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November 20, 2000

Docket Manager
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 5630 Fishers Lane, Rm. 1061
 Rockville, MD 20852

Re: Response of the International Academy of Compounding Pharmacists to
 Inquiries Made During the October 27, 2000, FDA Part 15 Hearing on the
 Prescription Drug Marketing Act; Docket No. 92N-0297

Dear Sir/Madam:

Enclosed for filing in the above-captioned docket, please find one original and three copies of (1) a letter from Shelly Capps, Executive Director of the International Academy of Compounding Pharmacists to Jane Axelrad, Associate Director for Policy, CDER and (2) Testimony of Shelly Capps at the October 27, 2000 FDA Part 15 Hearing on the Prescription Drug Marketing Act of 1987.

If you have any questions, please do not hesitate to contact me.

Sincerely,



Mary Kate Whalen

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November 20, 2000

Jane Axelrad
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Re: Response of the International Academy of Compounding Pharmacists to
Inquiries Made During the October 27, 2000, FDA Part 15 Hearing on the
Prescription Drug Marketing Act; Docket No. 92N-0297.

Dear Ms. Axelrad and Members of the Panel:

This responds to questions asked of the International Academy of Compounding Pharmacists ("IACP"), during the October 27, 2000, Food and Drug Administration ("FDA") Part 15 Hearing regarding FDA's December 3, 1999, final rule implementing the pedigree provisions of the Prescription Drug Marketing Act of 1988 ("PDMA"). The information presented below demonstrates that there is no reason to change the current industry practice regarding the distribution of bulk drug ingredients to compounding pharmacies.

At the outset, it is important to briefly reiterate the role of drug compounding in United States health care. Each day over 40,000 prescriptions are compounded - roughly one percent (1%) of the total prescriptions dispensed in the United States. Compounding is a necessary medical option for many patients. For example, some patients, because of allergies or other sensitivities, simply cannot tolerate standard drug formulations. If a patient is allergic to a preservative or a dye in a manufactured product, the compounding pharmacist, working with the treating physician, can prepare a dye-free or preservative-free dosage form. Other patients need drug formulations that manufacturers have discontinued

for economic reasons. Drug companies do not, and cannot, provide the same type of patient-specific drug therapies as compounding pharmacists.

Hospice patients who have difficulty swallowing a capsule can instead be prescribed pain medications, anti-emetics and antibiotics in compounded lozenges, lollipops, skin patches or suppositories. For example, phenytoin sodium USP is an anti-convulsant used in suppository form for terminal cancer patients who can no longer swallow. Through compounding, pharmacists can fill a physician's prescription for a suppository form with effective dosage strengths which are not commercially available. For such patients to obtain the same relief through a commercial product would require the insertion of 2-3 suppositories at a time.

As demonstrated below, as well as in the attached copy of my written statement from the October 27 hearing and the comments previously filed by IACP, adequate safeguards already exist to protect the public from damaged prescription medications, including those compounded from bulk drug ingredients. The FDA's final rule will not further Congress' or FDA's stated purpose of protecting the public health and safety. Instead, it can only serve to harm the public by disrupting the supply of bulk drug ingredients required to provide patients with medically necessary patient-specific drug therapies available only through compounders.

A. Sources of Supplies of Bulk Drug Ingredients to Compounding Pharmacists

The FDA panel for the October 27, 2000 Part 15 hearing ("the Panel") asked about the number of companies in the United States that supply bulk active pharmaceutical ingredients ("APIs") to compounding pharmacies and the sources of supply for these companies. There are an estimated 15-20 companies that supply bulk drug ingredients to compounding pharmacists.

One large supplier of bulk active pharmaceutical ingredients to pharmacies for use in compounding drugs distributes 415 different APIs. According to this supplier approximately 90% of all bulk APIs are procured from domestic sources. The remaining 10% of APIs are obtained from sources outside of the United States. Fifty percent of bulk APIs come directly from manufacturers, while the remaining 50% is obtained through secondary suppliers. On average the secondary suppliers carry a greater variety of bulk APIs than individual manufacturers. For example, one secondary supplier distributes 75 of the different APIs stocked by the company. These secondary suppliers of bulk APIs are the most vulnerable under the rule and are likely to be forced out of business if FDA implements the final rule and changes the past 12 years of industry practice.

B. Quality Control Procedures for Bulk API Suppliers

The Panel asked for information about quality control procedures used by repackagers of bulk drug ingredients sold to compounding pharmacists. Congress has recognized the important health benefits of compounded therapies, as demonstrated most recently by the passage of the Food and Drug Administration Modernization Act ("FDMA") of 1997. Under FDMA, licensed pharmacists compound medications pursuant to specific requirements implemented to ensure quality assurance and to safeguard the public. One such protection includes the use of bulk drug substances that comply with the standards of an applicable United States Pharmacopoeia ("USP") or National Formulary ("NF") monograph. Moreover all establishments must be registered under the Federal Food, Drug, and Cosmetic Act, including foreign establishments. Further, all bulk drugs received by repackagers must be accompanied by certificates of analysis. 21 U.S.C. § 353(b).

