

The following is a document created from a discussion of Pasteurella and the Bunny Vac that took place on the ARBA facebook board in May 2013. Contact information for the Bunny Vac is Bob Glass, Bglass@pavlab.com or (800) 856 9655.

The price as of May 2013 was: 20 dose vial, \$20; 50 dose vial, \$40. Shipping is \$10 for either size. Initial dose is followed up with another in 30 days and a booster once a year for the life of the rabbit.

5/11/2013

Hello, this is bob Glass with Pan American Vet Labs co developer of the BunnyVac Pasteurella vaccine. I've got tests running the lab now but will be back later. If anyone has questions post them here and I'll get to them ASAP. Thanks.

Study Data: We have submitted all the study data to USDA and based on that data USDA issued the product license. We have not published the data and plan to write a full paper and submit it to Veterinary journal for publication. I am not sure when we will get that done but if we publicize the data it will not be accepted for publication. So for now we are playing the middle and releasing some "summary" information but not the full data set. All the data is at USDA, has had a full review and has been accepted as supporting data for the product claims.

Youngest Age to vaccinate; In the study we used 70-90 day old rabbits but we see no indication that vaccination in young animals is a problem. Generally the rabbit immune system is at full competency at or near weaning. That is the earliest I would recommend vaccination. In my barn we will vaccinate at weaning (+/- 5 weeks).

Pregnant/nursing does My experience with rabbits is that any stress on pregnant does can be bad so I would not vaccinate any later than 7 days bred. Not because the vaccine is toxic but it will induce a strong immune response which could cause some level of stress. I have vaccinated pregnant does without a problem but I prefer to vaccinate at breeding or a week earlier to avoid stress while pregnant. I see no problem in vaccinating nursing does. There would seem to be advantage in does being at the highest level of immunity when the kits are born so that there is an abundance of antibody to go into the colostrum.

The USDA license is issued for Prevention of death and control/elimination of clinical disease in Pasteurella infected rabbits. Our goal is to minimize the impact of a Pasteurella outbreak in a herd. Certainly the greatest impact is death and in our study we had zero deaths in vaccinated animals versus 60% death rate in non vaccinated rabbit. The major symptom of clinical disease is sneezing and this is the main source of spreading the disease. In the study 100% of the non vaccinated rabbits had severe sneezing and respiratory congestion. In the vaccinated group small number of animals had very mild nasal exudate for a very short period (24-48 hours). All the vaccinated animals were completely clear of all symptoms by the end of the 14 day study period. The non vaccinated rabbits that did not die during the 14 days study period continued to suffer severe disease symptoms until the study was complete.

It is important to know that BunnyVac is not licensed to or do we claim that it will cure an ongoing infection. We have anecdotal (un proven) observations of diminished symptoms in clinically ill rabbits after treating with BunnyVac. The study to prove or refute this has yet to be done.

Side effects; We have not seen significant negative side effects in any animals. We have seen some minimal lethargy for +/-24 hours after injection. This is related to the immune response induced, not infection, as is seen with many vaccines.

No multi generational studies have been done, but Pasteurella vaccines have been employed in other species (cattal, sheep, goats) for many years with no reported impact on conception rates, Birth weight or weight gain.

The vaccine has a thimersol preservative but I will have to calculate the amount of mercury per dose. I'll get that later. this preservative is commonly used and approved by USDA. I recognize that there are concerns with vaccine preservatives but since this product is packaged in multidose vials a preservative is required. Single dose packaging would increase the cost 3-5 fold.

Cost: 20 dose vial = \$20 50 dose vial = \$40 \$10 shipping/handling for either size.

There is no need to isolate vaccinates as the product has only killed bacteria and cannot cause infection.

While we have not done a study to prove/disprove benefit in infected animals there is no indication that vaccination of sick animals will cause a negative effect.

BunnyVac is available to vets and non vets, no prescription is required.

The study we did was designed to prove efficacy in preventing death and clinical disease. The next step will be a study to determine if treatment completely blocks infection. This is in the planning stages but there is no date set for this study.

Immune response is dependent of several factors including the presentation of the infecting agent. many organism diminish the immune response by blocking the bodies ability to "see" the organism. this is done by "growing" a covering that is not recognized by the immune system. this covering "hides" most of the infecting organism so that only a small amount of the organism is seen and thus limits the degree of immune response. with a vaccine we can give huge doses of the killed organism without causing disease. This very large dose means more of the bacteria is "available" and results in a greater stimulation of the immune system and better protection against infection.

BunnyVac is not related to or derived from work done in Europe. The idea may be similar but we did not collaborate with anyone in Europe.

Sorry for not keeping up, I just finished the original questions. I see the question about curing infected rabbits. We have not done a complete study on this question, but we have treated infected animals and seen improvement. This is not a controlled study by any means and is not associated with USDA study.

Testing is not required for vaccination. That may be something individual owners decide to do or not do, but it is not a prerequisite for vaccination.

Blood test will not be able to differentiate between vaccine induced antibody and infection induce antibody

It is important to point out that this vaccine is a killed product, not a "live modified" product. It does not produce any infection only simulates infection by presenting the pasteurella to the immune system.

Sorry, I said this vaccine "is part of the Purdue study" and I meant "is NOT part of the Purdue study" it getting late...

