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Challenges confronting feline vaccination

James R. Richards

Cornell Feline Health Center, Cornell University College of Veterinary Medicine, Ithaca, NY 14853, USA

Abstract

Vaccination continues to be a major tool for controlling feline infectious diseases, but numerous factors present both challenges and opportunities for maintaining and expanding the market for veterinary biologicals. Developing novel vaccines is one approach, but in most cases the market for such products will be restricted to niche populations; the comparatively smaller quantity of vaccines sold may be offset somewhat if available from a limited number of manufacturers. A second approach is to produce better formulations of existing vaccines; such products would be applicable to larger populations of cats and have greater sales potential. But veterinarians must be convinced of the improved product's superiority for it to be successful in the marketplace. To ensure that high-quality, useful and necessary vaccines reach the marketplace, communication between veterinarians, the manufacturers of biologicals, and regulatory agencies must be enhanced.

Keywords: vaccination; vaccines; cats

Introduction

According to the *2000 Report of the American Association of Feline Practitioners Advisory Panel on Feline Vaccines*, the overall objectives of vaccination are to vaccinate the largest possible number of individuals in the population at risk, vaccinate each individual no more frequently than necessary, and vaccinate only against infectious agents to which individuals have a realistic risk of exposure and subsequent development of disease. The availability of the many safe and useful vaccines that help veterinarians meet these objectives is reliant upon this simple concept: that veterinarians depend on manufacturers to produce vaccines and manufacturers depend on veterinarians to purchase them. Not surprisingly, new vaccines will be developed only if manufacturers predict their commercial viability. After balancing development and production costs against expected revenues, what path should a manufacturer follow? To produce a novel vaccine—that is, one containing an antigen not present in any existing vaccines? Or to produce a better formulation of an existing product? And what other challenges confront manufacturers striving to bring new vaccines to market?

E-mail: jrr1@cornell.edu

Novel vaccines …

Novel vaccines will probably have application to comparatively small subsets of the owned cat population—that is, they will be classified as non-core vaccines in contrast to the so-called core vaccines recommended for use in all cats. As a result, sales volume may be relatively low. Nonetheless, commercial viability might be achievable if the product is available from only the manufacturer that developed it and if practitioners value the vaccine enough to pay a higher price. Traditionally, the vaccine that is first to market tends to maintain market share even after competing products become available.

It is increasingly difficult to identify new vaccine candidates for feline pathogens (examples might include *Mycoplasma haemofelis*, *Cytauxzoon felis*,

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Cryptosporidium spp., and selected fungal, endoparasitic and ectoparasitic agents). Therapeutic vaccines, such as anti-cancer vaccines, hold promise, as do vaccines against zoonotic agents; excepting rabies, the latter are largely unexplored. *Bartonella* spp., *Toxoplasma gondii*, *Yersinia pestis* and *Coxiella burnetii* are examples of zoonotic agents for which cats play a role in transmission to humans and for which no vaccines exist at the time of writing. But for zoonotic vaccines administered to cats to reduce human infections, the role that cats play in transmission must be thoroughly understood, and the population of cats most responsible must be the main vaccination targets. Unfortunately, this might be difficult to achieve, as exemplified by the following example. *Toxoplasma gondii* infections in humans are associated with eating contaminated meat and with ingesting sporulated oocysts passed in the feces of shedding cats. One could argue that cats defecating in pastures or feedlots and infecting food-producing animals are at least as important a source of human infections as are indoor cats with little access to prey and that eliminate in litter boxes. Yet the latter are more likely to be vaccinated because they live with humans who request vaccination.

… or better old ones?

Improved versions of existing vaccines may have application to a larger population of cats than would new novel vaccines, and thus have a greater potential sales volume. The following are examples of desirable features for existing (and new) vaccines.

They should induce broad protection. Feline calicivirus (FCV), feline coronavirus (FCoV) and feline immunodeficiency virus (FIV) are examples of feline pathogens that exist in nature as 'clouds of variants'. The antigenic diversity of these infectious agents complicates attempts to produce vaccines capable of inducing protection against the array of field isolates to which cats may be exposed.

Parenteral vaccines should not invoke local inflammatory responses at vaccine sites. The role, if any, that vaccine-induced inflammation plays in vaccine-associated sarcomas remains unclear; regardless, relieving clients and veterinarians of the need to monitor post-vaccination masses would be desirable.

Vaccination should not interfere with diagnostic testing. For example, an inactivated, whole-virus feline immunodeficiency virus vaccine currently available induces antibodies indistinguishable from those present in naturally infected cats. The inability to distinguish vaccinated cats from infected cats—and from those that are both vaccinated and infected—when using antibody-based diagnostic tests is an undesirable feature and complicates the decision to use the product.

