Investigator Reports Discussion from the U.S. Food and Drug Administration (FDA) 50 State Inter-governmental Working Meeting on Drug Compounding

Scott Denaburg, BA, PharmD, Investigator for the Tennessee Board of Pharmacy, attended the 2016 Inter-governmental Working Meeting on Drug Compounding that was held on September 20 - 21, 2016. During the discussion on sterile compounding, Denaburg was informed that the FDA, for the year 2016, had performed 77 inspections of 503"A" pharmacies with 20 follow up inspections. Although the "FDA Insanitary Conditions Guidance" may not have become final as of yet, the following information indicates how a 503A pharmacy may **currently be inspected by the FDA** for adulterated drugs which includes insanitary conditions.

As stated in the FDA "Background" heading regarding draft guidance (**Insanitary Conditions at Compounding Facilities; Draft Guidance for Industry; Availability**/A Notice by the Food and Drug Administration on 8/4/2016),

"...FDA is announcing the availability of a draft guidance for industry entitled "Insanitary Conditions at Compounding Facilities." Under section 501(a)(2)(A) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 351(a)(2)(A)), a drug is deemed to be adulterated if it has been prepared, packed, or held under insanitary conditions whereby it may have been contaminated with filth, or whereby it may have been rendered injurious to health. Drug products compounded under insanitary conditions could become contaminated and cause serious adverse events in patients, including death. Although sections 503A and 503B of the FD&C Act (21 U.S.C. 353a and 353b) provide exemptions for compounded drugs from specified provisions of the FD&C Act if certain conditions are met, neither section provides an exemption from section 501(a)(2)(A) of the FD&C Act. Any drug that is prepared, packed, or held under

insanitary conditions is deemed to be adulterated under the FD&C Act, including drugs produced by a compounding facility…"

Some noted conditions during inspections included the following:

- Drinking water from a 5 gallon bottle water dispenser used for sterile or injectable product not tested for purity or microbial/endotoxin content
- Wood-like surface on the underside of the Laminar Air Flow Workbench (LAFW) surface with what appeared to be stained
- An ISO class 7 ante-room hallway that was not wide enough to gown and keep from touching the walls. *(Investigator Note: This may be a good time to obtain a stainless steel bench or stool so as to not lean on the walls when garbing)*
- Soiled material observed on the metal grate covering the pre-filter of the ISO class 5 Laminar Flow Hood (LFH)
- Rusted nail observed on metal grate
- Clean room's positive pressure air handling system observed to be turned off
- Dead or alive insects found in the clean room
- Filth under the hood and in the pre-filter
- Glove box providing ISO class 5 conditions in a carpeted room with a wooden stool
- Glove box with damaged sleeves
- Gowned employee in cleanroom with exposed legs
- Toaster oven used to dry heat sterilize and depyrogenate glassware, but unable to reach temperature to be effective
- Exposed insulation above cleanroom entry door

- Failure to routinely use a sporicidal agent, correctly *(Careful to check if it actually kills spores as opposed to the name of the product)*
- Non-sterile wipes used to clean "aseptic" surfaces

During a Q and A session, Denaburg asked a question regarding how a sterile compounder might comply with FDA since USP 797 standards of garbing differ in allowing a non-sterile gown. Ian Deveau, Branch Chief Office of Compliance, Center for Drug Evaluation and Research (CDER)/FDA explained that the requirements more mirror the "proposed" guidelines of USP 797, which if unchanged, require the use of sterile sleeves. He indicated that the compounder would be required to keep his or her head and body out of the LAFW since the head, mask and beard covers are not required to be sterile. By adding the sterile sleeves to the regimen, only sterile garb would actually be inside the work area provided that the ISO Class 5 LAFW is working properly. Furthermore, Deveau discussed the use of sterile wipes as opposed to the non-linting wipes that are currently allowed under USP 797 guidelines. He noted that even if the compounder is spraying with sterile alcohol, he or she may be introducing microbes. (A slide was previously shown indicating that the FDA had tested a non-sterile wipe and found the presence of Bacillus species and other "spore-formers.")

Other issues included diluting certain cleaning agents that should not be diluted, and dwell time not being followed as directed by the manufacturer.

Physician Compounding: At this point, the FDA discussed that healthcare provider outbreaks of compounded drugs are on the rise, and "there are concerns about (the) ability to ensure quality of drugs compounded in (the) office setting, and physician awareness of applicable regulations," according to Emily Gebbia CDER, Office of Compliance. In a separate presentation slide, Gebbia conveyed the following, "…Section 503A of the Federal Food, Drug and Cosmetic Act

(FD&C Act) describes conditions that must be satisfied for drug products compounded by a licensed pharmacist in a State-licensed pharmacy or a Federal facility, **or by a licensed physician**, to be exempt from the following sections of the FD&C Act:

- 502(a)(2)(B) (concerning current good manufacturing practice requirements)
- 502(f)(1)(concerning the labeling of drug with adequate directions for use)
- 505 (concerning the approval of drugs under NDAs or ANDAs)

Even if the conditions of 503A are met, compounded drugs remain subject to other FD&C Act provisions (e.g., **insanitary conditions**)..." Denaburg noted other areas of discussion including the hospital guidance (one mile radius discussion), 503B facilities regulations/inspections, and other topics involving the Drug Quality and Security Act that may be discussed in the future.

(For additional questions, please contact the Board Office at (615) 741-2718 or contact Board of Pharmacy Executive Director Reggie Dilliard at Reginald.Dilliard@TN.GOV. Please note that the opinions and views expressed in this publication do not necessarily reflect the official views, opinions, or policies of the Board unless expressly so stated.