#191

Changes to Approved NADAs — New NADAs vs. Category II Supplemental NADAs

Guidance for Industry

This version of the guidance replaces the version made available February 2020. This revision reorganizes Appendix III for better clarity.

Submit comments on this guidance at any time. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number FDA-2008-D-0614.

For further information regarding this document, contact AskCVM@fda.hhs.gov.

Additional copies of this guidance document may be requested from the Policy and Regulations Staff (HFV-6), Center for Veterinary Medicine, Food and Drug Administration, 7500 Standish Place, Rockville MD 20855, and may be viewed on the Internet at either https://www.fda.gov/animal-veterinary or https://www.regulations.gov.

U.S. Department of Health and Human Services
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Table of Contents

Changes to Approved NADAs — New NADAs vs. Category II Supplemental NADAs

Guidance for Industry

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible for this guidance as listed on the title page.

I. Introduction

This guidance is intended to assist sponsors who wish to apply for approval of changes to approved new animal drugs that require FDA to reevaluate safety and/or effectiveness data. The guidance explains how the Office of New Animal Drug Evaluation (ONADE) categorizes possible changes to approved new animal drugs that require reevaluation of safety and/or effectiveness data and explains which administrative vehicle — a new original new animal drug application (new NADA) or a Category II supplemental application to the original new animal drug application (Category II supplemental NADA) — a sponsor should use when applying for approval of these changes.[1] The goal of this guidance is to create greater consistency in how such applications are handled by sponsors and by ONADE.

The recommendations in this guidance do not apply to changes to intentional genomic alterations in animals, regardless of whether they are heritable or non-heritable (e.g., gene therapies). For inquiries regarding such products, please contact AskCVM@fda.hhs.gov.

In general, FDA's guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. Background

In the past, applications for changes to approved new animal drugs may have been handled inconsistently by sponsors and the Agency. For example, in some instances, a sponsor may have

[1] This guidance does not apply to applications for *conditional approvals* under section 571 of the Federal Food, Drug, and Cosmetic Act (FFDCA).

filed an application for a specific change as a new NADA; in other instances, an application for a similar change was filed as a supplemental NADA. Inconsistency in handling such applications has been confusing for sponsors and for ONADE, particularly when reviewing and referencing the history of specific NADAs. This guidance is intended to improve consistency in the way applications for changes are handled. For these reasons, we believe that consistent handling of these types of applications also will help maintain clarity in the administrative record, which is an important part of protecting the public health.

For purposes of this guidance, a *new animal drug* is defined as any drug intended for use for animals other than humans, the composition of which is such that such drug is not generally recognized as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling of the drug (21 U.S.C. § 321(v); 21 CFR 510.3(g)(1)). A new animal drug as referenced in this document consists of the final dosage form. Before a new NADA can be approved by FDA, the submitted study data, which are reviewed by the Agency, must demonstrate that the new animal drug is safe and effective for use (21 U.S.C. § 360b(d)(1); 21 CFR 514.1(b)(8)).

When proposing a change to an approved new animal drug that may affect the safety and/or effectiveness of the drug, such changes generally must be submitted to FDA either as a new NADA or a supplemental application to the original NADA. Category II supplemental NADAs are the type of supplement that is used to propose changes that may require a reevaluation of certain safety or effectiveness data in the parent application. Specific changes meeting the requirements for a Category II supplemental NADA are described in 21 CFR 514.106(b)(2). This guidance provides examples and makes specific recommendations about when a change to an approved NADA that requires FDA to review safety and/or effectiveness data should be submitted as a new NADA and when such a change should be submitted as a Category II supplemental NADA. In addition, the guidance addresses how to handle submissions relating to certain types of proposed changes at the investigational stage.

Other guidances are relevant to this discussion. For example, CVM's guidance for industry (GFI) #82, "Development of Supplemental Applications for Approved New Animal Drugs,"[2] provides limited guidance on how to determine when changes to approved new animal drugs should be submitted as a Category I or Category II supplemental NADA (based on 21 CFR 514.106) or as a new NADA. GFI #82 primarily outlines the general information that should be included in each technical section when submitting a supplemental NADA. CVM GFI #83, "Chemistry, Manufacturing and Controls Changes to an Approved NADA or ANADA,"[3] also may be of interest.

This guidance makes recommendations that apply only to changes to approved new animal drugs that require the review of safety and/or effectiveness data. This guidance expands upon CVM's GFI #82 and more clearly defines which changes in approved new animal drugs will result in a new NADA or a Category II supplemental NADA. Furthermore, this guidance also addresses

[2] https://www.fda.gov/media/70308/download

[3] https://www.fda.gov/media/70323/download

appropriate submissions at the investigational stage. The recommendations in this guidance apply to any study (e.g., dose characterization, dose confirmation, target animal safety, palatability, residue, toxicology) submitted to FDA to fulfill effectiveness and/or safety technical sections for new animal drugs. Except for some noted exceptions, the recommendations generally are similar to those in CVM's GFI #82.[4]

Specifically, this guidance and its appendices discuss the following:

- When to submit an individual change to an approved NADA as a new NADA or as a Category II supplement to the original application, assuming nothing else about the new animal drug product is changed.
- Whether multiple concurrent changes to an approved NADA should be submitted as one or separate applications, and whether each of these applications should be a new NADA or a Category II supplemental NADA.
- How to handle submissions at the investigational stages of development (i.e., submissions to investigational new animal drug files (INADs)) relating to proposed changes in approved new animal drugs.
- Definitions for various dosage forms and routes of administration for new animal drugs, as well as information about the target animal classes of major food animals.

III. Definitions

For purposes of this guidance, the following definitions apply:

Active Pharmaceutical Ingredient (API) is the substance or mixture of substances in a drug product that is intended to furnish the direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease or to affect the structure or any function of the body. For the purposes of this document, the terms *active ingredient* and *API* are considered synonymous.

Dosage form is the pharmaceutical product type, or physical form, of an API as produced or given to the animal (Appendix I). A **new dosage form** contains the same API as included in an existing new animal drug previously approved by FDA but as a different pharmaceutical product type (see GFI #74, "Stability Testing of New Veterinary Dosage Forms," International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products [VICH] GL4[5]). Dosage forms are distinct from routes of administration (Appendix II).

[4] The recommendations in this guidance are consistent with the guidance *Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees*, issued by FDA's Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER), which addresses how sponsors should handle differences in human drugs and biologics when submitting an original application and when wishing to make changes to an approved product. (https://www.fda.gov/media/72397/download

[5] https://www.fda.gov/media/70255/download

A **new animal drug** is defined, in part, as any drug intended for use for animals other than man, the composition of which is such that such drug is not generally recognized as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling of the drug (21 U.S.C § 321(v); 21 CFR 510.3(g)(1)). All such drugs are called *new* animal drugs. A new animal drug as referenced in this document consists of the final dosage form.

