of the veterinarian-client-patient relationship, the veterinarian-employee is a part of the client, and the patients are his employer's animals. These veterinarians are typically poultry specialists, and are quite capable of assessing the field safety and efficacy of the vaccines they use. The tight profit margins in the poultry industries preclude the use of any product, including a vaccine, which does not appear to give a return. If a veterinarian employed by an integrator is using worthless vaccines, the problem is between that veterinarian and his employer, not between the manufacturer and the integrator. The prospects of a shyster foisting a worthless product on an unsuspecting or uneducated user are unlikely. Today, an unaffiliated practitioner or a vaccine manufacturer does

continued on page 3

continued from page 2

not approach the owners of poultry flocks (the integrators) with an offer to make an autogenous vaccine to solve a purported problem. Rather, the corporate veterinarian has identified the problem, determined the need for an autogenous vaccine, and approaches the manufacturer with a well-characterized organism in hand, asking the manufacturer to produce the vaccine for his operation. Given the resources and time, corporate veterinarians and consultants could legally produce these vaccines in their own laboratories for use in their own birds. It is preferable to have competent, experienced manufacturers produce them under commercial manufacturing practices. The regulations should foster this relationship, not hinder it, and could be modified to allow more efficient use without compromising prudent regulatory control.

Four specific concerns have been articulated by various members of the AAAP Biologics Committee. The first two were endorsed and sent forward to the agency by the Committee. The second two remain concerns of some individuals.

1. The regulations require that an autogenous vaccine be used only in the herd from which the organism was isolated [9 CFR 113.113 (a) (2) and (a) (3)], and impose extensive application procedures for use in adjacent and non-adjacent herds. The agency has been fairly liberal in interpreting this part of the regulation in terms of commercial poultry flocks. The special structures of the integrated industries (whether broilers, turkeys, layers, swine, or others) should be recognized and acknowledged in the regulation, rather than depending on the interpretation of future administrators. The structure of integrated operations makes the criteria in paragraph (a) (3) (iii) a permanent and ongoing feature. The integrated structure, by its very nature, always ensures that the "epidemiology of the disease situation ... links the designated geographic areas with the herd (i.e. flock) of origin..." An autogenous vaccine produced for any flock within an integrated production complex should be available for use anywhere in that complex.
2. The regulations limit vaccine production to 15 months from original isolation, or 12 months from production of the first serial, whichever comes first. Additional serials may be produced for up to 24 months upon presentation of supporting information to the Administrator, including a "documentation of continued

involvement". Extension beyond 24 months requires antigenicity and potency tests. These additional safeguards are not needed. If the vaccine is effective, it should be difficult or impossible to re-isolate that pathogen or otherwise "document continued involvement". It is quite possible and in many cases likely that the pathogen remains a threat. Under the current guidelines, the practitioner must stop vaccinating, allow some flocks to get sick, re-isolate the pathogen, and start over. If the pathogen has indeed disappeared, and the autogenous product is no longer needed, where is the real harm in the integrated system? There are likely no adverse effects whatsoever on the birds, farmers, or consumers from continued use of the vaccine. The only downside is the possibility of money ill-spent on an unneeded vaccine, and informed individuals who own the birds and stand the loss will have evaluated the risks and made the decision to continue use.

3. Some practitioners desire the ability to add an autogenous antigen to existing standard antigens. There are several rational reasons to do this, including spectrum of protection and bird handling and stress. Mixing of separately prepared preparations in the field is fraught with numerous dangers, such as contamination, incompatibility of emulsions, and homogenous distribution of components. Combination of autogenous and regularly licensed antigens by the manufacturer should be permitted. Appropriate testing of the regularly licensed fraction could be conducted as usual.
4. It is unclear whether a manufacturer can return an isolate to the owner. It is clear that isolates must be destroyed after the allowed 12 to 15 months (or 24-month extension). Some practitioners desire clear permission to retrieve isolates. The inability to do so precludes the ability to switch manufacturers, is an unnecessary restraint of commerce, and denies access to what is regarded as proprietary ownership of the isolate. If the time limits were to be rescinded as suggested, there should be no reason that an isolate could not be returned.

The objectives should be to produce autogenous vaccines that are pure and safe, and that meet the challenges of emerging or localized diseases, within a regulatory framework that maintains adequate regulatory control while recognizing the current structure of the industries.