

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:
22-315

OTHER REVIEW(S)

Date: January 21, 2009

From: Joe Hutter, Chemical Engineer

Subject: **IND 58663 Dexamethasone posterior segment drug delivery system
DEX PS DDS
Materials and Packaging Review**

To: The Record

Device Description

The device design was described briefly in the provided documents and also US Patent #7,468,065 (DA Webber et al. Apparatus for the delivery of ocular implants, US 2005/0154399 A1, July 14, 2005, Allergan, Inc.) The device is used to delivery an erodible (polylactic-glycolic acid) polymeric implant containing dexamethasone (Dex) into the posterior segment (vitreous) of the eye. The implant comes in 2 sizes, 0.35 mg Dex and 0.7 mg Dex. The delivery system is a syringe with a plunger which can be extended to push the implant out of a needle.

To use the device, the physician positions the needle to the appropriate place in the eye, then delivers the implant by pressing a button on the outside of the syringe. The implant is held in place in the syringe by a ~~_____ sleeve _____~~, the sleeve compresses the implant through a notch cut into the needle. The plunger is activated by compressing a button on the outside of the syringe, which compresses a polyethylene linkage, which lengthens and pushes the stainless steel plunger. The plunger pushes the implant out of the needle. The physician can then withdraw the syringe from the eye. The delivery device is single use only. The implant is loaded sterile at the factory. Air injection is minimized by designing the plunger and implant to be smaller than the needle so that air can flow around them when they are injected. In addition, the implant is not placed very far from the injection end of the needle. The needle is beveled to prevent coring of tissue so that the injection site is self-sealing.

b(4)

Analysis- Mechanical design of the device appears to be adequate for its purpose, the use of the device in actual clinical settings was described in the patent. The major safety issue appears to be risks of infection. The device is loaded sterile at the factory and this should minimize this problem. Also, the device is designed to be single use only.

Note to CDER- A microbiologist did not review the adequacy of the sterilization methods and its quality control since no documentation was provided.

Packaging

The packaging was described as a _____ aluminum foil pouch with a _____
_____ This package is contained in a larger _____
_____ shipping carton. The sterility was checked by completing integrity tests on the pouch, as well as a sterility test on the contents. The package was required to be a moisture and sterility barrier. A _____ was included in the package since it was determined in earlier studies that the DDS implant remained stable only when it was stored with a _____. The only reported failure of the DDS occurred in an accelerated test at 40 deg C/75% RH _____. (The PLGA (polylactic-glycolic acid) implant will undergo hydrolysis when contacted with water, therefore, it should be kept dry until it is delivered into the aqueous containing eye to assure proper erosion deliver of the drug.)

b(4)

The pouch was found to be intact after 24 mos. following an integrity creep test and sterility test.

The external _____ packaging was evaluated by shipping tests of the product at temperatures of 5, 20, and 38 deg C. The device was found to pass at the end of these tests. The device was able to function and remain in specifications even after drop tests during shipping.

Analysis- Packaging was found to be appropriate for this application.

Pre-Assembly Inspection of Components

Dimensional inspections are completed on the needle hub assembly, safety cap, and housing cap. Needle sharpness is tested by penetration testing of a Halar membrane. The actuation force to deploy the implant is tested with a mechanical analyzer. Implant position is tested after simulated shipping/dropping. Specifications were provided on p 10.

Analysis- Specifications and testing are appropriate for this device.

Toxicology

Allergan reported that the sleeve was tested by cytotoxicity, sensitization, and irritation and that the sleeve passed.

Analysis- Our toxicologist M Ghosh was consulted on these tests. It was her opinion that these tests were appropriate for the intermittent use of a syringe and sleeve. However, the testing of the silicone lubricant and stainless steel should be referenced to other applications (master file) to assure that these materials were adequately tested. Also, no tests were reported for the implant, so its biocompatibility could not be determined.

Conclusions

Packaging appears to be appropriate for this device. The design of the device appears appropriate for this application as well.

The sterility should be adequate, however, details of the sterilization procedures and validation were not reviewed. If these items are a concern for CDER, these items can be reviewed after further documents are provided by Allergan. Also, the biocompatibility testing reported for the sleeve appears adequate, however, no references were given to assure the lubricants and steel used was adequately tested. Also, no biocompatibility

testing of the implant itself was provided. If these items are also a concern for CDER, they can be reviewed after further documents are provided by Allergan.

**APPEARS THIS WAY
ON ORIGINAL**