In addition, we note that:

A **Category I supplemental NADA** ordinarily does not require a reevaluation of any of the safety or effectiveness data in the parent application (21 CFR 514.106(b)(1)).[6]

A **Category II supplemental NADA** may require a reevaluation of certain safety or effectiveness data in the parent application (21 CFR 514.106(b)(2)).

IV. New NADA or Category II Supplemental NADA – Which is Best?

In the following sections, we discuss when you should submit a new NADA and when you should submit a Category II supplemental NADA if you are requesting changes to an approved new animal drug that require review of safety and/or effectiveness data. We also discuss how to handle these types of changes at the investigational stage (i.e., INAD submissions). In addition, with regard to requests for multiple concurrent changes to an approved new animal drug, we offer examples to help determine whether such changes should be submitted as a single application or multiple applications, and how to handle these requests at the investigational stage. Before discussing specific cases, we note the following important considerations:

1. When you submit a new NADA or Category II supplemental NADA, you must own or have a *right of reference*[7] to the data that support the application. If a sponsor does not own or have a right of reference to data supporting an application, CVM will find the application to be deficient or incomplete. If you transfer ownership or lose the right of reference, you should consider the possible effect on pending, and future, submissions and applications. If you withdraw an approved NADA, you may no longer reference the data in that application (21 CFR 514.115(d)).
2. The sponsor's decision about whether to file a new NADA versus a Category II supplemental NADA ordinarily will not alter CVM's decisions as to what specific safety and/or effectiveness data will be needed to support the approval of an application.

Table 1 summarizes whether a new NADA or a Category II supplemental NADA would be appropriate for specific changes to an approved new animal drug that require review of safety and/or effectiveness data. The subsequent sections of this document provide details on handling each specific change.

[6] Because this guidance is only intended to address changes to approved new animal drugs that would generally require FDA to reevaluate safety and/or effectiveness data in the parent application, Category I supplemental NADAs are outside the scope of this guidance.

[7] 21 CFR 514.1(a)

Table 1. Summary of when to file a new NADA or a Category II supplemental NADA.

Proposed Change to Your Approved New Animal Drug	Submit as New NADA	Submit as Cat. II Supplemental NADA	Contact ONADE for Recommendations
New API	Yes	No	No
New Dosage Form	Yes	No	No
Variation of Previously Approved Dosage Form	No	Yes	No
New Major Route of Administration	Yes	No	No
Variation of Previously Approved Major Route of Administration	No	Yes	No
Add Target Animal	No	Yes	No
Add/Change Dose	No	Yes	No
Change Dosing Schedule	No	Yes	No
Add Indications	No	Yes	No
Change Rx/OTC/VFD Status	No	Yes	No
Replace, Add, Delete, or Change Concentration of Inactive Ingredient	No	No	Yes
Change Concentration of Active Ingredients	No	No	Yes
Multiple Changes	No	No	Yes

A. New Active Pharmaceutical Ingredient (API) — Submit as New NADA

If you are submitting a change that will create a new active pharmaceutical ingredient (API), we recommend you submit a new NADA. As noted previously, a *new animal drug* is any drug intended for use for animals other than man, the composition of which is such that such drug is not generally recognized as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling of the drug (21 U.S.C § 321(v); 21 CFR 510.3(g)(1)). Changes to the API drug molecule, as well as a change to the salt, ester, or enantiomer/racemic mixture of an existing API drug molecule, are considered to be a change in the API, which is a

basis for the "newness" of an animal drug (21 CFR 510.3(i)(1)). In such cases, a new NADA should be submitted, not a Category II supplemental NADA.[8, 9]

Similarly, a new combination of two or more active ingredients for use in animals should be submitted as a new NADA, not a Category II supplemental NADA.

During the investigational phase of development, sponsors of new animal drugs should establish separate investigational new animal drug files (INADs) for new animal drugs containing different APIs.

B. New Dosage Form — Submit as New NADA

New dosage forms of the same API typically result in delivery of the drug by a different route of administration or a different delivery system, which is another basis for the "newness" of an animal drug (21 CFR 510.3(i)(6)). Thus, your application for a different dosage form of an API for which you have already received approval for use in animals should be submitted as a new NADA, not a Category II supplemental NADA. Although a Category II supplemental NADA does provide for a "change in the…composition of the final product" and a "change in the treatment regimen (schedule of dosing)" (21 CFR 514.106(b)(2)(i) and (iv), respectively), CVM considers these situations to pertain to changes in composition that ***do not*** alter the dosage form of the new animal drug.

Special considerations may be appropriate for new animal drugs approved as medicated articles and feeds (21 CFR part 558). An application may be submitted for a new physical form of a Type A medicated article (e.g., liquid formulation versus dry formulation). If it is determined that the new physical form and inactive ingredient composition do not significantly affect the safety and effectiveness of the API (similar to some changes in inactive ingredients in other new animal drugs as described in section IV. I. *Replacing, Adding, Deleting, or Changing Concentrations of Inactive Ingredients*), the application should be submitted as a Category II supplemental NADA. However, if changes in the physical form and inactive ingredient composition significantly affect safety and/or effectiveness of the API compared to the previously approved Type A medicated article, the application should be submitted as a new NADA, not a Category II supplemental NADA (see section IV. I. *Replacing, Adding, Deleting, or Changing Concentrations of Inactive Ingredients*). Consult with ONADE to determine whether the application should be submitted as a new NADA or a Category II supplemental NADA. It may be necessary for CVM to review safety and effectiveness information relevant to

[8] In its October 17, 1990, policy letter regarding the implementation of the Generic Animal Drug and Patent Term Restoration Act (GADPTRA), CVM stated that a product that contains a different salt or ester form of the same drug in the finished new animal drug product is considered to contain a different active ingredient.

[9] CVM GFI #185 (VICH GL43), "Target Animal Safety for Veterinary Pharmaceutical Products" (https://www.fda.gov/media/70438/download), indicates: "Margin of safety studies are generally required for new salts or formulations of an API. Exceptions should be justified, for example, on the basis of known toxicology and target animal safety profiles for the API, widespread clinical use of existing products, and/or where the systemic or local exposure (as applicable) of the new product is proven to be equivalent to or less than that of the existing product."

the proposed change during the investigational (INAD) process to determine the appropriate administrative vehicle.

Applications for new free choice or liquid Medicated Type B and C feeds (21 CFR 510.455 and 21 CFR 558.5) derived from the same approved Type A Medicated Article should be submitted as Category II supplemental NADAs to the affected Type A Medicated Article NADA.

To improve clarity of the administrative record, sponsors of new animal drugs containing the same API should establish a separate INAD for each dosage form of the new animal drug.

