Finding of No Significant Impact (FONSI)
in support of an approval of a supplemental new animal drug application (NADA)
for
SYNOVEX® ONE GROWER
(trenbolone acetate and estradiol benzoate)
in
growing beef steers and heifers in a dry lot
for
increased rate of weight gain for up to 200 days

Zoetis Inc
Kalamazoo, MI

The Center for Veterinary Medicine (CVM) has considered the potential environmental impact of this action and has concluded that this action will not have a significant impact on the quality of the human environment and, therefore, an environmental impact statement will not be prepared.

Zoetis Inc is requesting the supplemental approval of a new animal drug application (NADA) for the use of SYNOVEX® ONE GROWER (trenbolone acetate and estradiol benzoate) as a single implant for increased rate of weight gain for up to 200 days in growing beef steers and heifers in a dry lot. SYNOVEX® ONE GROWER is administered by subcutaneous implantation in the middle-third of the ear and contains a total of 150 mg trenbolone acetate and 21 mg estradiol benzoate in six coated (extended-release) pellets. This product is dispensed over the counter.

In support of the application, Zoetis Inc has provided an environmental assessment (EA) titled, "Environmental Assessment for the Use of SYNOVEX® ONE Grower Implants in Growing Beef Steers and Heifers in a Dry Lot." A copy of the EA is attached. CVM provided guidance to and assisted Zoetis Inc by outlining the types of environmental information required for inclusion in the EA. CVM independently evaluated the EA to ensure the scope and content were adequate and to ensure that the information presented in the EA was accurate. CVM determined that the EA provides sufficient evidence to support a finding of no significant impact (FONSI).

The EA evaluates the potential for environmental impacts from the use of SYNOVEX® ONE GROWER as a single implant in growing beef steers and heifers in a dry lot through a comparison to the environmental risk analyses conducted as part of the EA prepared for the December 19, 2024, supplemental NADA for the use of SYNOVEX Choice® and SYNOVEX® PRIMER™ as single implants in growing beef steers and heifers on pasture (stocker, breeder, and slaughter)[1] (hereafter, referred to as the 2024 Pasture EA).[2]

[1] Hereafter, growing beef steers and heifers on pasture (stocker, feeder, and slaughter) may be simply referred to as pasture cattle.
[2] The 2024 Pasture Environmental Assessment (EA) is titled, "Environmental Assessment for Use of SYNOVEX® PRIMER™ and SYNOVEX Choice® Implants in Beef Steers and Heifers on Pasture (Stocker, Feeder, and Slaughter)." A copy of the EA may be obtained from the United States Food and Drug Administration's (FDA) Animal Drugs @ FDA website: https://animaldrugsatfda.fda.gov/adafda/views/#/environmentalAssessments

Summary of the 2024 Pasture EA

The 2024 Pasture EA conservatively evaluates the potential for significant environmental impacts to occur from the exposure of freshwater fish, the most sensitive non-target species, to the six major metabolites of trenbolone acetate and estradiol benzoate found in cattle manure (i.e., 17α-trenbolone, 17β-trenbolone, trendione, and 17α-estradiol, 17β-estradiol, and estrone, respectively) via a surrogate compound approach (i.e., a trenbolone surrogate compound and an estradiol surrogate compound). The 2024 Pasture EA includes an exposure and effects assessment and a risk characterization. The 2024 Pasture EA follows a similar risk assessment approach and uses many of the same assumptions as that described in the EA prepared for the July 31, 2014, original NADA of SYNOVEX® ONE FEEDLOT and SYNOVEX® ONE GROWER.[3,4]

In brief, the 2024 Pasture EA evaluated the potential aggregate environmental exposure of the surrogate trenbolone and estradiol compounds from the use of currently approved SYNOVEX® implants. Because SYNOVEX® implants are currently approved for use in growing beef steers and heifers fed in confinement for slaughter (feedlot cattle), growing beef steers and heifers in a dry lot (dry lot cattle), and growing beef steers and heifers on pasture (stocker, feeder, and slaughter) (pasture cattle), three exposure scenarios were modeled: (1) runoff from small and medium animal feeding operations (AFO) surfaces (feedlot scenario), (2) runoff from manure amended cropland and cropland irrigated with liquid manure (cropland scenario), and (3) runoff from manure excreted directly onto pastureland (pasture scenario). The predicted environmental concentrations in surface water (PEC_{sw}) values were estimated assuming that all three exposure routes occurred at the same time (i.e., the PEC_{sw} values for each exposure route were added together as an aggregate exposure). Because the proposed action subject to the 2024 Pasture EA was to allow for the use of SYNOVEX Choice® (100 mg trenbolone acetate and 14 mg estradiol benzoate) and SYNOVEX® PRIMER™ (50 mg trenbolone acetate and 7 mg estradiol benzoate) in pasture cattle, the pasture scenario conservatively assumed cattle were treated with the higher dose implant, SYNOVEX Choice®. To estimate the proportion of the surrogate trenbolone and estradiol compounds entering the environment from the feedlot and cropland scenarios, the 2024 Pasture EA assumed that several currently approved SYNOVEX® implants, including the higher dose implants (e.g., SYNOVEX® ONE FEEDLOT and SYNOVEX PLUS® (200 mg trenbolone acetate and 28 mg estradiol benzoate)) and those approved for use in reimplantation programs, were administered to feedlot cattle. The PEC_{sw} values were then divided by the predicted no effects concentration (PNEC) values established for the most sensitive non-target species (i.e., fish) for 17α-trenbolone, 17β-trenbolone, 17α-estradiol, and 17β-estradiol to estimate risk quotient (RQ) values. All of the RQ values estimated as part of the 2024 Pasture EA were <1.0, indicating no significant environmental impacts were expected, and a FONSI was prepared (dated November 13, 2024).

