

To summarize what I said at the AGF roundtable meeting on January 21, 2020

Colorado Serum Company is a Veterinary Biologics Company. We make vaccines, bacterins, toxoids and serum antibody products (antiserums or antitoxins) for farm animals. We make many biologics for small ruminants like CDT - *Clostridium perfringens* type C&D with Tetanus Toxoid (Essential 3+T), Bluetongue Vaccine (type 10), Bovi-Sera, Case-Bac Vaccine for CLA in sheep, *Campylobacter fetus-jejuni* Vaccine, *Chlamydia abortus* vaccine, Ovine Ecthyma vaccine, *Clostridium perfringens* type C&D Antitoxin, Tetanus Toxoid and Antitoxin, Pneumonia Bacterin (*Mannheimia haemolytica*-*Pasteurella multocida* Bacterin containing serotypes 1 and 2 for *M. haemolytica*), Anthrax Spore Vaccine and many other Clostridial combination Bacterin/Toxoid products. Veterinary Biologics are regulated by USDA/APHIS/CVB (Center for Veterinary Biologics) and Veterinary pharmaceuticals like dewormers, antibiotics and other medicines are regulated by FDA/CVM (Center for Veterinary Medicine). Colorado Serum Company is currently constructing a new BSL 2 (Biosafety level 2 laboratory) for small ruminant vaccine research and development. A couple of projects in the pipeline are a CLA vaccine for goats and a vaccine for tetracycline-resistant *Campylobacter jejuni* for sheep. Colorado Serum is always interested in any new R&D Veterinary Biologics that are developed by researchers at USDA or Universities that need a commercial partner to scale up and license to commercialize new products. Colorado Serum Company is also open to being a permittee and distributor for imported biologics that USDA/CVB might allow.

Coxiella burnetii, is the causative bacteria for Coxiellosis in ruminants and Q fever in people. It is a zoonotic which means the bacteria can cause disease and is contagious between animals and humans. The bacteria is an intracellular bacteria that likes to live inside the immune cells (phagocytic white blood cells) that are actually required to fight off infections. There is no vaccine for *Coxiella* in the United States but efforts for a vaccine are on-going at USDA/NADC/ARS. There is a vaccine for people in Australia and a killed vaccine in Europe made by Ceva in France that is used in ruminants. It is a phase 1 inactivated Bacterin which means it contains the outer LPS cell wall that makes it more immunogenic. Because this vaccine is a killed Bacterin it might have the possibility of consideration to be imported into the USA by USDA/APHIS/CVB. This is not something that CVB has been approached about, to my knowledge. Some of the problems with making a vaccine or importing a vaccine include the big problem that *Coxiella burnetii* is

classified as a select agent. This makes working with the vaccine very difficult and any host animal challenge efficacy studies extremely expensive since those studies would have to be done in a BSL-3 facility. There are only a few of these labs in the United States. Another problem with importing the vaccine is the fact that the organism used to make the vaccine in France is grown in eggs. CVB would have serious issues with this because of the potential to bring in foreign animal disease organisms from ingredients of animal origin – in this case eggs. This would be a big hurdle that CVB would have to sign off on. Historically they have not usually allowed imported biologics. In order for this to have any possibility for consideration it would require the sheep and goat industry associations to lobby USDA for consideration. It would most likely be cheaper than developing, testing and licensing a new U.S. vaccine. The expense of doing licensing studies in a BSL3 facility and also working with the organism in a BSL3 production facility (to grow it and attenuate or inactivate it) likely would make the expense of the vaccine cost prohibitive for most sheep and goat producers. One possible solution would be to have *Coxiella burnetii* added to the list of Program Diseases with USDA like *Brucella* and Tuberculosis currently are. As a Program Disease agent all efficacy and initial safety work could be done at the USDA/NADC/ARS BSL3 large animal facility using funds allocated to them under the Program Diseases program. (Dr. Plummer seemed to think this would be unlikely since the organism is so prevalent and ubiquitous in the environment.). A third option would be to have *Coxiella Brunetti* removed from the select agent list, which would allow for much less costly studies for vaccine development. The sheep and goat industries would be helpful along with organizations like the United States Animal Health Association (USAHA) in petitioning USDA and DHS to consider removing *Coxiella* from the select agent list.

We also discussed the Barbervax vaccine for help in controlling the barber pole worm in small ruminants. This parasite is increasingly resistant to dewormers and is difficult to control. The current vaccine is made in Australia. Petitioning USDA/CVB to allow importation into the United States would require them to approve the manufacturing and safety of the product. The vaccine is made from the dead worms inside infected goats collected usually at slaughter. This poses a big problem with USDA/CVB because it too would contain ingredients of animal origin and the concern would be introducing other possible foreign animal diseases into the United States. Dr. Miller also discussed how laborious it is to make the vaccine and it's difficult to make significant quantities. Probable issues

I can see with this vaccine are; **1.)** Owner compliance; the frequency of administration is every 6 weeks during the worm-risk season after 3 “priming” vaccinations initially given 4 weeks apart. This will be a problem, especially for sheep producers with large flocks grazing on large tracts of land. The frequency is due to a very short duration of immunity (only 6 weeks). **2.)** This is only labeled for use in sheep because of potential safety concerns in goats. **3.)** The vaccine contains saponin adjuvant. This can be reactive to goats in my experience. Saponin is an adjuvant in our CLA vaccine for sheep (Casebac) and it definitely is more reactive in goats which is why it is only labeled for sheep. **4.)** Cost of the vaccine and the market for it. For USDA/CVB to approve importation they would need to visit and inspect the facility and process. USDA/CVB would expect the permittee/importer or U.S. sheep industry to pay for this expense. By the time the vaccine reached the distributor and then the end user, the cost may be prohibitive for the end user especially if it will require 5 or 6 doses per animal every year. Because it is only labeled for sheep, the U.S. sheep industry would need to determine what the market would be for this. Since the majority of sheep are on dry western range lands where the barber pole worm isn’t as prevalent and sheep are not as easily rounded up to work with the frequency required for the Barbervax vaccine, would there even be much of a market for sheep? Goats would be off-label and how would USDA/CVB view this? Would it be allowed as an Rx by a veterinarian, the way it is in Australia? Would there be increased adverse reactions in goats compared to sheep? If used in goats what would that market be? Number of doses/year? The manufacturer in Australia would need this information before determining if they can do it or if it is even worth it to bother with the USDA/CVB inspection process and extra regulatory burden they may place on them.

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