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Alternative Means for FDA Approval of Pet Care Drugs – Part 2: Extended Conditional Approval

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This update is the second in a multi-part series exploring FDA approval of pet care drugs.

In this article, we look at how Expanded Conditional FDA Approval has the potential to incentivize drug development and provide veterinarians with legally-marketed new animal drugs to treat serious or life-threatening diseases or conditions and to fill treatment gaps where currently no therapies are available.

In part one of our series about alternative means for FDA approval of pet care drugs, we discussed that before an animal drug product can be legally marketed for use in animals, a New Animal Drug Application (NADA) for the drug must be approved by the FDA. If the proposed drug product meets certain qualifications, the FDA may provide a company with the option of seeking conditional approval of the drug.

In 2018, to incentivize development of new animal drugs for serious or life-threatening conditions or unmet animal health needs, Congress enacted legislation reauthorizing FDA's animal drug user fee program for an additional five years. This legislation also amended section 571 of the Federal Food Drug, and Cosmetic Act (FFDCA) to include provisions for expanded conditional approval of new animal drugs. Eligibility for conditional approval has been expanded beyond minor uses in major species and use in minor species (MUMS) to also include certain major uses in major species.

Conditional approval, including approval under the new expanded pathway, allows an animal drug sponsor to legally market its product after demonstrating that the drug is safe and manufactured in accordance with full approval standards, and that there is a reasonable expectation of effectiveness for use. The initial conditional approval is valid for one year with the potential for four annual renewals. During this time, the animal drug sponsor must demonstrate that it is actively working toward collecting the remaining efficacy data needed to achieve full approval. The animal drug sponsor must attain full approval within five years after receiving conditional approval, otherwise the conditional approval will be terminated.

To be eligible for expanded conditional approval, section 571 of the FFDCA requires that the non-MUMS drug meets two criteria:

1. The drug is intended to treat a serious or life-threatening disease or

condition OR addresses an unmet animal health need; AND

2. A demonstration of efficacy would require a complex or particularly difficult study or studies.

Additionally, the conditional approval pathway cannot be used for transgenic animals, meaning an animal whose genome contains a nucleotide sequence that has been intentionally modified in vitro. The Act further states that drugs containing an antimicrobial active ingredient are not eligible for expanded conditional approval.

The FDA provides these definitions to help clarify the eligibility criteria and application process for extended conditional approval:

Serious or life-threatening disease or condition: FDA interprets "serious or life-threatening disease or condition" to mean a disease or condition that is associated with morbidity that has substantial impact on day-to-day functioning or is associated with mortality in the target animal. Short-lived and self-limiting morbidity will usually not be sufficient unless the disease or condition is persistent or recurrent. Whether a disease or condition is serious is a matter of clinical judgment, based on its impact on such factors as survival, day-to-day functioning, or the likelihood that the disease, if left untreated, will progress from a less severe condition to a more serious one. A disease or condition may be considered serious based on the magnitude of its effect on the target animals that would receive the drug, its potential to affect humans if they were to contract the disease or condition from an affected target animal, or its potential to adversely impact the food supply.

The following are considered serious or life-threatening diseases or conditions:

- A disease or condition associated with mortality or morbidity that has substantial impact on day-to-day functioning in the target animal; or
- A disease or condition in animals that is zoonotic (infections that are shared between animals and people) and that presents a risk of a serious or life-threatening disease or condition to human beings, whether it also presents a risk of harm to the target animal receiving the drug; or
- A disease or condition that causes widespread morbidity in food-producing animals that presents a risk of regional or national disruption to food production, even if the effect of the disease or condition on an individual-animal basis is minor.

Unmet animal health need: FDA interprets "unmet animal or human health need" to mean a disease or condition whose treatment, control, or prevention is not adequately addressed by available therapy. This is a disease or condition that affects individual or defined groups of animals or humans, or a condition that more broadly affects animal or human health (e.g., antimicrobial resistance).

For this guidance, a disease or condition is one for which treatment, control, or prevention is "not adequately addressed" by available therapy

when: 1) available therapy does not exist for the same intended use proposed for the drug, or 2) available therapy does exist for the same intended use but the drug for which expanded conditional approval is sought is reasonably expected to provide a meaningful advantage over available therapy.

Complex or particularly difficult study or studies: Center for Veterinary Medicine (CVM) intends to determine whether a study or studies is complex or particularly difficult on a case-by-case basis by considering the extent to which one or more of the following factors apply to demonstrating substantial evidence of effectiveness:

- The nature of the disease or condition makes it unusually time consuming or difficult to enroll enough eligible animals to provide substantial evidence of effectiveness.
- The demonstration of effectiveness is unusually difficult or complex due to logistical challenges, such as needing an unusually large number of animals in the study or studies or the need for use of advanced or complicated tests.
- It is necessary to develop and qualify effectiveness endpoints (e.g., clinical endpoints, biomarkers) to conduct the study or studies.
- It is necessary to develop and validate or qualify novel methods to adequately evaluate effectiveness outcomes (e.g., complex animal models, technologies, or diagnostic tests).
- The endpoint being evaluated is a delay in progression of a chronically progressive disease or condition where evaluation of effectiveness for an individual animal will likely take an extended period (typically a year or more). CVM intends to take into consideration the frequency and complexity (including logistical or technical difficulty) of monitoring the disease or condition during the study when considering this factor.
- There is a need to evaluate the treatment of a disease or condition over an extended period of drug administration where evaluation of effectiveness for an individual animal will likely take an extended period (typically a year or more). CVM intends to take into consideration the frequency and complexity (including logistical or technical difficulty) of monitoring the disease or condition during the study when considering this factor.
- The drug will be indicated for mitigating transmission of a zoonotic disease from animals to humans and it and it is necessary to conduct a study(ies) to evaluate the human aspect of effectiveness.

In our third and final installment of this series, we will seek to define and understand the difference between major and minor species when seeking approval for new pet care drugs.
