

REGISTERED MAIL
RETURN RECEIPT REQUESTED

[Address]

RE: Implementation of FDA Guidance for Industry #213

Dear [Sponsor Contact]:

We appreciate your help in making FDA's judicious use strategy successful. This letter describes a process for coordinating the timing of actions on the supplemental applications to align products with Guidance for Industry (GFI) #213¹ and transitioning to new labeling. We are contacting you because you are the sponsor of one or more New Animal Drug Application(s) (NADAs) or Abbreviated New Animal Drug Application(s) (ANADAs) affected by GFI #213 and you have indicated your intention to engage in the voluntary process outlined in GFI #213.

At the time we finalized GFI #213, we said that we anticipated sponsors would complete changes to approved applications to implement the judicious use strategy (i.e., removing production indications for use and changing marketing status from over-the-counter (OTC) to veterinary feed directive (VFD) or prescription (Rx)). In the interest of effectively communicating the timing of these changes to affected stakeholders, we have set **January 1, 2017** as the implementation date. Our goal is that by January 1, 2017, all supplemental applications (or alternatively, as may be requested, voluntary application withdrawal requests) will have been processed so that all approved affected applications are aligned with the principles outlined in GFI #209².

To ensure that a clear, consistent, and equitable process is applied to implement these changes by the January 1, 2017 target date, CVM has outlined the process in the attached Appendices. Appendix 1 outlines the administrative process for aligning the conditions of approval and labeling for (or voluntary withdrawal of) affected NADAs or ANADAs in accordance with

¹ "New Animal Drugs and New Animal Drug Combination Products Administered in or on Medicated Feed or Drinking Water of Food-Producing Animals: Recommendations for Drug Sponsors for Voluntarily Aligning Product Use Conditions with GFI #209" - <http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM299624.pdf>

² "The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals" - <http://www.fda.gov/downloads/AnimalVeterinary/GuidanceComplianceEnforcement/GuidanceforIndustry/UCM216936.pdf>

GFI #213. Appendix 2 outlines a plan for transitioning approved products to the new (GFI #213 – aligned) labeling requirements by January 1, 2017. Please note that these process documents provide an overall framework for facilitating implementation and recognize that ongoing engagement will be needed to address specific issues as they arise.

Thank you for your commitment to aligning your new animal drug applications with FDA's GFI #213. We are pleased to be able to work collaboratively with you to address this important public health issue.

Sincerely,

William T. Flynn, D.V.M., M.S.
Deputy Director for Science Policy
Office of the Center Director
Center for Veterinary Medicine

Appendices (2)

Appendix 1

Administrative Process for Aligning the Conditions of Approval of Affected NADAs/ANADAs with GFI #209 under GFI #213

To ensure our target implementation date of January 1, 2017 is met, and to ensure that a clear and consistent process is applied to align affected NADAs/ANADAs, CVM has outlined a recommended administrative process below. We believe this process will address one of the concerns voiced during the comment period for GFI #213, specifically, that this strategy is implemented in a manner that is equitable to all affected drug sponsors. In addition, this process is intended to coordinate labeling updates to related pioneer, generic, and combination drug products to minimize the potential for disruption and confusion in the marketplace.

There are two potential paths you may choose to align your affected product(s): 1) request approval of aligning changes to the labeling and request withdrawal of the portions of the application associated with the production claims (if applicable); or 2) request that the entire application be withdrawn (no longer approved). As an option, for those products remaining approved, you may additionally choose to seek approval of a new therapeutic claim.

For supplemental NADAs or ANADAs to change the marketing status from OTC to VFD or Rx and to remove production claims (if applicable):

1. **Request pre-submission conference(s) to reach agreement on a specific plan and labeling revisions needed to align the affected product(s):** If you intend to submit a supplemental application to change the marketing status of your product and to remove production claims (if applicable), please submit a separate request for a presubmission conference for each affected NADA or ANADA (STARS (A)NADA file, Z submission, PS meeting type) in order to review and agree on the future approvability of revised facsimile labeling for each product³. We recommend that you consider requesting that these meetings occur in a teleconference. In person meetings are always acceptable if you choose. Teleconferences may be more cost effective for you and will allow more flexibility in scheduling and (if needed) rescheduling.