Appendix I provides the names and definitions of dosage forms of currently approved new animal drugs (21 CFR parts 520, 522, 524, 526, 529, and 558), including medicated articles and feeds. Dosage forms are distinguished from routes of administration (Appendix II, see below). In general, if you intend to add a dosage form or change the dosage form of your approved API to any other dosage form listed in the far-left column of the table in Appendix I, the application should be submitted as an NADA. There are *variations* of specific dosage forms (second column), such as *Bolus* and *Tablet, Coated* within *Tablet, Compressed*. If you intend to add or change from one variation to another within the same dosage form of an approved API (e.g., from capsule to coated capsule), the application should be submitted as a Category II supplemental NADA.

Appendix I is not intended to include all possible dosage forms of new animal drugs. Contact ONADE[10] on how to handle applications for dosage forms not listed.

C. New Major Route of Administration — Submit as New NADA

CVM considers adding or changing to a different major route of administration to be a change to "the newness of a … method … of administration or application…" (21 CFR 510.3(i)(6)). Thus, your application for approval of a different major route of administration for a new animal drug for which you have previously received approval should be submitted as a new NADA, not a Category II supplemental NADA.

To improve clarity of the administrative record, sponsors of a new animal drug should establish separate INADs for different major routes of administration of the drug product.

Appendix II describes some major routes of administration for new animal drugs. In general, if you intend to add or change a major route of administration of your approved new animal drug to any other major route of administration specified in Appendix II, you should submit the application as a new NADA. There are variations within some major routes of administration, such as *Intramuscular* and *Subcutaneous* within *Injection*. An application to add or change a variation within a major route of administration of a new animal drug for which you have already received approval within that major route should be submitted as a Category II supplemental NADA, not a new NADA.

[10] Typically, you should contact the reviewer assigned to the approved new animal drug and/or that reviewer's Team Leader from the Target Animal Division in ONADE, i.e., the Division of Therapeutic Drugs for Non-Food Animals, Division of Production Drugs, or the Division of Therapeutic Drugs for Food Animals.

Appendix II is not intended to include all routes of administration for new animal drugs. Contact ONADE on how to handle applications for routes of administration of new animal drugs not listed.

D. Adding Target Animals — Submit as a Category II Supplemental NADA

The regulations regarding Category II supplemental applications provide for the addition of a new species (21 CFR 514.106(b)(2)(vii)), i.e., the animals for which the new animal drug is approved, or the "target animals." Thus, your application for approval of the use of a new animal drug in a new target animal should be submitted as a Category II supplemental NADA, not a new NADA.

Sponsors should consult with ONADE as to whether it would increase administrative clarity to establish separate INADs for each target animal being investigated for treatment with a specific new animal drug. General recommendations are as follows:

- Major food animals

CVM provides terms and definitions for major food-producing animals in Appendix III (a copy of Appendix III is also available at https://www.fda.gov/animal-veterinary/new-animal-drug-applications/classes-major-food-producing-animals-new-animal-drug-applications, specifically for cattle, swine, chickens, and turkeys. You should contact the applicable Target Animal Division to determine when separate INADs are appropriate for different subclasses, or subclass variants,[11] of major food animals. For example, if a new animal drug is being investigated for use only in specific subclasses or subclass variants of a major food animal, it may be appropriate to establish separate INADs for each subclass or subclass variant. If the new animal drug is being investigated for use in all subclasses of a major food animal (e.g., beef cattle), an INAD established for the major food animal, but not subclass or subclass variant within the major food animal, may be adequate.

- Companion animals

Classes or breeds of companion animals generally are not distinguished in new animal drug indications. Thus, unless a new animal drug is intended for use in a specific class (e.g., kitten versus mature cat) or breed of companion animal, separate INADs for each species (e.g., cat, dog, horse), but not class or breed within species, should be adequate.

- Minor species

In general, a separate INAD should be established for each minor species of animals being investigated for treatment with a specific new animal drug. For aquaculture, it is recommended

[11] CVM uses the term "class" to refer to a species of animal (e.g., cattle). A class may have a further delineated "subclass", a category generally defined by the physiologic status or production purpose of the animals (e.g., beef steers vs. beef heifers). A subclass may be further delineated (i.e., a "variant") by a production purpose or animal husbandry/management practice (e.g., growing beef steers in dry lot/grow yard).

that separate INADs be established for finfish, crustaceans, and mollusks. Separate life stages, including eggs, may be included within a single INAD.

E. Adding or Changing Doses — Submit as a Category II Supplemental NADA

As provided for in 21 CFR 514.106(b)(2)(iii), your application for approval of the use of a new animal drug at a dose different from your previous approval should be submitted as a Category II supplemental NADA, not a new NADA. A single INAD may also be used for different doses of the same new animal drug product intended for use in the same target animal for the same indication.

F. Changing Dosing Schedule — Submit as a Category II Supplemental NADA

Your application for approval of the use of a new animal drug with a dosing schedule different from your previous approval should be submitted as a Category II supplemental NADA, as provided for in 21 CFR 514.106(b)(2)(iv), not a new NADA.

Examples of changing the dosing schedule include the following:

- Original approval was for giving 2 tablets a day, 12 hours apart; change would allow 2 tablets to be given once a day at the same time.
- Original approval was for an injectable sustained release suspension to be given every 14 days; change would allow injections every 10 days.
- Original approval was for the drug to be given for a limited amount of time, such as the first 7 days postsurgery; change would allow the drug to be given for the life of the animal.

Consult with ONADE as to whether it would increase administrative clarity to establish separate INADs for different dosing schedules of a specific new animal drug.

G. Adding Indications — Submit as a Category II Supplemental NADA

The Category II supplemental application regulations provide for additions of therapeutic and production claims (21 CFR 514.106(b)(2)(v) and (vi)). Thus, your application for approval of the use of a new animal drug for additional indications should be submitted as a Category II supplemental NADA, not a new NADA.

To increase administrative clarity for both CVM reviewers and new animal drug sponsors, sponsors should at least establish a separate INAD for therapeutic indications in food animals, a separate INAD for therapeutic indications in nonfood animals, and a separate INAD for animal production indications. Contact ONADE for indications handled within the same Target Animal Division to determine which indications may be included in the same INAD and which should be in separate INADs.

H. Changing (Rx, OTC, VFD) Status — Submit as a Category II Supplemental NADA

Category II supplemental applications include changes from prescription (Rx) or over-the-counter (OTC) status (21 CFR 514.106(b)(2)(viii)). Thus, your application for approval of such a change in the status of your previously approved new animal drug should be submitted as a Category II supplemental NADA, not a new NADA.

This recommendation also applies to change in status of Veterinary Feed Directives (VFD) to OTC or OTC to VFD for medicated articles/feeds.