[3] SYNOVEX® ONE GROWER was previously known as SYNOVEX® ONE GRASS.
[4] The environmental assessment (EA) prepared for the July 31, 2014, original new animal drug application (NADA) of SYNOVEX® ONE FEEDLOT and SYNOVEX® ONE GROWER is titled, "Environmental Assessment for SYNOVEX® ONE (Estradiol Benzoate and Trenbolone Acetate Extended Release Implant) Feedlot and Grass for Beef Steers and Heifers." A copy of the EA may be obtained from the United States Food and Drug Administration's (FDA) Animal Drugs at FDA website: https://animaldrugsatfda.fda.gov/adafda/views/#/environmentalAssessments

Summary of the Current EA

The current EA was prepared to evaluate the potential environmental impacts from the use of SYNOVEX® ONE GROWER as a single implant in growing beef steers and heifers in a dry lot. The EA briefly summarizes the risk assessment approach described in the 2024 Pasture EA, which the current EA relies upon. The EA states that growing beef steers and heifers in a dry lot were conservatively considered as part of the feedlot scenario in the 2024 Pasture EA.

A dry lot is an animal management technique that may be used during periods of drought or forage dormancy in pasture cattle. The dry lot area may be defined by a large pen and is either covered with grass or packed dirt. Cattle may be held in a dry lot for several months before either returning to pasture or being transferred to a feedlot. After cattle are removed from the dry lot, the manure may be left in place or scraped and applied to cropland. Based on the animal and manure management practices of cattle in a dry lot, the environmental exposure routes of the six major metabolites of trenbolone acetate and estradiol benzoate from growing beef steers and heifers in a dry lot is expected to be the same as cattle on feedlots (e.g., runoff from feedlot surfaces, runoff from manure amended cropland). As a result, the feedlot scenario is considered to be conservative and inclusive of the environmental exposure expected from dry lots.

The EA concludes that although SYNOVEX® ONE GROWER was not directly evaluated as part of the 2024 Pasture EA, the PEC_{sw} and RQ values were estimated for a higher dose implant, SYNOVEX® ONE FEEDLOT (i.e., SYNOVEX® ONE GROWER contains 150 mg trenbolone acetate and 21 mg estradiol benzoate vs. SYNOVEX® ONE FEEDLOT contains 200 mg trenbolone acetate and 28 mg estradiol benzoate). Because no significant environmental impacts were expected for the higher dose implant, the same conclusion can be made for the lower dose implant in the same scenario (i.e., feedlot scenario).

In addition to the justifications provided in the current EA for why significant environmental impacts are not expected from the current proposed action, additional aspects related to dry lot operations in the United States (US) that also limit the potential for significant environmental impacts were considered by CVM.

First, cattle in a dry lot are expected to be held for much shorter durations than cattle on a feedlot or pasture. Thus, the evaluation in the 2024 Pasture EA, which assumed that cattle on feedlots and pasture were treated every day with a SYNOVEX® implant over a 30-year period, represents a much longer potential environmental exposure duration.

Second, the proportion of dry lot operations compared to the proportion of feedlot and pasture operations in the US is expected to be much less. Therefore, the total number of cattle in dry lots that could be administered SYNOVEX® ONE GROWER, is much less than those on feedlots and pasture, thus reducing the overall environmental exposure and risk.

These aspects considered collectively demonstrate that the overall environmental introduction of the six major metabolites of trenbolone acetate and estradiol benzoate for the use of SYNOVEX® ONE GROWER in growing beef steers and heifers in a dry lot is expected to be substantially lower than that estimated as part of the 2024 Pasture EA. As a result, the RQ values reported in the 2024 Pasture EA are considered to be highly conservative as it relates to the current proposed action because they represent the use of a higher dose product (i.e., SYNOVEX® ONE FEEDLOT) in a higher number of individual animals, in an overall higher number of animal operations (i.e., feedlot and pasture), over a longer environmental exposure duration.

Conclusion

Based on the information and evaluation conducted as part of the current EA in combination with that in the 2024 Pasture EA, no significant environmental impacts are expected from the proposed use of SYNOVEX® ONE GROWER as a single implant for increased rate of weight gain for up to 200 days in growing beef steers and heifers in a dry lot.

{see appended electronic signature page}

Matthew Lucia, DVM
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Electronic Signature
Addendum for Submission ID

Signing Authority (Role)	Letter Date
Matthew Lucia (Office Director)	02/23/2026

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