New England Compounding Center

Customized Pharmacy Services

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BY FACSIMILE/CONFIRMATION COPY BY MAIL

Ms. Daryl A. Dewoskin
Investigator
Food and Drug Administration
2224 Pawtucket Avenue, Suite 201
East Providence, Rhode Island 02914

Ms. Kristina M. Joyce, PharmD
Investigator
Food and Drug Administration
One Montvale Avenue
Stoneham, Massachusetts 02180

Re: Inspection of New England Compounding Center ("NECC")

Dear Ms. Dewoskin and Dr. Joyce:

This letter supplements our initial written response dated February 27, 2003, to the FDA-483 delivered to NECC on February 10, 2003. As discussed in our initial response, we had taken a variety of corrective steps, and were proceeding to implement additional standard operating procedures (SOPs). With the assistance of (b) (4) an experienced and well-credentialed expert in the field of pharmacy compounding of sterile and other medical preparations, we have completed the implementation of those SOPs.

We have implemented an aseptic process validation protocol (SOP 5.120), similar to (b) (4) and those set forth in FDA Compliance Policy Guides for aseptic processing. To date, we have conducted three sterile media fill validation tests simulating our process for compounding sterile betamethasone acetate

suspension in aqueous betamethasone phosphate solution (betamethasone respule), with passing results. (b) (4) concurs that the process described in NECC SOP 7.200 is now validated as an aseptic process. Additional sterile media-fill validation tests of the aseptic processes used by NECC to compound sterile ophthalmic combination drug preparations as well as injectable solutions are underway.

Sterile media-fill process simulation will be repeated (b) (4) as a means of regularly re-validating the process.

Additionally, representative samples of sterile medication preparations compounded by NECC are regularly submitted to a qualified third-party testing laboratory for sterility testing (b) (4) and all have passed to date.

Please note that while we are validating NECC sterile parenteral preparation processes, we are not subject to (nor are we voluntarily subjecting ourselves to) current good manufacturing practices (cGMPs) as promulgated by the FDA, since we are a compounding pharmacy, not a manufacturer.

We have also implemented a policy and procedure for the evaluation of the aseptic compounding technique for individual compounding personnel prior to their compounding sterile parenterals (SOP 5.010). Compounding personnel must demonstrate, by performing multiple sterile media transfers and manipulations, that they are competent to aseptically compound before being permitted to prepare sterile parenteral drug products.

Additionally, as mentioned in our initial response, NECC has developed and implemented an SOP requiring regular monitoring of the compounding environment and personnel for bioburden consistent with similar guidelines for compounding pharmacies (b) (4) (b) (4) The intent is to ensure that the compounding environment is controlled such that sterile products cannot become contaminated with environmental microflora during the compounding process.

Since early 2003, NECC has been monitoring the content of active ingredients contained in its compounded sterile parenteral preparations by submitting samples to a qualified outside testing laboratory. The results of those tests indicate that the compounded preparations prepared in the NECC pharmacy are within acceptable ranges relative to label claims for content and potency. The pharmacy has also developed and is implementing a protocol that validates the potency of "like" preparations when they are subjected to the same compounding processes and storage practices, to a) ensure as much conformity of potency in similar products as possible, subject to the idiosyncrasies inherent in extemporaneously compounded products; and b) establish an additional basis for expiration

dating beyond that available from third-party reference sources. Finally, NECC has developed and is implementing a quality management program to ensure that all compounded injectable medications meet the appropriate compendial or other reference standards for quality, content, and purity. The quality management program includes the measurement of pH for all applicable preparations, including sterile parenterals; as well as, where appropriate, endotoxin levels, color, clarity, the absence of visible foreign particulate matter, and closure integrity.

We hope that this information is satisfactory and we consider the matter closed unless we hear from you. If you have further questions or would like further information, including copies of our new SOPs, please do not hesitate to contact me.

Sincerely,

New England Compounding Center, Inc.
Barry Cadden, R.Ph., Manager

cc: Leslie Doyle, R.Ph.
(b) (4)