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April 6, 2016

Gay Dodson, R.Ph.
Executive Director
Texas State Board of Pharmacy
William P. Hobby Building, Suite 3-600
333 Guadalupe Street
Austin, Texas 78701

Dear Mr. Dodson:

Public Citizen, a consumer advocacy organization with more than 400,000 members and supporters nationwide, strongly urges the Texas State Board of Pharmacy to suspend immediately the pharmacy license for I.V. Specialty — a compounding pharmacy based in Austin that produces a wide range of sterile drugs for home infusion to patients located within a two-hour radius of Austin[1] — and the licenses of Pharmacist-in-Charge Carlos H. Garcia[2] and any other pharmacists employed by the company. These state regulatory actions are urgently needed to protect patients from potentially life-threatening infections: A recent inspection of I.V. Specialty by the Food and Drug Administration (FDA) found multiple serious violations of standard procedures for producing sterile injectable drugs, and the company recklessly refused to follow the FDA's March 7 recommendations to discontinue production of injectable drugs and to recall all of its unexpired injectable drug products.[3]

As you may know, the FDA first inspected I.V. Specialty in July 2014, after the company registered with the agency as an outsourcing facility.[4] At that time, FDA investigators identified numerous "serious deficiencies" in the company's practices for producing sterile drug products.[5] Inspection findings included:[6]

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[1] I.V. Specialty, Ltd., webpage. http://www.ivspecialty.com/. Accessed March 31, 2016.
[2] Food and Drug Administration. Form FDA 483 issued to I.V. Specialty, Ltd. on February 15, 2016. http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofGlobalRegulatoryOperationsandPolicy/ORA/ORAElectronicReadingRoom/UCM489814.pdf. Accessed March 31, 2016.
[3] Food and Drug Administration. FDA alerts health care professionals and patients not to use human and animal sterile drug products produced and distributed by I.V. Specialty, Ltd., Austin, Texas. http://www.fda.gov/Drugs/DrugSafety/ucm489951.htm. Accessed March 31, 2016.
[4] Food and Drug Administration. Form FDA 483 issued to I.V. Specialty, Ltd. on July 22, 2014. http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofGlobalRegulatoryOperationsandPolicy/ORA/ORAElectronicReadingRoom/UCM410372.pdf. Accessed March 31, 2016.
[5] Food and Drug Administration. Warning letter to I.V. Specialty, Ltd. April 21, 2015. http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2015/ucm449675.htm. Accessed March 31, 2016.
[6] Food and Drug Administration. Form FDA 483 issued to I.V. Specialty, Ltd. on July 22, 2014. http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofGlobalRegulatoryOperationsandPolicy/ORA/ORAElectronicReadingRoom/UCM410372.pdf. Accessed March 31, 2016.

- "Clothing of personnel engaged in the manufacturing, processing, packing, and holding of drug products is not appropriate for the duties they perform. Specifically, [s]terile garb (i.e. gowns, booties, head bonnet, facemask, goggles) is not worn during aseptic processing of sterile drug products in the ISO 5 horizontal laminar airflow (LAP) hoods."
- "Procedures designed to prevent microbiological contamination of drug products purporting to be sterile do not include adequate validation of the sterilization process."
- "Aseptic processing areas are deficient regarding the system for cleaning and disinfecting the room and equipment to produce aseptic conditions."
- "Equipment and utensils are not cleaned and sanitized at appropriate intervals to prevent contamination that would alter the safety, identity, strength, quality or purity of the drug product."
- "Each batch of drug product purporting to be sterile is not laboratory tested to determine conformance to such requirements. Specifically, given the observed inadequate environmental controls and aseptic practices, testing is deficient in that:
  a. Your firm does not conduct finished drug product testing for sterility and endotoxins. Sterility testing only includes base solutions. …
  b. Your firm's test method for sterility… has not been validated to demonstrate it is equivalent to or better than the USP test method (i.e., Membrane Filtration or Direct inoculation)."

In a belated warning letter sent to I.V. Specialty on April 21, 2015 — after the company was no longer registered with the FDA as an outsourcing facility — the agency indicated that these deficiencies "put patients at risk."[7] The FDA's warning letter hammered home this point by stating that "drug products compounded in [the company's] facility that were intended or expected to be sterile were prepared, packed, or held under insanitary conditions, whereby they may have become contaminated with filth or rendered injurious to health, causing them to be adulterated within the meaning of section 501(a)(2)(A) of the FDCA [21 U.S.C. § 351(a)(2)(A)]."