- (a) ***Points of contact⁴: Please submit your application-specific presubmission conference requests (and any informal questions you may have) to the following divisions:***

³ If you have a portfolio of affected applications that you wish to align, you may optionally contact the Office of New Animal Drug Evaluation (ONADE) Project Management Team (NADA sponsors) or the ONADE Division of Generic Animal Drugs (ANADA sponsors) to discuss general strategy plans and questions you may have for alignment of your portfolio of affected applications. If a formal meeting is desired, please submit these requests as a STARS General Correspondence (GC) file, Z submission, PS meeting type code. Definitive labeling review will not occur at these portfolio overview meetings; CVM will review and agree on labeling revisions in the application-specific presubmission conferences.

⁴ For optional portfolio overview meetings, the point of contact for pioneer (NADA) portfolios is Aila Albrecht, Leader, ONADE Project Management Team (HFV-109) at 240-402-0625 or Aila.Albrecht@fda.hhs.gov; and the point of contact for generic (ANADA) portfolios is Sharon Ricciardo, Team Leader, ONADE Division of Generic Animal Drugs (HFV-170), at 240-402-0854 or Sharon.Ricciardo@fda.hhs.gov

- Pioneer (NADA) Type A medicated articles and water medications:
Address submissions to Cindy Burnsteel, Director, ONADE Division of Therapeutic Drugs for Food Animals (HFV-130);
Contact John Mussman at 240-402-0589 or John.Mussman@fda.hhs.gov with questions;
- Pioneer (NADA) medicated feed combinations:
Address submissions to Linda Wilmot, Director, ONADE Division of Production Drugs (HFV-120);
Contact Ashley Shaw at 240-402-0812 or Ashley.Shaw@fda.hhs.gov with questions;
- Generic (ANADA) Type A medicated articles, water medications, medicated feed combinations:
Address submissions to John (Ken) Harshman, Director, ONADE Division of Generic Animal Drugs (HFV-170);
Contact Sharon Ricciardo at 240-402-0854 or Sharon.Ricciardo@fda.hhs.gov with questions.

(b) **Timing of presubmission conference(s):** In order to meet the final implementation target date of January 1, 2017, we request that you schedule meetings as soon as possible. At minimum, they should be requested early enough so that we can review and agree on the approvability of facsimile labeling in time for you to submit your labeling supplement(s) by June 30, 2016, and have time (as applicable) to share the agreed-upon labeling with sponsors of affected ANADA products and NADA or ANADA combination medicated feed applications such that they too may submit their labeling supplements by the same date. To this end, if you are a sponsor of a product that has affected generic(s) or feed combination(s) please submit your presubmission conference request no later than March 2016.

As changes to ANADA product labeling and to NADA or ANADA combination medicated feed application labeling depend on the specific changes that will be made to the pioneer (reference listed or component product) application, if you are the sponsor of an ANADA product or NADA or ANADA combination medicated feed application, please wait to submit your product specific presubmission conference request until after CVM contacts you to advise of the needed changes.

2. Include revised labeling and any necessary supporting information in each application-specific presubmission conference request:

The goal of the presubmission conference is to 1) reach agreement that the submitted facsimile labeling—as amended, if needed—would be considered approvable in a future labeling supplement, and 2) discuss and agree on the submission timing and content of the labeling supplement for the application.

- (a) ***Draft Revised Labeling:*** Please provide us with draft revised labeling for all affected labeling components. Any of the following is acceptable for initial review: clean revised color facsimile labeling, marked up facsimile labeling, or photos/copies of final printed labeling (FPL) showing hand marked “redline” changes. For products changing to VFD status, in addition to the labels, please also include a draft new VFD labeling component (VFD template) consistent with the recently revised VFD regulation. For products that will have production claims withdrawn, please indicate in your submission which corresponding representative (Blue Bird) Type B and Type C medicated feed labels will no longer be approved (it is not necessary to include revised labeling for indications that will be withdrawn, i.e., no longer be approved).