I am looking over all the comments and see a great deal of skepticism from some. Thats ok. Some of this is due to my not making some things clear and some is from a healthy level of "Prove it first". My late dad was blessed with a healthy level of "Prove it first" and I learned a lot from him. I am more than willing to speak directly with anyone who wants to seek a better understanding of this whole thing. I can assure you of two things: I am not some "fly by night" snake oil salesman

and this vaccine is not a panacea that will eliminate *Pasturella* from every rabbit. It is just one more tool that each producer should evaluate as an addition to their management program. Good hygiene cannot be replaced and certainly should not be replaced, but use of vaccines in livestock pets and humans has been proven beneficial and this one while not perfect can be beneficial also.

We decide to use SC only in our study. The reasons are: most people are better able to do SC than IM, many breeders raise rabbits for meat and the IM injection can cause a blemish in the meat, Intranasal has consistently been shown to be less efficacious than SC or IM. It is acceptable with highly immunogenic agents but not with lower immunogenic agents.

The question of impact on litter size, conception rates etc are good one and I don't have an answer specifically related to rabbits. *Pasteurella* vaccines are commonly used in other species without these problems. There no reason to expect these problems in rabbits.

The study we did was a short term; inject on day 0, boost on day 30, challenge 2 weeks later and observe for 14 days. 10 non vaccinated and 2 groups of 10 each vaccinated. Safety studies were 2 injections as above and observe for +/- 70 days. This was done in 300 hundred rabbits (Californian and New Zealand) in three separate rabbit farms. We did not see any negative side effects in either study

Injections are given on day 0, day 30 and annually after that.

We will be doing more testing but no concrete plans or time table just yet. Honestly I need some time to see how widely this is accepted before I invest another chunk of money into this research. We have another product for a completely different disease that we working on that takes time and money. If you are interested you can see information on Pythiosis at www.pavlab.com (check the Pythium page) or the facebook group Pythiosis.

The BunnyVac label calls for a withdrawal period of 21 days after injection. There is no data that shows a problem if consumed earlier than that, just a standard "for sure safe" withdrawal period.

The bunnyVac is "one size fits all". We are stimulating an immune response and need to present the antigen to a number of cells that will accomplish this goal. That number is essentially the same regardless of the size of the animal. The

dose is 1/2 cc per injection. We use a smaller volume (most vaccine are 1 cc) to accommodate the small breeds.

Great questions/discussion for so early in the morning! Pasteurella has two pathology modes: skin infections (abscesses) and respiratory infection. The site of infection appears to be at least partially determined by the strain of Pasteurella: certain strains like the skin others like the mucous membranes of the respiratory system (lungs/nasal passage/sinuses). The skin strains appear to be close closely related to each other than they are to the respiratory strains and the same is true of the respiratory strains. We have focused on the respiratory infection with this vaccine. since the respiratory strains are fairly closely related it is possible to induce antibodies that will recognize/fight many or that group. Thus we can produce a vaccine that some level of benefit for many if not all of the reparatory strains. The immunity induced by infection or by vaccination is present in the blood stream in the form of antibodies (humoral immunity) and immune active cells (cellular immunity). In many cases the cellular immunity is more effective than the humoral.

Antibodies can directly kill bacteria but they also serve to "tag" bacteria so the immune cells can "see" them. The cells are very effective because they not only kill the bacteria but also engulf the bacteria, digest it and send pieces out in "packets" which are taken in by not yet activated immune cells which are then imprinted with the bacteria's pieces and join the fight. The problem with Pasteurella infection is that the bacteria can be attacked in those areas where there is good blood supply, unfortunately Pasteurella colonizes the sinus cavities where there is very limited blood supply. In this area the immune cells and antibodies are not able to get to all the bacteria, thus the carrier state. this is also why many rabbits initially have really snotty noses and congestion; this is due to infection in the nasal passages and lungs. the immune response can kill the bacteria in these areas and the symptoms clear. but the bacteria remains in the sinuses. Then the immune response goes into a "surveillance" mode with lower number of activated cells and decreased antibody levels. It does maintain a memory of the infecting agent and can be activated by re exposure. So, the carrier rabbit is asymptomatic until something allows the bacteria to take off. In rabbits this is "stress" in any of many forms. Did you ever wonder way rabbits reproduce so fast? it's because they get sick and die easily; they have to have lots of babies to survive. the purpose of the vaccine is induce a level of immunity in non infected rabbits so that the initial exposure to live Pasteurella finds them with a level of

immunity that blocks the infection. We do not know what percentage of animals will emerge from the initial exposure without being carriers, that will be the subject of a further study. What we know is that the severity of the initial exposure will not result in death and the degree of disease will be significantly lessened. The lesser symptoms mean less infectious snot in the air from sneezing which in turn means less chance that additional rabbits will become infected, especially because they also will have an existing immunity.

The question of developing an anti *Pasturella* rich immunoglobulin as a treatment is an interesting one. This is done for many diseases with good success. However it is generally not needed in animals that have successfully vaccinated. It also is a rather expensive product and the benefit is short lived, days to weeks only. My thought is that you can get better benefit through vaccinating in advance of infection. I am studying the idea of an immunoglobulin product for Rabbit Epizootic Enteropathy.

That's a whole new project that will take a long time. But it would be interesting to see if serum from a rabbit that has recovered from this disease imparts any benefit to one sick with it.