

Toxicology Review of Sci-B-Vax Vaccine

BLA125737

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Applicant: VBI Vaccines, Inc.

Product: Sci-B-Vac^R, 10 ug/mL

Cross references: IND 17542

Proposed indication for use: Prevention of infection caused by all known subtypes of the hepatitis B virus (HBV) in adults, age \geq 18 years old

Reviewer: Ching-Long Joseph Sun, Ph. D., Division of Vaccines and Related Products Applications

Précis

The sponsor submitted three toxicity studies and an intramuscular embryo-fetal developmental and pre- and post-natal reproductive toxicity study in rats. The study reports had been addressed or reviewed in IND 17542.

All three toxicity studies were not GLP compliant. In the first two toxicity studies, the dosing regimen was not mimicking the proposed trial and the test article was not the intended clinical formulation. Thus, they are irrelevant. The 8-week repeated dose toxicity study, the testing facility was not GLP certified at time when it was performed in 2004. The report did not contain line listings of the individual data points, including laboratory data points. Based on the limited data submitted, the vaccine caused typical local reactions at the injection sites but did not cause any systemic effects other than the expected lymphoid hyperplasia.

In the embryo-fetal developmental toxicity study, three groups of female rats were administered intramuscularly placebo control, placebo adjuvant control or 10 ug HBsAg and ^{(b) (4)} ug aluminum hydroxide 30 days and 15 days prior to mating, and on gestation days 4 and 15. Half of the pregnant rats were sacrificed on gestation day 21 for embryo-fetal development assessment and the other half were delivered for pre- and post-natal development assessment. It did not have any effects on female reproductive effect, fetal/embryonal development and postnatal development up to day 23.

Conclusion and recommendation

The application is approvable from a preclinical toxicological perspective.

The embryo-fetal developmental toxicity study results can be reflected in sections 8.1 and 13.1. The recommended revision is shown.

8.1 Pregnancy

Risk Summary

Developmental toxicity studies have been performed in female rats administered TRADEMARK on four occasions; twice prior to mating, twice during gestation. Each dose

was the adult human dose. The study revealed no evidence of harm to the fetus due to TRADEMARK [see *Animal Data below*].

Data

Animal Data

Developmental toxicity study has been performed in female rats at a dose equivalent to the adult human dose. In the study, female rats received TRADEMARK (10 mcg/occasion) by intramuscular injection 30 days and 15 days prior to mating and on gestation days 4 and 15. No adverse effects of pre-weaning development were observed. There was no evidence of fetal malformations or variations.

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

TRADEMARK has not been evaluated for carcinogenic, mutagenic potential or male fertility in animals. It had no effect on female fertility in rats [see 8.1 *Animal Data*].

Concurrence: Martin David Green, Ph. D., Division of Vaccines and Related Products Applications