Prior to purchasing any bulk APIs from any source - foreign or domestic - the large API distributor requests proof of registration with the FDA and/or labeler codes from that source. Further, as a repackager of bulk APIs, the company has implemented additional quality control procedures, as detailed below, which provide safeguards for bulk APIs obtained through either domestic or international sources and distributed to compounding pharmacies. These procedures adequately protect the public from the threat of counterfeit, damaged or adulterated bulk drugs.

This distributor requires certificates of analysis from all of its suppliers. To promote consistency in format, the company is creating standardized certificates of analysis and making them available on the company web site for all of its customers. The certificates of analysis are made available to the compounding pharmacists.

The following procedures ensure quality control of the APIs and to comply with Good Manufacturing Practices ("GMPs"):

1. Upon receipt, all chemicals are visually inspected for product and container integrity and put into quarantine.
2. The chemical's documentation is examined for completeness and accuracy.
3. A sample is taken to the Quality Control laboratory where the physical properties of the chemical are compared with the chemical's description given on the Certificate of Analysis, USP, NF or other reference document.

4. The chemical is then put through a variety of tests to confirm its identity. Depending on the substance, tests may include IR spectra, UV-VIS spectra, meltpoint, specific gravity, and various chemical tests.
5. Once the chemical meets the necessary criteria, the lot number is activated and it is released from quarantine.
6. Prior to repackaging, the bulk container's barcode is scanned against the package labels to verify the information.
7. After the repackaging process is complete, a random sample is pulled and its identity is again confirmed.
8. While filling an order, the chemical's barcode is scanned which ensures that the correct part number, size, and lot number has been pulled for the corresponding order.
9. A final quality control audit is performed by again scanning all barcodes to validate order completeness.

In light of these quality control procedures, imposing a pedigree requirement would provide no additional protection. The controls established by repackagers to meet GMPs assure product quality.

C. Recalls of Bulk APIs

The Panel also inquired about the ability of suppliers of bulk APIs to compounders to track drugs in the event of a recall. For example, this large distributor has successfully completed recalls regarding bulk drug ingredients. One recall of an API was initiated by a vendor. After receiving the recall letter from the vendor identifying the lot number of the substance, the company was able to pull the corresponding lot numbers for the API obtained from that vendor, identify specific purchasers and amounts of the substance ordered, and issue a recall on the same day. IACP is aware that other API distributors can also track shipments.

D. Impact on health care

As demonstrated in my written statement from the October 27 hearing, along with the statements of the American Pharmaceutical Association, the Pharmaceutical Distributors Association and Purity Wholesaler, the pedigree requirements of FDA's

December 3, 1999 final rule will result in a disruption of supplies of both finished prescription drugs and bulk drug ingredients to pharmacies. The inability of compounding pharmacists to purchase bulk drug ingredients will risk the health of patients whose access to vital compounded medications would be seriously disrupted. Taking into account the numerous areas in which drugs are routinely compounded - such as home-health centers and hospitals - this will affect approximately 10,000 pharmacies resulting in tens of thousands of patients who will not be able to obtain medical treatment necessary for quality health care. Any benefits that could be gained through this rule would be substantially outweighed by the public health costs, preventing patients from receiving the prescribed medications.

CONCLUSION

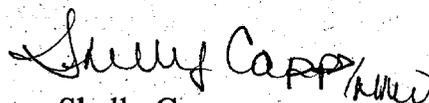
The burdensome pedigree requirements for the distributors of bulk drug ingredients are unnecessary and will not further Congress' intent in protecting the public from unsafe drugs. Sufficient quality control and antidiversion safeguards and penalties exist under current FDA record keeping, licensing and GMP regulations pertaining to initial manufacturers, repackagers and pharmacies to ensure that damaged, adulterated or counterfeit bulk drug ingredients are not processed into compounded medications for distribution to consumers. The PDMA legislative history did not discuss a single instance of any injury or adverse event associated with adulterated, damaged, subpotent or counterfeit bulk drug ingredients used in compounded drugs. Nor has FDA, through the course of this rulemaking or during recent Congressional hearings regarding FDA's monitoring of imported bulk pharmaceutical chemicals, provided any evidence of adulterated, damaged, counterfeit or subpotent bulk drug ingredients that were subsequently used in compounded drugs or any adverse events reported from patient use of such compounded drugs. There is no evidence whatsoever that requiring pedigree information would provide any benefits for APIs used in compounding.

Accordingly, we again urge that the FDA final rule be amended so that it is consistent with Congressional intent to clearly indicate that the pedigree requirements apply only to distributors of finished form prescription drugs, not to the distribution of bulk drug ingredients. If FDA chooses to ignore the will of Congress, the rule should at least be consistent with industry practice over the past 12 years and allow authorized distributor status to be demonstrated by two or more transactions with a manufacturer or other authorized distributor during a 24 month period, and require that unauthorized distributors only go back to the last authorized distributor for pedigree information.

Jane Axelrad
November 20, 2000
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Thank you for the opportunity to present the position of the IACP on this crucial final rule.

Sincerely,

A handwritten signature in cursive script that reads "Shelly Capps". To the right of the signature, there are some initials that appear to be "HWD".

Shelly Capps
Executive Director

cc: FDA Part 15 Panel
Docket Manager 92N-0297