How closely do results of vaccine efficacy trials reflect real-world effectiveness? For most diseases, experimental results compare favorably with what veterinarians experience in practice. As examples, efficacy tests of FPV vaccines indicate that vaccine-induced immunity is sufficient to completely protect most cats against challenge exposure. Similarly, tests of the efficacy of FHV-1 and FCV vaccines demonstrate protection from serious disease in most vaccinated cats. Both of these results parallel the experience of most practitioners. However, many variables influence a cat's response to vaccination, so efficacy trials may not tell users how vaccination will affect a specific animal or population of animals.

Purity—Pure cultures of an infectious agent ("master seed stocks") are used to produce a vaccine. An extensive array of tests are conducted to be as certain as possible that the organism in these cultures is indeed the intended agent and that no adventitious agents are present. The cells used in establishing and manufacturing the master seeds ("master cell stocks") undergo similar stringent testing to ensure that they have been correctly identified and are themselves free of contamination. Once a manufacturer has established a master cell or master seed stock, the USDA performs its own confirmatory testing; if results are acceptable, the USDA releases the master stock for use by the manufacturer. To produce a vaccine, the manufacturer then creates working cells and seeds from the master stocks, which subsequently are frozen and stored in liquid nitrogen.

Although purity testing is extensive, it is not without potential error. Contaminants that are closely related to the intended infectious agent are occasionally missed, and adventitious agents that are present at levels below the threshold of detection may not be identified. This is particularly important if an adventitious agent is pathogenic—a major risk associated with manufacturing of MLV vaccines. Improvements in test methodologies have made creation of master stocks more difficult but also more precise, and have allowed detection of contaminates missed by previous testing methods.

Potency—Potency testing determines the quantity of antigen in a vaccine. Potency and efficacy are closely related, but there are important differences. Potency is usually an in vitro assessment made during the manufacturing process, whereas efficacy is an in vivo assessment of how a vaccine performs in animals. The USDA must approve all potency test procedures, and requires that the manufacturer demonstrate a correlation between potency test results and vaccine efficacy. Each batch of vaccine manufactured is tested for potency, and once the potency exceeds a predetermined limit, the vaccine can be sold.

One factor that makes in vitro potency testing attractive is that prior to use of potency testing, each batch of vaccine had to be tested for efficacy—an expensive requirement that cost the lives of many thousands of animals. Unfortunately, the correlation between potency and efficacy is not always strong. First, potency tests are usually comparisons between production batches of vaccine and a reference vaccine. Because of the way reference vaccines are made and approved, subsequent reference vaccines may contain more antigen mass than previous batches, with a resulting upward shift in the potency of manufactured vaccines. Increased potency may raise safety concerns. Second, vaccines of unequal efficacy may receive equivalent potency tests results. For instance, although a heated or frozen vaccine may maintain potency, its efficacy may be compromised. Third, potency tests tend to ignore the role that an adjuvant plays in vaccine efficacy. As an example, a vaccine adjuvant may be adversely affected by storage, yet potency test results may remain unaffected. For these reasons, potency test results parallel efficacy only under the limited set of conditions under which they were originally approved.

Safety—Vaccine safety is demonstrated by monitoring vaccinates for clinically significant problems. Both laboratory safety data (eg, reversion-to-virulence studies, evaluation for local or systemic reactions, and shedding of live vaccine antigens) and field safety data must be generated. A standard field safety test must include a number of animals vaccinated at various geographic locations, usually multiple veterinary practices. Historically the requisite number of test animals has been relatively small (no fewer than 300 animals), but recently the number has been increased, with 1000 animals now being the common standard. In most instances, test animals are vaccinated by a veterinarian and observed for a brief period, usually 30 minutes. The owners are then instructed to monitor the animals at home and to report any unusual signs to the veterinarian. Other vaccines or medications are often administered simultaneously with the test vaccine, a practice that often complicates data analysis, but which more accurately reflects the way the product will be used.

Safety testing of this nature is likely to demonstrate problems that occur with considerable frequency during the immediate post-vaccination period; it is less likely to reveal rare or subtle vaccine problems, or those that occur a long time after vaccination. Therefore, safety testing should be considered exclusionary. In other words, if safety problems are encountered during the test period, then the vaccine will probably be unsafe in practice as well. But having successfully completed safety tests does not necessarily ensure that a vaccine will be completely safe—or even adequately safe—in a clinical setting. Safety is never absolute; rather, it is a subjective balance between frequency and severity of adverse events on the one hand and the benefits of disease reduction or prevention on the other.

Vaccine Labels

The set of rules under which a vaccine was developed influences the amount and type of information included on the label. When comparing vaccines, it is important to understand how the information presented on the label was obtained.