Finding of No Significant Impact (FONSI)

In support of the supplemental approval of a new animal drug application (NADA) for SYNOVEX® ONE Grower (estradiol benzoate and trenbolone acetate extended-release implant) in growing beef steers and heifers fed in confinement for slaughter 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 (estradiol benzoate and trenbolone acetate extended-release implant) for increased rate of weight gain for up to 200 days in growing beef steers and heifers fed in confinement for slaughter. One implant (six pellets) contains a total of 21 mg estradiol benzoate and 150 mg trenbolone acetate. Each pellet contains 3.5 mg estradiol benzoate and 25 mg trenbolone acetate in an extended-release coating. SYNOVEX® ONE Grower is administered via subcutaneous implantation in the middle one-third of the ear by means of an implant applicator.

In support of the application, Zoetis Inc. has provided an Environmental Assessment (EA) dated July 21, 2021. A copy of the EA is attached. We have reviewed the EA and find that it supports a FONSI.

The EA for SYNOVEX® ONE Grower indirectly evaluated the potential environmental impacts of the proposed action (i.e., the use of SYNOVEX® ONE Grower in growing beef steers and heifers) through a comparison to the environmental risk analyses conducted in the SYNOVEX® ONE Feedlot and Grass EA dated May 29, 2014.[1] The 2014 SYNOVEX® ONE Feedlot and Grass EA was prepared by Zoetis in support of an original NADA for two similar extended-release implant products, SYNOVEX® ONE Feedlot (28 mg estradiol benzoate and 200 mg trenbolone acetate extended-release implant) and SYNOVEX® ONE Grass (21 mg estradiol benzoate and 150 mg trenbolone acetate extended-release implant), which resulted in a FONSI by CVM on June 9, 2014. In the 2014 SYNOVEX® ONE Feedlot and Grass EA, it was assumed that 100% of beef steers and heifers held on feedlots and in

[1] The 2014 EA prepared for SYNOVEX® ONE FEEDLOT and GRASS is titled "Environmental Assessment for Synovex® ONE (Estradiol Benzoate and Trenbolone Acetate Extended Release Implant) Feedlot and Grass for Beef Steers and Heifers." Herein, this EA is referred to as the 2014 SYNOVEX® ONE EA. Copies the SYNOVEX® ONE EA and FONSI can be accessed from CVM's Listing of Environmental Assessments and Findings of No Significant Impact website located at: https://animaldrugsatfda.fda.gov/adafda/views/#/environmentalAssessments

pastures in a watershed were implanted 365 days a year with SYNOVEX® ONE Feedlot and GRASS, respectively (i.e., SYNOVEX® ONE Feedlot and Grass accounted for 100% of the market share). In the SYNOVEX® ONE Grower EA, it was assumed that the use of SYNOVEX® ONE Grower would replace that of SYNOVEX® ONE Feedlot in part or entirely. Because any use of SYNOVEX® ONE Grower instead of SYNOVEX® ONE Feedlot will result in lower overall environmental concentrations of trenbolone acetate, estradiol benzoate, and their metabolites (because the overall payout of SYNOVEX® ONE Grower is lower than that of SYNOVEX® ONE Feedlot) the potential aggregate exposures and cumulative impacts from use of both products have already been indirectly evaluated.

Because the amount of estradiol benzoate and trenbolone acetate is reduced as compared to SYNOVEX® ONE Feedlot, it expected that the daily concentrations of the metabolites of estradiol benzoate and trenbolone acetate excreted in the manure of cattle administered SYNOVEX® ONE Grower would also be less than that excreted by cattle administered SYNOVEX® ONE Feedlot. Thus, the daily excretion rates of estradiol benzoate and trenbolone acetate metabolites on both the farm and watershed level would be reduced and predicted environmental concentrations and risk quotients in water would be smaller than those estimated for SYNOVEX® ONE Feedlot. Accordingly, if no significant impacts were expected from the use of SYNOVEX® ONE Feedlot, then no significant impacts should also be expected from the use of SYNOVEX® ONE Grower. Based on the analyses in the 2014 SYNOVEX® ONE Feedlot and Grass EA, CVM has previously determined that the proposed uses of SYNOVEX® ONE Feedlot and Grass are not expected to result in significant impacts on the human environment, and has prepared a FONSI for the approval of an NADA for these products; therefore, a similar conclusion is made for the proposed use of SYNOVEX® ONE Grower.

Based on the information and analysis contained in the SYNOVEX® ONE Grower EA in combination with that in the 2014 SYNOVEX® ONE Feedlot and Grass EA, no significant environmental impacts are expected from the proposed use of SYNOVEX® ONE Grower in growing beef steers and heifers fed in confinement for slaughter for increased rate of weight gain for up to 200 days.

{see appended electronic signature page}

Matthew Lucia, DVM
Director
Office of New Animal Drug Evaluation
Center for Veterinary Medicine
U.S. Food and Drug Administration

Electronic Signature
Addendum for Submission ID

Signing Authority (Role)	Letter Date
Matthew Lucia (Office Director)	9/9/2021

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