We will review your initially submitted labeling components and, if necessary, contact you to request an amendment to provide final clean color facsimile labeling containing any necessary revisions. If desired, an informal teleconference may be scheduled at this time to discuss our comments for revision. We will review your revised labeling when the amendment is received and assess its future approvability.

The formal presubmission conference may be rescheduled as necessary such that you and CVM will be able to reach 100% agreement on the approvability of the labeling (i.e., agreement on the acceptability of the labeling for submission “as is” in your future labeling supplement). Administrative agreements and any other agenda items will also be discussed at the formal meeting. As a result of these goals, these presubmission conferences generally will be initially scheduled for a date that is beyond 30 days from submission receipt.

- (b) ***Supporting information for any additional labeling changes (other than new therapeutic claims⁵) that are beyond the scope of GFI #213:*** If you are proposing additional labeling changes that require supporting information or justification (for example, if you desire to administratively rephrase the wording of an existing therapeutic claim while remaining consistent with the intent of the original approval), please include this information in the meeting request.
- (c) ***Permission to Contact Sponsors of Generics/Combinations:*** In your meeting request, please include written permission for CVM to contact the sponsors of affected generic and combination medicated feed applications (if applicable) in advance of approval to tell them of the forthcoming supplemental application and to share with them copies of the agreed-upon (acceptable for future approval) facsimile labeling you have submitted in the meeting request or amendment. This will give us time to coordinate action with respect to any

⁵ If you are interested in discussing major changes such as addition of a new therapeutic claim or revision of a withdrawal period, please submit a separate presubmission conference request to discuss these project plans. See also below for information regarding adding a new therapeutic claim under GFI #213.

necessary corresponding changes to those generic and combination applications.

3. **CVM will document the future approvability of submitted labeling:** We will document that the labeling submitted in the meeting request (as revised in an amendment, if applicable) would be considered approvable for purposes of inclusion in your future labeling supplement. These agreements will be documented in the Presubmission Conference Agreements section of the Memorandum of Conference (MOC). The MOC will allow us to “bank” all agreements and take coordinated action on all similar products at the same time.

Within 45 days of the meeting date, CVM will transmit the MOC to you with a cover letter that reaffirms that the agreed-upon labeling is expected to support approval of the future supplemental labeling application (i.e., that a supplemental application containing such labeling would be considered approvable).

4. **Submit supplemental labeling applications:** In order to meet the final implementation target date of January 1, 2017, we request that you submit all supplemental labeling applications before June 30, 2016, according to the schedule agreed upon at the presubmission conference. This will allow us to coordinate action on all impacted applications. For workload management purposes, we generally will recommend that you submit your labeling supplement soon after the meeting is held. CVM will then review applications as they are received and in general will work toward coordinated approval dates for all similar applications over a three-day window by the end of December 2016. Our goal is to meet the January 1, 2017 implementation date.

- (a) ***Process for submitting supplemental applications:*** As agreed upon at the pre-submission conference, submit supplemental application(s) (STARS NADA or ANADA file, C submission, NF subclass code, 180 day review clock⁶) to the applicable division in ONADE (see points of contact earlier in this appendix).

In each supplement, you should include the following:

- A request to voluntarily change the marketing status from OTC to VFD (if a medicated feed)⁷ or from OTC to Rx (if a water medication);⁸ Your request should include your rationale for requesting the changes (e.g., it would be acceptable to cite your desire to align the conditions of use with the principles of judicious use described in GFI #209).

⁶ Sponsors who use eSubmitter for this process should not check yes for the question on the template that asks if they are submitting a “Qualifying Labeling Supplement” (QLS). If this option is inadvertently selected, we will change the STARS due date to 180 days when the submission is received. Generic (ANADA) sponsors will need to submit NF supplements with a 270-day review clock; however, CVM will internally work to review these submissions as though they have a 180 day review clock.

⁷ Published in 21 CFR Part 558.