I. Replacing, Adding, Deleting, or Changing Concentrations of Inactive Ingredients

Replacing, adding, deleting, or changing the concentration of inactive ingredients from that found in an approved new animal drug may result in a new animal drug composition that is not generally recognized as safe and effective. Such a change may be considered a new animal drug (21 U.S.C. § 321(v); 21 CFR 510.3(g)(1)). However, the Category II supplemental application regulations also provide for changes in "composition of the final product" and changes in "quality, purity, strength, and identity specifications of the active or inactive ingredients" (21 CFR 514.106(b)(2)(i) and (ii)). Furthermore, these regulations provide for changes in active ingredient concentration (21 CFR 514.106(b)(2)(i)), which will usually occur with a concurrent change in the concentration of inactive ingredients (see section IV.J. *Changing Concentrations of Active Ingredients*). Therefore, as discussed below, the nature of the changes to the inactive ingredient composition of a new animal drug product will determine whether it is submitted as a new NADA or a Category II supplemental application.

CVM recognizes that many changes to the inactive ingredient composition of a new animal drug product do not significantly affect the safety and effectiveness of the API. In such situations, a new NADA would not be warranted. For example, the deletion or reduction of an ingredient intended to affect only the color of a product can be reported in an annual report (21 CFR 514.8(b)(4)(ii)(B)).[12] In some situations, additional safety and/or effectiveness data may need to be submitted to CVM for a new formulation. For these types of changes to the inactive ingredient composition that require review of safety and/or effectiveness data due to such changes in drug delivery and/or distribution of the API, an application should be submitted as a Category II supplemental NADA.

However, some changes in inactive ingredient composition of a previously approved new animal drug may significantly affect the safety and/or effectiveness of the formulation compared to the previously approved formulation. In such situations, your application for an API formulation in which inactive ingredients have been replaced, added, deleted, or their concentration changed from the new animal drug for which they have already received approval should be submitted as a new NADA, not a Category II supplemental NADA.

[12] Additionally, changes consistent with GFI #83 may be submitted as Category I or Category II supplemental NADAs.

Because of the potential difficulty in determining the significance of replacing, adding, deleting, or changing the concentration of inactive ingredients of your previously approved new animal drug, consult with ONADE to determine whether the application should be submitted as a new NADA, a Category II supplemental NADA, or another appropriate administrative vehicle.[13] The reason for the proposed change may be considered during the review process. It may be necessary for CVM to review safety and effectiveness information relevant to the proposed change during the investigational (INAD) process to determine whether the application should be a new NADA, Category II supplemental NADA, or another appropriate administrative vehicle (see e.g., 21 CFR 514.8).

Consult with ONADE to determine whether separate INADs should be established for APIs with different inactive ingredient compositions. During the early stages of development of a new animal drug formulation, it may be acceptable to use one INAD until a specific formulation is selected for further investigation.

J. Changing Concentrations of Active Ingredients

The Category II supplemental application regulations provide for changes in active ingredient concentration in addition to changes in the composition of the final product (21 CFR 514.106(b)(2)(i)). A change in the concentration of an active ingredient is necessarily accompanied by a change in the concentration of one or more inactive ingredients, and/or by a change to the ratio of active ingredients if two or more active ingredients are used in the formulation. These secondary changes may or may not significantly affect the function of the API or the safety and/or effectiveness of the new formulation compared to the previously-approved formulation. Therefore, the nature and degree to which the proposed changes to the *inactive ingredients* affect the function of the API(s) or safety of the new formulation should be used to determine whether an application to change the active ingredient concentration should be submitted as a new NADA or a Category II supplemental NADA. Refer to section IV.I. *Replacing, Adding, Deleting, or Changing Concentrations of Inactive Ingredients* for guidance.

Sponsors should consult with ONADE to determine whether separate INADs should be established for new animal drug formulations with different concentrations of active ingredients.

K. Multiple Changes

You can request multiple concurrent changes to an approved new animal drug. For changes that require FDA to reevaluate safety and/or effectiveness data, ONADE will consider whether the requested changes are *related* to each other and, therefore, should be submitted in a single application (new NADA or Category II supplemental NADA). If the concurrent requested changes are not related to each other and could be filed individually as *stand-alone* submissions, they should be submitted as separate applications (new NADA(s) and/or Category II supplemental NADA(s)). The decision as to whether an application should be submitted as a

[13] For example, as a category I supplemental NADA or in an annual report.

new NADA or Category II supplemental NADA should be based on how the ***specific*** changes within the application are usually handled if submitted individually.

In deciding whether multiple requested changes to an approved new animal drug should be submitted in a single or multiple application(s), ONADE will consider the relationship between the proposed changes, e.g., whether one change is necessary to allow the other change. If the proposed changes are unrelated (i.e., one change is not necessary to allow approval of the other change), separate safety and/or effectiveness data sets typically will be needed for each change, and each change should usually be submitted in separate applications. For example:

> **Example 1.** In this example, assume a sponsor requests to expand usage of their approved new animal drug in an additional target animal for the same indication, and the safe and effective dose for the additional target animal is different from the dose originally approved for the first target animal. In this case, the request is for two concurrent changes from the original approval: a new target animal and a new dose for that target animal. These requests are related and cannot stand alone because a new dose is necessary to gain approval in the new target animal, and the same safety and effectiveness data set will support the two concurrent changes. Thus, the request for these two related changes from the original approval (target animal and dose for that target animal) should be submitted in the same application.
>
> **Example 2.** In this example, assume a sponsor requests approval of a new dosage form of their approved new animal drug and that the new dosage form has different inactive ingredients and is safe and effective at a different dose of the API than the approved dosage form. In this case, the request is for three changes from the original approval: a new dosage form, changes in inactive ingredients, and a new dose. These requests are related and cannot stand alone because a new dose and different inactive ingredients are necessary to gain approval of the new dosage form, and the same safety and effectiveness data set will support the three concurrent changes. Thus, the sponsor's request for these three related changes from the original approval (dosage form, inactive ingredients, and dose) should be submitted in the same application.
>
> **Example 3.** In this example, assume a sponsor wishes to expand the approved dose range for an already approved product (original dosage form) as well as gain approval of a new dosage form of the API (with changes in inactive ingredients and dose necessary to allow approval of the new dosage form). In this scenario, the request for the change in dose range for the original dosage form is unrelated to, and can stand alone from, the request for a new dosage form (and associated changes in inactive ingredients and dose). Separate safety and/or effectiveness data sets would be necessary to gain approval of the expanded dose range for the original dosage form versus the new dosage form. Thus, the request for the expanded dose range for the original dosage form should be submitted in a separate application from the request for approval of the new dosage form (and associated changes in inactive ingredients and dose).
>
> **Example 4**. In this example, assume a sponsor has an approved new animal drug to treat a specific disease in dogs. The sponsor wishes to expand the approved dose range for

dogs, as well as gain approval of use of the drug to treat the same disease in cats. The requested change in the dog approval is unrelated to, and can stand alone from, the request for the cat approval. Separate safety and effectiveness data sets would be necessary to gain approval of the expanded dose range for dogs versus gaining approval for use in cats. Thus, the request for expanding the approved dose range for dogs should be submitted in a separate application from the request for approval in cats.

