

**Finding of No Significant Impact (FONSI)
in support of a supplemental New Animal Drug Application for**

**SYNOVEX CHOICE
(estradiol benzoate and trenbolone acetate implant)**

for

Increased rate of weight gain and improved feed efficiency in heifers
fed in confinement for slaughter

NADA 141-043

**Zoetis
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 is requesting the approval of a supplemental new animal drug application (NADA) for the use of SYNOVEX CHOICE [estradiol benzoate (EB) and trenbolone acetate (TBA) implant] for increased rate of weight gain and improved feed efficiency in heifers fed in confinement for slaughter. SYNOVEX CHOICE is currently approved under NADA 141-043 for increased rate of weight gain in steers fed in confinement for slaughter. Each implant is administered subcutaneously in the ear and consists of four uncoated pellets containing a total of 14 mg EB and 100 mg TBA (3.5 mg EB and 25 mg TBA per pellet). The labeled duration of efficacy is 120 days. This product is dispensed over the counter.

In support of the application, Zoetis has provided an Environmental Assessment (EA) dated June 3, 2014. A copy of the EA is attached. We have reviewed the EA and find that it supports a FONSI.

The EA for SYNOVEX CHOICE has indirectly evaluated the potential environmental impacts of the proposed action (i.e., the use of SYNOVEX CHOICE in beef heifers) through a comparison to the environmental risk analyses conducted in the SYNOVEX ONE EA dated May 29, 2014¹. The SYNOVEX ONE EA was prepared by Zoetis in support of an original NADA for two similar extended release implant products, SYNOVEX ONE FEEDLOT (28 mg EB and 200 mg TBA extended release implant) and SYNOVEX ONE GRASS (21 mg EB and 150 mg TBA extended release implant)², which resulted in a FONSI by CVM on June 9, 2014. In the SYNOVEX ONE EA, it was assumed that 100% of beef steers and heifers held on feedlots and in pastures in a watershed were implanted 365 days a year with SYNOVEX ONE FEEDLOT and

¹ The EA prepared for the SYNOVEX ONE products 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 SYNOVEX ONE EA.

² SYNOVEX ONE FEEDLOT is proposed for increased rate of weight gain and improved feed efficiency in steers and heifers fed in confinement for slaughter for a period up to 200 days. SYNOVEX ONE GRASS is proposed for increased rate of weight gain for up to 200 days in pasture cattle steers and heifers (stocker, feeder and slaughter).

GRASS, respectively (i.e., SYNOVEX ONE accounted for 100% of the market share). In the SYNOVEX CHOICE EA, it was assumed that the use of SYNOVEX CHOICE would entirely replace that of SYNOVEX ONE FEEDLOT, which was already assumed to have a 100% market share for beef cattle held on feedlots; therefore, the potential aggregate exposures and cumulative impacts from use of both products have already been indirectly evaluated.

Based on the results of an explant study that measured the daily release rate of EB and TBA from two SYNOVEX products (see Table 3 in Section 3.2 of the EA), it was estimated that the daily release rates of EB and TBA in SYNOVEX CHOICE would be approximately 6% and 10% less than those from SYNOVEX ONE, respectively. Because the daily release rates are reduced, it can be assumed that the daily concentrations of EB and TBA metabolites excreted in the manure of cattle administered SYNOVEX CHOICE would also be less than that excreted by cattle administered SYNOVEX ONE FEEDLOT. Thus, if the SYNOVEX CHOICE implants were substituted for the SYNOVEX ONE implants in the analysis conducted in the SYNOVEX ONE EA, the daily excretion rates of EB and TBA on both the farm and watershed level would be slightly reduced, ultimately resulting in reduced environmental exposures to the metabolites of EB and TBA (i.e., smaller predicted environmental concentrations in water) and smaller risk quotient values. Therefore, if no significant impacts were expected from the use of SYNOVEX ONE, then no significant impacts should also be expected from the use SYNOVEX CHOICE. Based on the analyses in the SYNOVEX ONE 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 CHOICE.

Based on the information and analysis contained in the SYNOVEX CHOICE EA in combination with that in the EA prepared for SYNOVEX ONE, it is concluded that no significant environmental impacts are expected from the proposed use of SYNOVEX CHOICE implants for increased rate of weight gain and improved feed efficiency in heifers fed in confinement for slaughter.

{ see appended electronic signature page }

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Center for Veterinary Medicine
U.S. Food and Drug Administration

Electronic Signature
Addendum for Submission ID

Signing Authority (Role)	Letter Date
Steven Vaughn (Office Director)	6/9/2014

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