⁸ Published in 21 CFR Part 520.

- A request to voluntarily withdraw approval of those portions of the NADA or ANADA pertaining to the production indications.
- An appropriate claim of categorical exclusion (CE) from the requirement to submit an Environmental Assessment (EA) and appropriate certifying statements regarding the existence of no extraordinary circumstances. (Details of this and appropriate language will be discussed with you at the presubmission conference, and you may contact ONADE at any time with questions.)
- Clean color facsimile (i.e., PDF) labeling [or final printed labeling if you choose] that is identical to the labeling agreed upon and documented in the MOC. For review efficiency and to help ensure that your supplement is approvable without amendment, we recommend that you do not introduce additional changes beyond those agreed upon in the MOC. However, if you choose to request additional changes, please describe them clearly in your cover letter.

- (b) ***Interim supplemental applications or amendments to previously submitted GFI #213 labeling supplements:*** Between the time that the presubmission conference is held and June 30, 2016, if you identify additional labeling changes you would like to make, we ask that such changes be limited as much as possible and be restricted to minor changes only. Please contact the applicable ONADE review division to discuss the best administrative path for approval of any interim changes (i.e., whether to submit a stand-alone labeling supplement, or include the changes in your future GFI #213 labeling supplement, or amend a GFI #213 labeling supplement already under review).

After June 30, 2016, we ask that sponsors refrain from submitting new stand-alone labeling supplements or amendments to GFI #213 labeling supplements under review. If amendments are made after June 30, 2016, we cannot ensure that the labeling supplements will be processed in coordination with other applications by the target dates in December 2016.

B. If you intend to submit a supplemental application to add a new therapeutic claim:

1. Follow current project development procedures (i.e., request a separate pre-submission conference and (if possible) work under the INAD or JINAD to submit applicable technical section submissions toward approval). If your existing application is not associated with an open INAD or JINAD file, you should request the pre-submission conference under the NADA or ANADA to discuss the best administrative pathway for review. Technical section considerations for new therapeutic indications are discussed in section IV.B. of GFI #213.
2. We request that you contact the assigned ONADE project manager (or the ONADE Division of Generic Drugs, as applicable) to discuss timing of the technical section submissions and the supplemental application, especially if you want to coordinate

the timing of the review of the new therapeutic claim with the other GFI #213 related changes. If you wish to seek approval prior to the timed approval of GFI #213 related supplements in December 2016, CVM will need to consider the implications of the product in question on related generics and/or combination drug approvals. Conversely, as you may know from experience, new claim development often requires significant time and may require generation of new data. If you are interested in pursuing a new therapeutic claim but do not foresee completing all necessary technical sections in time for approval near December 2016, please contact CVM as soon as possible to discuss your plans and options under GFI #213.

3. Once all applicable technical sections are complete or likely to be complete, you should submit your request to approve a new therapeutic indication as a separate supplemental application (STARS C submission, B1 subclass code). In some cases, new indications and GFI #213 alignment changes may be approved in the same supplement. If this may apply to your plans, please discuss best administrative practices (submission content and statements, etc.) with the applicable division in ONADE before submitting your supplement.
4. Given the timing constraints associated with such “B1” supplements, we request that you submit a meeting request to discuss your proposed new indication as soon as possible to help maximize time for project development, submission and review of the supporting information, and coordination of the approval as appropriate.

C. If you choose to withdraw the entire NADA or ANADA:

1. We encourage you to contact the Center for Veterinary Medicine (CVM), Office of Surveillance and Compliance (OS&C), Division of Surveillance, HFV-212, to discuss the process for requesting voluntary withdrawal of approved applications (vWOA) before you submit your request. You can reach the CVM’s OS&C, Division of Surveillance, HFV-212, by contacting Sujaya Dessai at 240-402-5761 or Sujaya.Dessai@fda.hhs.gov.
2. If you are a sponsor of a product that has affected generic(s) or feed combination(s): At the time you contact CVM, OS&C, Division of Surveillance about the process for submitting a vWOA (or if you do not contact HFV-212 first, at the time you submit the vWOA), we request that you submit written permission for us to contact the sponsors of the affected generic(s) and/or feed combination(s) to tell them of the forthcoming vWOA.
3. We encourage you to submit a vWOA as soon as possible. However, to meet the final implementation target date of January 1, 2017, we request that you submit all requests for a vWOA no later than June 30, 2016. Please note: we will process vWOAs as quickly as possible once they are received. We do not intend to coordinate the processing of these requests to provide for a common effective date.