Example 5. In this example, assume a sponsor who has an approved new animal drug for increased rate of weight gain in growing beef steers and heifers on pasture (stocker, feeder, and slaughter) wishes to add an indication of increased carcass leanness in growing beef steers and heifers on pasture (stocker, feeder, and slaughter) plus gain approval of the increased rate of weight gain and carcass leanness indications in growing beef steers and heifers fed in confinement for slaughter. The requested change for growing beef steers and heifers on pasture (stocker, feeder, and slaughter) is unrelated to, and can stand alone from, the request for approval in growing beef steers and heifers fed in confinement for slaughter. The requested new indication for growing beef steers and heifers on pasture (stocker, feeder, and slaughter) would require separate safety and/or effectiveness data from the request for growing beef steers and heifers fed in confinement for slaughter. Thus, the request for adding the carcass leanness indication for growing beef steers and heifers on pasture (stocker, feeder, and slaughter) should be submitted in a separate application from the request for approval of the increased rate of weight gain and carcass leanness indications in growing beef steers and heifers fed in confinement.

Once a determination is made as to whether multiple proposed changes may be submitted as one or separate applications, contact ONADE if you need help deciding whether each application should be submitted as a new NADA or a Category II supplemental NADA. In general, if any one of the changes proposed within an application could, on its own, be submitted as a new NADA, the application should be submitted as a new NADA, not a supplemental NADA. In summary, using the previous examples:

Example 1. A request to approve a new animal drug for use in an additional target animal at a different dose than for the original approval should be submitted as a single Category II supplemental NADA.

Example 2. A request to approve a new dosage form of a new animal drug with necessary changes in inactive ingredients and dose from the approved dosage form should be submitted as a single new NADA.

Example 3. A request for additional doses of an approved dosage form should be submitted as a Category II supplement to the original NADA, whereas the request for the new dosage form should be submitted as a new NADA.

Example 4. The request to expand the approved dose range for an approved new animal drug in dogs should be submitted as a Category II supplement to the original NADA; the request to gain approval of use of the drug to treat the same disease in cats should be submitted as a separate Category II supplemental NADA.

Example 5. The request to add a production indication in growing beef steers and heifers on pasture (stocker, feeder, and slaughter) should be submitted as a Category II supplement to the original NADA; the request for production indications in growing beef steers and heifers fed in confinement for slaughter should be submitted as a separate Category II supplemental NADA.

An exception may apply for multiple requested changes such as described in Examples 4 and 5 where:

1) Essentially the same product applies to each request (i.e., same API, dosage form, and route of administration, and no differences in inactive ingredient composition that significantly alter the safety and effectiveness of the new animal drug);
2) All safety, effectiveness, and chemistry, manufacturing and control information for each request has been reviewed under one or more INADs;
3) Technical section complete letters have been issued by ONADE for each of these technical sections for each request under one or more INADs;
4) All requests would be reviewed by the same Target Animal Division in ONADE; and
5) You plan to submit an administrative NADA (or administrative Category II supplemental NADA, if appropriate).[14]

If these criteria are met, you may be able to submit multiple requests as one administrative NADA or one administrative Category II supplemental NADA. Consult with ONADE if you believe your requests meet these criteria and you wish to submit your requests as one administrative NADA or one administrative Category II supplemental NADA.

You should also consult with ONADE as to whether it would increase administrative clarity to establish one or more separate INAD(s) for investigation of multiple proposed changes to an approved new animal drug. In general, changes that should be submitted as a new NADA should be investigated under a separate INAD.

V. Conclusions

By applying the recommendations in this guidance, we believe that applications for changes to approved new animal drugs will be handled in a more consistent manner. This in turn will improve the clarity of the administrative record for new animal drug applications. You are encouraged to contact ONADE with any further questions regarding the most appropriate administrative vehicle for proposed changes to approved new animal drugs.

[14] See CVM GFI #132, "Administrative Applications and the Phased Review Process" (https://www.fda.gov/media/70029/download).

Appendix I. Examples of Dosage Forms of New Animal Drugs

DOSAGE FORM [1]	VARIATIONS [2]	DEFINITION
Block	none	A solid dosage form usually in the shape of a square or rectangle that animals consume voluntarily; but not a Type C Medicated Feed.
Capsule	Capsule	A dosage form in which the drug is enclosed within either a hard or soft soluble container or shell made from a suitable form of gelatin.
Capsule	Capsule, Coated	A capsule with an additional designated coating.
Cream	none	A semisolid dosage form where the drug is dissolved or dispersed in a base, usually consisting of emulsions of oil and water, where water is the main ingredient.
Culture	none	Microorganisms or living tissue cells in special media conducive to their growth.
Emulsion	none	A liquid dosage form with a two-phase system in which one liquid is dispersed throughout another liquid in the form of small droplets.
Gel	none	A semisolid dosage form consisting of either suspensions made up of small inorganic particles or large organic molecules interpenetrated by a liquid; usually water-based and thickened without oil or fat.
Liquid	none	A liquid dosage form consisting of a pure neat chemical in its liquid state (an intermediate state entered as matter goes from solid to gas). Do not use this term to describe solutions.
Ointment	none	A semisolid dosage form, usually consisting of emulsions of oil and water, where oil is the main ingredient; intended for topical application.
Packing	none	A solid dosage form consisting of a material, covered by or impregnated with a drug, that is inserted into a body cavity or between the tooth enamel and the gingival margin.
Particulates	Crumbles	A solid dosage form consisting of small irregularly shaped fragments or particles; but not a Type C Medicated Feed.
Particulates	Granule	A solid dosage form consisting of particles or grains smaller and more uniform than crumbles; but not a Type C Medicated Feed.