The dose volume should be appropriate for the patient and the site and method of administration. Topical (e.g. intranasal, conjunctival) products are usually available in 0.5 ml doses, a volume that usually cannot be fully administered to cats. Also, if administering parenteral vaccines to small kittens or into distal extremities with limited subcutaneous space, a dose of 1 ml may cause more patient discomfort than would a smaller volume.

Intranasal/conjunctival vaccines with reduced incidence and severity of post-vaccinal reactions (e.g. sneezing, conjunctivitis) are desirable.

Vaccines should have revaccination intervals consistent with the actual duration of protection they induce.

For improved vaccines to have a competitive edge and to sell in volumes that justify their production, veterinarians must be convinced of their superiority. Educational efforts on the part of manufacturers, and confirmation of the product's superiority by independent and unbiased investigators, are tools of proven effectiveness.

What will be acceptable?

Costs of novel and improved vaccines will expectedly be higher than those of current products, partly so that manufacturers can counteract lower sales volumes resulting from niche markets and reduced frequency of administration. How much are veterinarians and clients willing to pay? Most current vaccines cost only a few dollars; will veterinarians be willing to purchase those that cost several times more? What if a manufacturer produces a vaccine that induces protection extending beyond a year? If protection lasts 5 years, say, will veterinarians be willing to spend five-fold more for it? Most important of all, perhaps: do veterinarians actually want vaccines that do not require frequent administration? And if not, will manufacturers suffer for producing them? These are all questions with which feline biologicals manufacturers must grapple.

The frequency and route of vaccine administration must be acceptable to both veterinarians and clients. An initial series of two to four subcutaneous vaccines given at intervals of 3–4 weeks, followed by annual to triennial administration, is of proven acceptability. However, resistance may be met if a greater (or lesser) number or frequency of vaccinations is required; so, too, if a novel route of administration (e.g. intradermal or oral) or one perceived to be distressful to the cat (e.g. intranasal) is required.

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Regulatory challenges

The United States Department of Agriculture (USDA) is charged with regulating veterinary vaccines marketed for interstate sale. The laudable quality of the majority of veterinary biologicals affirms the processes by which USDA approves and monitors vaccines. Traditionally, vaccine efficacy is determined by challenging (usually with a laboratory-adapted isolate of the pathogen) a small number of both vaccinates and controls (usually of uniform age and background), then comparing the rate of infection, severity of clinical signs or serological response to vaccination. But new technologies and rising expectations will continue to challenge regulatory processes.

Novel vaccine types

Certain recombinant vaccines may not induce antibody production; thus, measuring a serological response in vaccinated animals would not be a useful means of determining efficacy.

Pathogens that exist as a cloud of variants (such as FIV, FCV and FCoV)

Predicting vaccine performance in the field is impossible when only one isolate is used in a laboratory challenge.

Vaccines for zoonotic diseases in which infected cats show minimal or no signs of disease

Infection prevention or a reduction of shedding in vaccinates compared with controls would be the yardstick rather than a reduction in clinical signs.

Cultural challenges

Veterinarians are increasingly and rightly considering vaccination to be an important elective medical procedure rather than simply a way to encourage annual client visits. Not surprisingly, a new vaccine that would have been welcomed in the past may now be met with skepticism. Some reasons, though multiple and complex, include:

Adverse events associated with vaccination.

Incomplete understanding of factors that lead to vaccine-associated sarcomas.

Recognition that effective immunization of the feline population does not require every cat to receive every vaccine antigen every year.

Increasing awareness of the shortcomings of the regulatory process.

Conflicting vaccination recommendations arising from industry and professional organizations.

Marketing strategies that create dissatisfaction among veterinarians.

- vaccines with non-core application being marketed as core
- incomplete information regarding the influence of vaccination on diagnostic tests
- misleading information regarding breadth of coverage
- manufacturers creating unrealistic expectations about the performance of the vaccine in the field
- direct-to-consumer marketing—welcome by veterinarians wishing to use the product, unwelcome by those who do not.

Confronting the challenges

A vaccine reaches the marketplace when (i) a manufacturer decides to make it, and (ii) when the USDA (in the USA) is satisfied that the product meets defined standards for efficacy, safety, purity and potency. The manufacturer need not demonstrate that the protection induced by vaccination will be clinically apparent or even relevant to an individual cat, nor that the use of the vaccine will reduce the prevalence of disease. Though usually satisfactory, this method of licensure has allowed vaccines of questionable value to reach the market. Over time, problematic vaccines tend to be withdrawn by the manufacturer, usually because veterinarians fail to purchase them. But in the meantime, much time and expense is wasted in product development, production and marketing. Plus, competing manufacturers may be reluctant to explore similar—although perhaps superior—vaccines, fearing veterinarians will fail to purchase them as well. Manufacturers do not want to risk releasing vaccines that will be rejected, so lines of communication must be strengthened to assure that high-quality, useful and necessary vaccines remain in the arsenal. Successful confrontation of these many challenges will require a strong partnership between practicing veterinarians, biologicals manufacturers and regulatory agencies.

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