D. If you choose to request a waiver of any applicable user fees:

CVM intends to grant fee waivers provided the application (e.g., supplemental application to add a new indication or application for a new combination use) in question is appropriately linked to the implementation of GFI #213.

Consistent with the normal process for requesting waivers of fees, we ask that sponsors direct requests for such fee waivers to our ADUFA Waiver Officer.

ADUFA Waiver Officer
Office of New Animal Drug Evaluation, HFV-100
7500 Standish Place
Rockville, MD 20855

Such requests would most appropriately be submitted subsequent to the pre-submission conference in which agreement is reached on the overall plan for aligning the affected product in question with GFI #213. Including a reference to this agreement in your fee waiver request would help support the linkage of the application in question to the GFI #213 initiative. In addition, if all GFI #213 changes are not implemented concurrently with or prior to the approval of the applications for which the fee waiver is requested, it is important that fee waiver request include written commitment to implement such changes by the January 1, 2017 deadline.

Appendix 2

Plan for Transitioning to New (GFI #213 – aligned) Labeling by January 1, 2017

CVM's primary goal is that on January 1, 2017, all affected products are being used in the market in accordance with the principles outlined in GFIs #209 and #213. This means that such products will no longer be used for production (growth promotion/feed efficiency) purposes and will only be used with the prior authorization of a licensed veterinarian.

We appreciate the cooperation that you (affected sponsors) have demonstrated in helping to successfully implement this important initiative. We acknowledge the large number of products that are affected by these changes and the complex nature of the task to effectively transition product inventories to the new (GFI #213-aligned) labeling. We believe that by working collaboratively with you, and utilizing several strategies described below, this transition can be accomplished in a manner that is orderly, that limits industry impact, and avoids supply chain disruption or loss of product inventory.

Given the planned nature of this initiative, we expect that you will consider strategies for proactively managing product inventories in an effort to effectively transition to new labeling by the target deadline. We believe there are number of steps that you can take as we progress towards the January 1, 2017 implementation date to facilitate the transition to new labeling. We have outlined below the key time periods leading up to January 1, 2017, and have outlined a number of actions you may consider to manage product inventories and facilitate transition to new labeling by the target deadline.

To discuss issues related to transitioning to new labeling, please contact Neal Bataller, OS&C Division of Surveillance (HFV-210), at 240-402-5745 or Neal.Bataller@fda.hhs.gov.

A. Between now and June 30, 2016

Transitional labeling: You may consider notifying your customers (product users) of the changes expected to take effect on January 1, 2017. Between now and the time that we reach agreement on new GFI #213-aligned labeling for specific products (target deadline of June 30, 2016), we acknowledge that you may find it necessary to label additional inventory of affected product. In such cases, we would not object if information about the expected changes were provided with the existing product labeling and/or information was printed on or affixed to the product labeling in a manner that does not obscure any existing information. If such “transitional labeling” is used, we would expect such labeling to include language that is consistent with the following statements:

Statement that applies to feed products: Beginning January 1, 2017, this product will require a veterinary feed directive issued by a licensed veterinarian and will be subject to the following restriction:

"Caution: Federal law restricts medicated feed containing this veterinary feed directive (VFD) drug to use by or on the order of a licensed veterinarian." ⁹

Statement that applies to water products: Beginning January 1, 2017, this product will require a prescription issued by a licensed veterinarian and will be subject to the following restriction:

"Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian." ¹⁰

Statement that applies to all products with production indications: Effective January 1, 2017, this product will no longer be approved for [insert all production indications as they appear on labeling] which means the use of this product for that [/these] purpose[s] will no longer be legal.