DOSAGE FORM [1]	VARIATIONS [2]	DEFINITION
Paste	none	A semisolid dosage form that is a fatty, viscous, or mucilaginous base, or a mixture of starch and petrolatum.
Pellet	none	A solid dosage form in a small mass consisting of highly purified drug with or without excipients, made by compression, molding, and/or extrusion; but not a Type C Medicated Feed.
Powder	none	A solid dosage form consisting of an intimate mixture of dry, finely divided drugs and/or chemicals.
Powder, Aerosol	none	A powder product packaged under pressure and released upon activation of an appropriate valve system.
Solid Matrix	none	A solid dosage form in a special shape (e.g., ring, cylinder, cartridge, etc.) and embedded with the drug. It is typically placed in a body cavity or under the skin, where the medication is released for localized or systemic effects.
Solution	Solution	A liquid dosage form in which the drug is dissolved in a solvent or mixture of mutually miscible solvents; but not a Type C Medicated Feed.
Solution	Solution, Concentrate	A solution in which the concentration of drug is increased by the evaporation of nonactive ingredients. The concentrated solution is diluted with appropriate vehicles before the drug is administered.
Solution	Powder, for Solution	A powder product, which upon the addition of suitable vehicles, yields a solution.
Sponge	none	A solid dosage form in which the drug is embedded in an absorbent pad of natural or synthetic materials.
Spray	none	A liquid dosage form in which the drug is minutely dispersed by a jet of air or steam.
Spray, Aerosol	none	A spray which utilizes a compressed gas as the propellant to provide the force necessary to expel the product as a wet spray.
Suspension	Suspension	A liquid dosage form that consists of solid particles dispersed throughout a liquid phase, in which the particles are not soluble.
Suspension	Suspension, Concentrate	A suspension in which the concentration of drug is increased by the evaporation of nonactive ingredients. The concentrated suspension is diluted with appropriate vehicles before the drug is administered.

DOSAGE FORM [1]	**VARIATIONS** [2]	**DEFINITION**
Suspension	Powder, for Suspension	A powder product, which upon the addition of suitable vehicles, yields a suspension.
Suspension, Extended Release	none	A suspension formulated to allow a reduction in dosing frequency.
Syrup	none	A liquid dosage form consisting of a solution with high concentrations of sucrose or other sugars.
Tablet, Compressed	Tablet	A solid dosage form containing a mixture of the drug and diluents that are granulated and compressed.
Tablet, Compressed	Bolus	A large tablet.
Tablet, Compressed	Tablet, Coated	A tablet that is covered with a designated coating.
Tablet, Compressed	Tablet, Flavored	A tablet that contains compounds intended to improve palatability.
Tablet, Extruded	none	A tablet that is formulated by extrusion and typically is intended to be chewable.
Tablet, Effervescent	none	A tablet that contains mixtures of acids (e.g., citric acid, tartaric acid) and sodium bicarbonate, which release carbon dioxide when dissolved in water; it is intended to be dissolved or dispersed in water before administration.
Tablet, Sustained Release	Tablet, Sustained Release	A tablet formulated to allow continued release of the drug over time.
Tablet, Sustained Release	Bolus, Sustained Release	A bolus formulated to allow continued release of the drug over time.
Medicated Article/Feed [3]	Type A Medicated Article	Intended solely for use in the manufacture of another Type A Medicated Article or a Type B or Type C Medicated Feed. It consists of a new animal drug(s), with or without carrier (e.g., calcium carbonate, rice hull, corn, gluten) with or without inactive ingredients, as defined in 21 CFR 558.3(b)(2).
Medicated Article/Feed [3]	Type B Medicated Feed	Intended solely for the manufacture of other Medicated Feeds (Type B or Type C). It contains a substantial quantity of nutrients including vitamins and/or minerals and/or other nutritional ingredients in an amount not less than 25 percent of the weight. It is manufactured by diluting a Type A Medicated Article or another Type B Medicated Feed, and meets the additional requirements defined in 21 CFR 558.3(b)(3).

DOSAGE FORM [1]	VARIATIONS [2]	DEFINITION
Medicated Article/Feed [3]	Type C Medicated Feed	Intended as the complete feed for the animal or may be fed *top dressed* (added on top of usual ration) on or offered *free-choice* (e.g., supplement) in conjunction with other animal feed. It contains a substantial quantity of nutrients including vitamins, minerals, and/or other nutritional ingredients. It is manufactured by diluting a Type A Medicated Article or a Type B Medicated Feed. A Type C Medicated Feed may be further diluted to produce another Type C Medicated Feed, as defined in 21 CFR 558.3(b)(4). A dosage form that meets this definition may be considered a Type C Medicated Feed even if it is provided in the physical form of blocks, crumbles, granules, pellets, or other dosage forms described above.

[1] When changing from one dosage form to another in this column, the application should be submitted as a new NADA.

[2] When changing from one variation to another within the same dosage form of an approved new animal drug, the application should generally be submitted as a Category II supplemental NADA.

[3] See section IV.B. *New Dosage Form — Submit as New NADA* regarding Medicated Articles/Feeds.

Appendix II. Examples of Routes of Administration for New Animal Drugs

MAJOR ROUTE [1]	DESCRIPTION	VARIATIONS [2]	CFR REFERENCE
Oral	Through the mouth.	Oral: into the mouth or pharynx and swallowed. In Feed: by application in, on, or with feed. In Drinking Water: by dissolving or diluting in drinking water. By Intubation: by tube inserted through the mouth or nose into the gastrointestinal tract.	21 CFR 558 (Animal Feeds); 21 CFR 520 (Oral)
Injection	Placing a non-formed (liquid or semisolid) drug product into a tissue or body cavity through a needle.	Intramuscular: in a muscle. Intravenous: in a vein. Subcutaneous: directly under the skin. Intraarterial: in an artery. Intraarticular: in a joint. Intraperitoneal: in the peritoneal cavity. Intradermal: in the dermis of the skin. Intraruminal: in the rumen. Subconjunctival: under the conjunctiva.	21 CFR 522
Implantation	Placing a formed (solid) drug product into a tissue or body cavity.	none	21 CFR 522
Topical	Directly to a particular area of the external body surface; affects only the area to which it is applied (in contrast to *transdermal*); includes otic administration.	none	21 CFR 524
Transdermal	On or into the skin resulting in a systemic action (in contrast to *topical*).	none	21 CFR 524
Transmucosal, Oral	Across the oral mucous membrane resulting in systemic action.	none	21 CFR 529

MAJOR ROUTE [1]	**DESCRIPTION**	**VARIATIONS** [2]	**CFR REFERENCE**
Intramammary	Into the mammary gland, including mammary infusion into a quarter through the teat canal.	none	21 CFR 526
Nasal	Into or through the nose, localized to the nasal passages.	none	21 CFR 529
Inhalant	Through the respiratory system.	none	21 CFR 529
Ophthalmic	To the eye.	none	21 CFR 524
Rectal	Into the rectum.	none	21 CFR 529
Intravaginal	Into the vagina.	none	21 CFR 529
Intrauterine	Into the uterus.	none	21 CFR 529
Aquatic Exposure	Immersion therapy administered to aquatic animals via bath treatment (exposure).	External-Systemic: absorbed through the skin, gills, etc., and intended action is systemic. External-Topical: direct contact with the external surfaces of skin, gills, etc., and intended action is local.	21 CFR 529
In ovo	Into a fertilized egg (poultry) after laid by the female.	none	none
Egg Dip	Submerged and/or coated with the drug.	none	21 CFR 529

[1] When changing from one major route of administration to another in this column, the application should be submitted as a new NADA.

