Finding Of No Significant Impact

In support of an approval of a
New Animal Drug Application (NADA) related to
the SBC LAL-C line of genetically engineered chickens (*Gallus gallus domesticus*), which
are carrying a single copy of the *hLAL* rDNA construct integrated at a single genomic site
that directs the expression of a recombinant human lysosomal acid lipase protein

NADA 141-453

Alexion Pharmaceuticals, Inc.
Lexington, MA

Based on the conclusions of the Environmental Assessment (EA) of the approval of NADA 141-453 related to the SBC LAL-C line of genetically engineered (GE) chickens producing a recombinant human lysosomal acid lipase protein in their egg whites, the Center for Veterinary Medicine (CVM) has made the finding that this action will not have a significant impact on the quality of the human environment in the United States. Therefore, preparation of an environmental impact statement is not required, and the agency is issuing this Finding of No Significant Impact (FONSI).

Alexion Pharmaceuticals, Inc. has requested the approval of a New Animal Drug Application (NADA) related to the SBC LAL-C line of genetically engineered chickens (*Gallus gallus domesticus*), which are carrying a single copy of the *hLAL* rDNA construct integrated at a single genomic site that directs the expression of a recombinant human lysosomal acid lipase protein (rhLAL). A formulation of purified rhLAL, called sebelipase alfa, is intended for use in enzyme replacement therapy for humans with Lysosomal Acid Lipase deficiency. This product is the subject of a Biologic License Application (BLA) that is currently under review by the Center for Drug Evaluation and Research (CDER). CDER will separately comply with its National Environmental Policy Act (NEPA) obligations associated with the BLA submitted by Alexion Pharmaceuticals, Inc.

In support of the application, Alexion Pharmaceuticals, Inc. submitted an Environmental Assessment (EA) dated August 18, 2015 that focuses on the potential environmental effects associated with production of SBC LAL-C chickens and egg white harvest at the sponsor's four facilities. Three of these facilities are located in Georgia and one in Massachusetts. SBC LAL-C hens lay eggs for egg white harvesting. Eggs are collected, and cracked; egg whites are separated from the yolks and stored for further purification and production of sebelipase alfa. The following risk-related questions were considered in the EA:

- What are the risks to personnel involved with animal husbandry, other animals, and environment associated with production of the SBC LAL-C line of GE chickens while under containment?
- What is the likelihood that SBC LAL-C GE chickens will escape the conditions of containment?
- What is the likelihood that SBC LAL-C GE chickens will survive and disperse if they escape the conditions of containment?

- What is the likelihood that SBC LAL-C GE chickens will reproduce and establish if they escape the conditions of containment?
- What are potential impacts on the environment of the United States should SBC LAL-C GE chickens escape the conditions of containment?

As indicated in the EA, the hazards and risks associated with production of SBC LAL-C chickens under described conditions of containment are highly dependent on the expression product of the *hLAL* rDNA construct and the ability of the *hLAL* rDNA construct to mobilize and spread to other animals. Therefore, the EA considered the risk of gene flow to other animals, the risk of diseases spread to other animals, risks of direct toxicity associated with increased environmental concentration of rhLAL, and risks associated with disposal of GE animals and GE animal waste. CVM determined that the available data and information indicate that the *hLAL* rDNA construct is not likely to mobilize and spread to other animals and its expression is not intrinsically hazardous. Therefore, the production of SBC LAL-C GE chickens under conditions of containment described in the EA is not expected to pose any significant risks to personnel involved with animal husbandry, other animals, or the environment.

All production facilities have multiple redundant forms of containment to prevent the escape of SBC LAL-C chickens. Containment includes physical barriers (perimeter fences, buildings, dedicated rooms, and chicken housing enclosures), security systems with video surveillance, and daily observations by personnel. All GE chickens have multiple forms of identification that include neck or two wing bands. Based on the review of materials submitted in the EA and FDA's inspections of the sponsor's facilities in Georgia and Massachusetts, CVM concluded that the probability of SBC LAL-C chickens escaping the conditions of containment is extremely low.

In the highly unlikely event that SBC LAL-C chickens were to escape from production facilities, their survival and dispersal in the environments around the production facilities is highly unlikely because they are not expected to possess traits needed for survival in the natural environment. Lack of ground cover, harsh winter climate (Massachusetts) and the presence of carnivorous predators (Georgia and Massachusetts) that would likely eliminate any escaped animals further decrease the probability of their survival and spread in the environment. CVM therefore concludes that the likelihood that SBC LAL-C chickens will survive and disperse if they escape the conditions of containment is extremely low.

Reproduction and establishment of escaped chickens in the natural environment is highly unlikely due to the lack of potential mates for SBC LAL-C chickens. There are no known populations of feral chickens around the production facilities. Any closely related species (e.g., partridges, pheasants, grouses, and wild turkeys) that may be found around the production facilities and that could theoretically mate with escaped chickens are not anticipated to produce any viable offspring. In the highly unlikely event that escaped SBC LAL-C chickens have offspring, it is likely that they will be subjected to natural predation. CVM therefore concludes that the probability of reproduction and establishment of SBC-LAL chickens in the environment around the production facilities is extremely low.

Conclusion

Based on CVM's review of information and analyses presented in the sponsor's EA, data submitted by the sponsor in support of the steps of the hierarchical risk-based review process, and FDA's inspections of the sponsor's production facilities, CVM concludes that the approval of the NADA related to the SBC LAL-C line of GE chickens is not expected to have a significant impact on the quality of the human environment in the United States. CVM therefore issues this Finding of No Significant Impact (FONSI) and determines that preparation of an environmental impact statement is not required.

08/24/2015

Date

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