Even though I.V. Specialty is no longer a registered outsourcing facility, the FDA, invoking its authority to inspect any facility that makes or sells drug products, reinspected the company from January 25 through February 5, 2016.[8] Once again, the agency uncovered multiple egregious, life-threatening problems in the company's processes for making sterile drugs. Inspection findings included:[9]

- "Aseptic processing areas are deficient regarding systems for maintaining any equipment used to control the aseptic conditions."
- "Each batch of drug product purporting to be sterile and pyrogen-free is not laboratory tested to determine conformance to such requirements. Specifically,

[7] Food and Drug Administration. Warning letter to I.V. Specialty, Ltd. April 21, 2015. http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2015/ucm449675.htm. Accessed March 31, 2016.
[8] Food and Drug Administration. Form FDA 483 issued to I.V. Specialty, Ltd. on February 15, 2016. http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofGlobalRegulatoryOperationsandPolicy/ORA/ORAElectronicReadingRoom/UCM489814.pdf. Accessed March 31, 2016.
[9] *Ibid.*

1) Your firm does not conduct sterility and endotoxin testing of finished drug products purporting to be sterile. …
2) Your firm conducts sterility testing using the … method which has the following deficiencies."

- "Clothing of personnel engaged in the manufacturing, processing, packing, and holding of drug products is not appropriate for the duties they perform. Specifically,
  1) Gowning garments are stored and donned in the ISO 8 ante room and worn during aseptic operations were not sterile …
  2) During aseptic processing [of drug products]… we observed the pharmacy technician to be operating with exposed hair, ears, neck and forehead."
- "Procedures designed to prevent microbiological contamination of drug products purporting to be sterile are not established, written, and followed. Specifically, … [y]our cleanroom practices are deficient to prevent product contamination."
- "Aseptic processing areas are deficient regarding the system for cleaning and disinfecting the room and equipment to produce aseptic conditions."

Lacking the authority to order I.V. Specialty to recall its injectable drugs and being unable to force the company to cease operations without undertaking a lengthy legal process, the FDA on March 7 recommended that the company take these actions voluntarily, but the company refused to do so. Therefore, in an attempt to protect patients from the risk of life-threatening infections, the FDA on March 9 issued an alert that stated the following:[10]

> The U.S. Food and Drug Administration is alerting health care professionals and patients not to use drug products intended to be sterile that are produced and distributed by I.V. Specialty Ltd., Austin, Texas, due to lack of sterility assurance.
>
> Health care professionals and consumers should immediately check their medical supplies, quarantine any drug products labeled as sterile from I.V. Specialty, and not administer them to patients. Health care professionals should make alternative arrangements to obtain any medications they administer to patients from reliable sources that adhere to proper quality standards.
>
> During FDA's recent inspection of I.V. Specialty, investigators observed insanitary conditions, including poor sterile production practices, which raise concerns about I.V. Specialty's ability to assure the sterility of the drug products it produces. Administration of a non-sterile product intended to be sterile may result in serious and potentially life threatening infections or death.

In light of the FDA's inspection findings, the injectable drug products made by I.V. Specialty represent an immediate threat to the health and welfare of patients in Texas, and the company's recalcitrance is unacceptable. Therefore, given the FDA's lack of authority to order I.V. Specialty to immediately recall its injectable drugs and cease operations, the Texas State Board

[10] Food and Drug Administration. FDA alerts health care professionals and patients not to use human and animal sterile drug products produced and distributed by I.V. Specialty, Ltd., Austin, Texas. http://www.fda.gov/Drugs/DrugSafety/ucm489951.htm. Accessed March 31, 2016.

of Pharmacy must use its legal authority to force the company to cease operations by suspending immediately the pharmacy license for I.V. Specialty and the licenses of all the company's pharmacists.

We also are concerned that there is generally a lack of adequate coordination and communication between the FDA and state pharmacy boards in responding to companies such as I.V. Specialty. To help us advocate for improvements in these areas, please address the following questions:

(1) Did the FDA inform the Texas State Board of Pharmacy in advance of its two inspections of I.V. Specialty and invite a representative of the board to participate in the inspections?

(2) Did the FDA communicate to the Texas State Board of Pharmacy the findings of its inspections? If so, when were the findings communicated to the board, and did the board receive unredacted copies of the FDA Form 483 for each inspection?

(3) What measures could be taken to improve the coordination and communication between the FDA and state pharmacy boards in responding to companies such as I.V. Specialty?

Thank you for your prompt attention to these important public health matters.

Sincerely,

Michael Carome, M.D.
Director
Public Citizen's Health Research Group

Sidney M. Wolfe, M.D.
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