[2] When changing from one variation to another within the same major route of administration of an approved new animal drug, the application should generally be submitted as a Category II supplemental NADA.

Appendix III. Target Animal Classes of Major Food Animals

CVM has posted these tables on our website for easy access by users (https://www.fda.gov/animal-veterinary/new-animal-drug-applications/classes-major-food-producing-animals-new-animal-drug-applications).

Please note that the labeling for some approved animal drugs includes "legacy terms" that have been used since before FDA established the terminology in these tables; therefore, the tables do not encompass all terminology for all classes of major food-producing animals.

Cattle

There are three major subclasses of cattle: veal calves, beef cattle, and dairy cattle.

Veal Calves

Veal calves are typically dairy breeds of immature male or female cattle that are raised to produce meat (veal) for human consumption. Most are pre-ruminating; but, depending on management, age, and diet, they may be ruminating.

The following subclass of veal calves may be used to further define this major subclass:

Subclass	Definition
Bob Veal	Veal calves less than 2 weeks of age and pre-ruminating.

Beef Cattle

Beef cattle are defined as cattle that are raised primarily to produce meat (either beef or dairy breeds) for human consumption or to produce offspring (beef breeds) that will produce meat intended for human consumption.

The following subclasses of beef cattle may be used to further define this major subclass:

A. Beef Calves

Beef cattle (beef breeds only) nursing their dams from birth until weaning. May be pre-ruminating or ruminating. Formerly referred to as "suckling beef calves." *Excludes veal calves*.

The following variants of beef calves may be used to further define this subclass:

Variant	Definition
Beef Calves less than 2 months of age	Beef calves considered pre-ruminating and nursing their dams from birth until 2 months of age.
Beef Calves 2 months of age and older	Beef calves considered ruminating and nursing their dams from 2 months of age to weaning.

B. Beef Steers

Weaned castrated male cattle (beef and dairy breeds) intended for slaughter, housed in any setting and receiving their diet from any source(s).

The following variants and subsets of variants of beef steers may be used to further define this subclass:

Variant	Subset	Definition
Growing Beef Steers on Pasture (stocker, feeder, and slaughter)	No subsets	Weaned growing beef steers (beef and dairy breeds) maintained on pasture and receiving the majority of their diet from grazing. Refers to cattle considered to be "*stocker, feeder, and slaughter*" cattle, and these words are always included in the parenthetical portion of the class name. "*Stocker*" refers to weaned growing cattle grazing pasture prior to finishing and slaughter; they are usually younger, weigh less, and are of lower condition (finish) than "*feeder*" cattle. *"Feeder"* refers to weaned growing cattle grazing pasture and of sufficient weight and maturity to be placed on high-energy rations for finishing; they are generally older, weigh more, and carry more condition (finish) than "*stocker*" cattle. *"Slaughter"* refers to weaned growing cattle grazing pasture and suitable for slaughter.
Growing Beef Steers in a Dry Lot	No subsets	Weaned growing beef steers (beef and dairy breeds) maintained in a dry lot. They receive the majority of their diet from harvested forage (possibly with a supplement).
Growing Beef Steers Fed in Confinement for Slaughter	Includes all subsets	Weaned growing and finishing beef steers (beef and dairy breeds) intended only for slaughter and confined in group pens and fed a progressively high-energy diet *ad libitum* as their sole ration until slaughter. May also be referred to as feed yard or feedlot cattle in the industry. *Includes growing beef steers in a grow yard (see definition below).*
Growing Beef Steers Fed in Confinement for Slaughter	**Growing Beef Steers in a Grow Yard**	A subset population of growing beef steers fed in confinement for slaughter, these are weaned growing beef steers (beef and dairy breeds) confined in group pens and fed a moderate- to high-roughage diet *ad libitum* as their sole ration prior to the finishing stage. Grow yards may also be referred to as starter yards or backgrounding yards in the industry.

C. Beef Heifers

Weaned female beef cattle intended for breeding (beef breeds) or slaughter (beef and dairy breeds) that have not yet calved, housed in any setting and receiving their diet from any source(s).

The following variants and subsets of variants of beef heifers may be used to further define this subclass:

Variant	Subset	Definition
Replacement Beef Heifers	Includes all subsets	Weaned female beef heifers (beef breeds only) that are intended only for breeding to produce calves for meat production. If reproductive safety is not evaluated, an age restriction of less than 1 year will apply.
Replacement Beef Heifers	**Replacement Beef Heifers on Pasture**	Weaned replacement beef heifers maintained on pasture and receiving the majority of their diet from grazing. If reproductive safety is not evaluated, an age restriction of less than 1 year will apply.
Growing Beef Heifers on Pasture (stocker, feeder, and slaughter)	No subsets	Weaned growing beef heifers (beef and dairy breeds) intended only for slaughter (i.e., not for reproductive purposes) maintained on pasture and receiving the majority of their diet from grazing. Refers to cattle considered to be "*stocker, feeder, and slaughter*" cattle, and these words are always included in the parenthetical portion of the class name. "*Stocker*" refers to weaned growing cattle grazing pasture prior to finishing and slaughter; they are usually younger, weigh less, and are of lower condition (finish) than "*feeder*" cattle. *"Feeder"* refers to weaned growing cattle grazing pasture and of sufficient weight and maturity to be placed on high-energy rations for finishing; they are generally older, weigh more, and carry more condition (finish) than "*stocker*" cattle. *"Slaughter"* refers to weaned growing cattle grazing pasture and suitable for slaughter.
Growing Beef Heifers in a Dry Lot	No subsets	Weaned growing beef heifers (beef and dairy breeds) maintained in a dry lot. They receive the majority of their diet from harvested forage (possibly with a supplement).
Growing Beef Heifers Fed in Confinement for Slaughter	Includes all subsets	Weaned growing and finishing beef heifers (beef and dairy breeds) intended only for slaughter (i.e., not for reproductive purposes) and confined in group pens and fed a progressively high-energy diet *ad libitum* as their sole ration until slaughter. May also be referred to as feed yard or feedlot cattle in the industry. *Includes growing beef heifers in a grow yard (see definition below).*
Growing Beef Heifers Fed in Confinement for Slaughter	**Growing Beef Heifers in a Grow Yard**	A subset population of growing beef heifers fed in confinement for slaughter, these are weaned growing beef heifers (beef and dairy breeds) confined in group pens and fed a moderate- to high-roughage diet *ad libitum* as their sole ration prior to the finishing stage.

Variant	Subset	Definition
		Grow yards may also be referred to as starter yards or backgrounding yards in the industry.

D. Beef Bulls

Weaned intact male beef cattle intended for breeding (beef breeds) or slaughter (beef and dairy breeds), housed in any setting and receiving their diet from any source(s).