As noted in Appendix 1, we expect all agreements on new labeling to be in place and labeling supplements submitted by June 30, 2016, the targeted deadline. Therefore, after June 30, 2016, we ask sponsors to use discretion in deciding whether to continue to apply “transitional labeling” to new product inventory. It would be desirable to begin labeling new product inventory with the new GFI #213-aligned labeling, provided such inventory is not expected to enter the marketplace until after January 1, 2017. However, if the inventory is expected to enter marketplace before January 1, 2017, it would be preferable to label such inventory with “transitional labeling”.

Given the unique circumstances and the temporary nature of this “transitional labeling”, we would not object to sponsors immediately labeling affected product with the above information. In addition, although we do not expect a supplemental application to be submitted for this transitional labeling, we do ask that sponsors submit a copy of such labeling to the appropriate DER file.

B. Between June 30, 2016 and January 1, 2017

As outlined under the administrative process above, agreements regarding the new GFI #213-aligned labeling for specific products will be documented in the MOC for the pre-submission conference and labeling supplements should be submitted by June 30, 2016. In addition, the acceptability of such labeling for supporting approval of the associated supplemental application (to be submitted at a later date) will be affirmed by letter to the drug sponsor.

As noted above, the primary goal is to target implementation of the new labeling on January 1, 2017. However, we understand that inventory supplies can’t always be accurately predicted. Therefore, once this agreement is in place, we would not object if you began labeling product inventory within your control with the new agreed-upon labeling language prior to approval of the supplemental application. Applying the new

⁹ 21 CFR Sec. 558.6 (a) (6)

¹⁰ 21 CFR Sec. 201.105 (a)(2)

labeling to product could be accomplished by affixing the new labeling language to existing product labeling utilizing stickers and/or the generation of new printed labeling. CVM would not expect agreed-upon new labeling to enter the market prior to June 30, 2016 and would prefer that none of the newly-labeled product to enter the market prior to January 1, 2017. However, CVM understands that it may be necessary for a limited amount of the newly-labeled product to enter the market prior to January 1, 2017 and would not object to this.

It is our expectation that you will ensure that product inventory that is still within your control (after agreement on new labeling) is appropriately re-labeled by January 1, 2017. If stickers are used, please ensure that such stickers are affixed to the product before it is distributed to the end user.

For medicated feed products, updated Blue Bird labels would also need to be generated. We would consider it helpful if you would make available advance copies of the updated Blue Bird labels for feed manufacturers. The availability of updated Blue Bird labels is critical so that feed manufacturers are prepared to implement the changes by January 1, 2017.

While we would not object to new labeling entering the market between June 30, 2016 and January 1, 2017, you should consider that a product labeled with new VFD drug labeling (restricting medicated feed containing the VFD drug to use by or on the order of a licensed veterinarian) will not include a “transitional statement” indicating the implementation begins January 1, 2017. A veterinary feed directive is not required to be issued by a licensed veterinarian for new products transitioning to VFD until January 1, 2017. We believe that a strategy for proactively managing product inventories will ensure an orderly transition and limit labeling entering the market that may be confusing to the veterinarians and feed manufacturers using the product prior to January 1, 2017.

C. After January 1, 2017

As noted above, our primary goal is that on January 1, 2017, all affected products are being used in the market in accordance with the principles outlined in GFIs #209 and #213. This means that feed manufacturers discontinue use of old Blue Bird labels and begin labeling medicated feeds with the new GFI #213-aligned Blue Bird labels.

Our expectation is that after January 1, 2017, product in distribution channels (i.e., no longer in the sponsor’s control) either is 1) labeled with “new” final printed label, 2) has a sticker affixed to the product that includes the “new” final label language, or 3) is labeled with “transitional label” statement(s).

Recognizing the complexity and scale of this effort, CVM intends to exercise as much flexibility as possible in relation to this transition period. However, we ask that affected drug sponsors exercise due diligence to transition to the new labeling in an expedient manner.