Prescription Platform Vaccines

Using Next Generation Technology in the Ongoing War Against Animal Diseases

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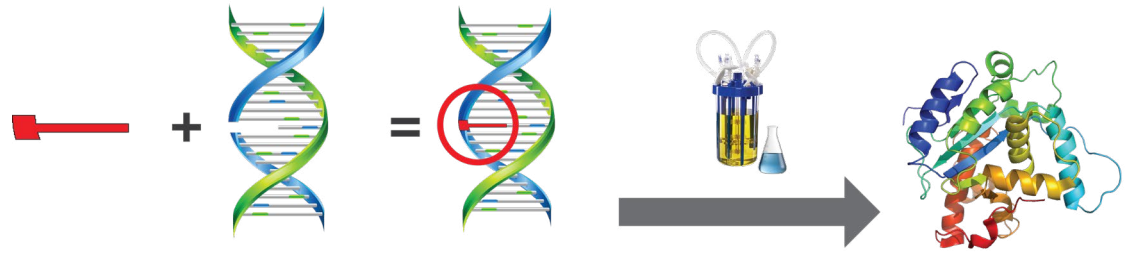
Since the beginnings of animal domestication, owners and producers have been dealing with the effects of animal diseases. Past efforts to combat them have included such things as herbal and antibiotic treatments, dietary modifications, alterations in management practices, and vaccination. Until recently, vaccination has been limited to the use of either commercial or autogenous vaccines, both of which have their own distinct advantages and drawbacks. The USDA Center for Veterinary Biologics (CVB), with the most recent in a long history of regulations designed to support innovation in veterinary biologics, has released guidance documents allowing for the development and licensure of Prescription Platform Vaccines (RxPP).

A Prescription Platform Vaccine is a platform-based, standardized vaccine that is nonviable and non-replicating (i.e., "killed"). By CVB definition, a production platform is a manufacturing process that relies on a single vector or expression system ("backbone") and a standard process for inserting a gene or genes of interest (GOI) into the system to generate different recombinant Master Seeds or Sequences, which are then used to produce product following a standardized method for manufacture. The GOI is selected to be one that codes for a protein that is known to convey immunity against the agent in question, so that the final product will be expected to produce disease coverage in vaccinated animals. See Figure 1 for a graphic explanation.

Figure 1: Graphic depiction of RxPP technology



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The GOIs for RxPP vaccines are derived from diagnostic submissions by veterinarians.

In order to provide RxPP vaccines, a biologics manufacturer must first develop an Initial Product, which is a fully-licensed product that establishes factors including a standardized manufacturing method, the "backbone" used for the product, and other parameters such as minimum age, maximum antigen level, dose size, route of administration, and adjuvant type. This Initial Product must also demonstrate both safety and effectiveness. Once the Initial Product has been completed, the same licensed procedures are followed to manufacture RxPP vaccines using other GOIs. These RxPP vaccines can then be prescribed by attending veterinarians for use in at-risk animals out in the field.

The GOIs for RxPP vaccines are derived from diagnostic submissions by veterinarians. Viruses and bacteria detected by virus isolation, PCR, or metagenomics are sequenced for the GOIs by diagnostic laboratories using next generation diagnostic methods. These sequences can then be transferred to a RxPP manufacturer, by permission from the attending veterinarian, for RxPP vaccine development.

As the name implies, Prescription Platform vaccines require a written prescription from a veterinarian. This veterinarian must have an established and legitimate Veterinarian-Client-Patient Relationship (VCPR) with the end-user of the RxPP, as defined by both government regulations and the American Veterinary Medical Association. The veterinarian and the manufacturer work together to determine the GOI used in the product, as detailed above. After this GOI is approved by CVB, the manufacturer produces a construct

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(the "backbone" plus the selected GOI). All parameters for the fully-licensed Initial Product must be followed, other than the use of the new GOI. The construct is then incubated to produce antigenic proteins, the final product is inactivated and adjuvanted, and it is ready to be administered to animals. Since these RxPP vaccines are made using a different GOI than the fully-licensed Initial Product, they have not shown potency or efficacy (which is indicated on the label); however, since they are made using identical processes to the Initial Product they do have expectations that they will provide both. RxPP vaccines are tested for both safety and purity before being released for use.

Autogenous vaccines must be made from disease agents actually isolated from an affected farm, and can only be used on that farm or, with special CVB and state veterinarian approval, in adjoining and/or non-adjacent herds also considered at risk due to epidemiologic connections. RxPP vaccines can be used in herds at risk for a disease but not yet affected, meaning they are a much more proactive disease-fighting agent without the laborious paperwork and approvals required for autogenous vaccines. Since RxPP vaccines are developed from a fully-licensed Initial Product platform, with the only variation being the GOI used, they also have the associated expectations of effectiveness which are not seen in autogenous vaccines.

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Unlike autogenous vaccines, RxPP vaccines may be used in any animals that the attending veterinarian determines could benefit from their use. RxPP vaccines can also fulfill a need in cases where commercially-available (off the shelf) vaccines are not a viable option. Commercial vaccines can take years to develop, and may not be available when needed for new, emerging diseases. Also, commercial vaccines that have been available for many years can contain outdated antigens that do not reflect the strains currently causing issues in the field. RxPP vaccines, on the other hand, can use GOIs from these new strains to develop current vaccines without the long wait times. In many cases, production of a RxPP vaccine can be done in less than twelve weeks from start to finish.
Another distinct advantage to RxPP products is that they can be used for many emerging diseases where there is no other way possible to create a vaccine. Many agents causing emerging diseases cannot be grown *in vitro*, so a traditional autogenous vaccine cannot be used and a commercial vaccine cannot be developed. However, these agents can be detected by molecular sequencing, from which the GOIs can be derived and inserted into the RxPP backbone, thus allowing the manufacture of a vaccine to combat the disease.

Additional general information regarding Prescription Product Vaccines can be found in Veterinary Services Memorandum Nos. 800.213 and 800.214. Medgene is in the process of licensing RxPP products for the ISPRIME service with the USDA. For more information on Medgene, please visit www.medgenelabs.com.

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