The following variants of beef bulls may be used to further define this subclass:

Variant	Definition
Beef Bulls Intended for Breeding	Weaned intact male beef bulls (beef breeds only) intended only for breeding. If reproductive safety is not evaluated, an age restriction of less than one year will apply.
Beef Bulls Intended for Slaughter	Weaned intact male beef cattle intended only for slaughter (beef and dairy breeds).

E. Beef Cows

Beef breed female cattle that have calved.

Dairy Cattle

Dairy cattle are defined as cattle that are raised primarily to produce milk for human consumption and/or to produce offspring that will produce milk or meat (including veal) for human consumption.

The following subclasses of dairy cattle may be used to further define this major subclass:

A. Dairy Calves

Pre-ruminating dairy cattle from birth until weaning being fed a ration that includes milk or liquid milk replacer. *Excludes veal calves.*

B. Replacement Dairy Heifers

Weaned female dairy cattle that have not yet calved and are intended only for breeding and future milk production, housed in any setting and receiving their diet from any source(s). If reproductive safety is not evaluated, an age restriction of less than 1 year will apply.

The following variants of replacement dairy heifers may be used to further define this subclass:

Variant	Definition
Periparturient Replacement Dairy Heifers	Replacement dairy heifers approximately 3 weeks before calving. After calving they become periparturient dairy cows.
Replacement Dairy Heifers on Pasture	Weaned replacement dairy heifers maintained on pasture and receiving the majority of their diet from grazing.

C. Dairy Bulls

Weaned intact male dairy cattle intended for breeding. If reproductive safety is not evaluated, an age restriction of less than 1 year will apply.

D. Dairy Cows

Female dairy cattle that have calved.

The following variants of dairy cows may be used to further define this subclass:

Variant	Definition
Lactating Dairy Cows	Dairy cows that are producing milk for human food.
Dry Dairy Cows	Dairy cows that have previously lactated, but which are not currently producing milk for human food (i.e., dairy cows between two lactations).
Periparturient Dairy Cows	Dairy cows that have previously lactated, and are in the transition period from approximately 3 weeks before to approximately 3 weeks after calving.

Swine

Swine are defined as animals of the *Sus* genus, either *Sus scrofa domesticus* or *Sus domesticus*, that are raised primarily to produce meat for human consumption or to produce offspring that will produce meat for human consumption.

The following subclasses of swine may be used to further define this class:

A. Nursing Piglets

Swine from birth until weaning. May be referred to as weanling pigs, baby pigs, or suckling piglets in the industry.

B. Nursery Swine

Swine intended for slaughter, from weaning to end of nursery phase at approximately 40 to 70 lbs (18 to 32 kg). May be referred to as starter pigs in the industry.

C. Growing Swine

Swine intended for slaughter, from approximately 40 to 70 lbs (18 to 32 kg) to 120 to 150 lbs (55 to 68 kg).

D. Finishing Swine

Swine intended for slaughter, from approximately 120 to 150 lbs (55 to 68 kg) to market weight.

E. Boars

Intact male swine intended for breeding or slaughter.

The following variants of boars may be used to further define this subclass:

Variant	Definition
Boars Intended for Breeding	Boars intended for breeding.
Boars Intended for Slaughter	Boars intended for slaughter, including chemically castrated males and those removed from breeding service. May also be referred to as culled boars in the industry.

F. Barrows

Surgically castrated male swine intended for slaughter.

G. Gilts

Female swine intended for breeding or slaughter that have never farrowed a litter.

The following variants of gilts may be used to further define this subclass:

Variant	Definition
Replacement Gilts	Gilts intended for breeding.
Gestating Replacement Gilts	Replacement gilts that are pregnant.
Gilts Intended for Slaughter	Gilts intended for slaughter.

H. Sows

Female swine that have farrowed.

The following variants of sows may be used to further define this subclass:

Variant	Definition
Gestating Sows	Sows that are pregnant.
Lactating Sows	Sows that are producing milk.
Weaned Sows	Sows that have farrowed and completed nursing a litter.
Sows Intended for Slaughter	Sows that have been removed from breeding service. May also be referred to as culled sows in the industry.

Chickens

Chickens are defined as animals of the subspecies *Gallus gallus domesticus* that are raised primarily to produce meat and/or eggs for human consumption or to produce offspring that will produce meat and/or eggs for human consumption.

The following subclasses of chickens may be used to further define this class:

A. Embryonated Chicken Eggs

Eggs containing a chicken embryo at any stage of embryonic development.

B. Chicks

Chickens from hatch until they are able to survive in ambient temperature (no longer brooded). This is the initial post-hatch phase of the subclasses identified in the remainder of this table.

When used on approved labeling, the term “chicks” only refers to chicks of the chicken species. If a drug product is approved for use in chicks of another species, the labeling should clearly state “(species) chicks” (e.g., quail chicks).

C. Broiler Chickens

Chickens raised from hatch, grown to a marketable weight, and intended for meat production. Includes Rock Cornish game hen or Cornish game hen, broiler or fryer, roaster or roasting chicken, and capon.

D. Replacement Chickens

Chickens raised from hatch to sexual maturity and intended to become laying hens or breeder chickens.

The following variants of replacement chickens may be used to further define this subclass:

Variant	Definition
Breeder Replacement Chickens	Male and female chickens intended to become breeder chickens.
Laying Hen Replacement Chickens	Female chickens intended to become laying hens.

E. Laying Hens

Mature female chickens that produce non-fertilized eggs for consumption.

F. Breeder Chickens

Sexually mature male and female chickens intended to produce fertilized eggs for hatching.

The following variants of breeder chickens may be used to further define this subclass:

Variant	Definition
Broiler Breeder Chickens	Chickens intended to produce fertilized eggs for hatching into broiler chickens or broiler breeder replacement chickens.
Layer Breeder Chickens	Chickens intended to produce fertilized eggs for hatching into laying hen replacement chickens or layer breeder replacement chickens.

Turkeys

Turkeys are defined as animals of the species *Meleagris gallopavo* that are commonly raised primarily to produce meat for human consumption or to produce offspring that will produce meat for human consumption.

The following subclasses of turkeys may be used to further define this class:

A. Embryonated Turkey Eggs

Eggs containing a turkey embryo at any stage of embryonic development.

B. Turkey Poults

Turkeys from hatch until they are able to survive in ambient temperature (no longer brooded). This is the initial post-hatch phase of the subclasses identified in the remainder of this table.

C. Growing Turkeys

Turkeys raised from hatch and growing to a marketable weight and intended for meat production. Includes fryer-roaster, young turkey, and yearling turkey.

D. Breeder Replacement Turkeys

Turkeys raised from hatch to sexual maturity and intended to become breeder turkeys.

E. Breeder Turkeys

Sexually mature male and female turkeys intended to produce fertilized eggs for hatching into growing turkeys or breeder replacement turkeys.