

VIA FEDERAL EXPRESS
AND FACSIMILE TO 301-827-8904

Mr. Melvin Szymanski
Compliance Officer
U.S. Food and Drug Administration
Center for Drug Evaluation and Research
Office of Compliance, HFD-310
5600 Fishers Lane
Rockville, Maryland 20857

October 21, 2003

Dear Mr. Szymanski:

I am writing in response to the warning letter of September 16, 2003, copies of which were addressed to me, Robert Howard, and Joseph Todd. Future correspondence can be directed to me at the above address. Thank you for the courtesy of extending the time to respond.

The letter makes specific allegations regarding actions by CanaRx and individuals acting on its behalf, in addition to stating the agency's more general objection to U.S. consumers' purchase of prescription drugs from Canada, and the role CanaRx may play in that for some consumers. I will respond to both in some detail, but also am compelled to state at the outset a very important general proposition: we at CanaRx share FDA's interest in the health and safety of U.S. consumers. Contrary to the agency's assumptions and assertions, we take numerous steps to safeguard our customers' health and safety, and what we do creates no risk beyond that faced by U.S. consumers conducting similar transactions domestically. With that in mind, we look forward to working with FDA to resolve this situation.

How CanaRx Does Business

The letter alleges a chain of events that purports to describe the manner in which CanaRx conducts its business. Unfortunately, those allegations, which serve as the basis for many of the letter's assertions of illegality and risk, do not accurately reflect either how CanaRx functioned in the past or how we operate at present. Reflecting recent changes in how we do business (some of which have been instituted since issuance of the warning letter), please be aware that:

- CanaRx does not use a U.S. mail post office box. The information required of consumers (which includes the U.S. prescription, important patient medical information, enrollment forms, and written confirmation that the patient has read CanaRx's representations) is received by CanaRx in Canada.
- The U.S. prescriptions and pertinent medical information are reviewed by a duly licensed Canadian doctor, who exercises independent medical judgment in determining whether to issue a prescription. On many occasions, the doctor has

contacted the patient for clarification, and in some instances has declined to issue the prescription on the basis of the additional information.

- CanaRx does not act as a pharmacy. We do not fill prescriptions, nor do we ship the drugs or otherwise take possession of them at any time. We obtain the necessary information and provide it to a Canadian doctor, who in the appropriate circumstances issues a prescription. That prescription is provided to a pharmacy, which ships the drugs directly to the patient. CanaRx does, however, require the pharmacies make provision for proper shipment, so that drugs requiring special shipping arrangements (such as insulin, which is shipped in insulated packaging via overnight delivery) are handled appropriately.
- CanaRx limits the formulary of drugs for which it will process prescriptions, in two important ways. First, we do not process prescriptions for controlled substances or immediate-use antibiotics. Second, we only process prescriptions to be filled by drugs that are the subject of an approved NDA or ANDA, manufactured by the FDA-approved manufacturer, at the manufacturing location required by the approval, and in accordance with requirements of the approval relating to formulation, source and specifications of active ingredients, processing methods, manufacturing controls, container/closure system, and appearance. Some of these drugs are manufactured in the U.S., while others are manufactured in foreign facilities, but all are manufactured in facilities that are within the scope of the applicable approval, and all are subject to GMP requirements and FDA inspection for compliance, and to regulation and oversight by Health Canada.
- CanaRx limits the quantities of drugs for which it will process prescriptions. In order to provide additional safeguards, with rare exception, we process prescriptions only for quantities of drug that can be provided without opening the sealed container in which the pharmacy receives the drug. For example, Nexium comes in sealed containers of 84 capsules each. If a patient's prescription calls for one pill a day (the typical dose), we would process a prescription only for 84 days of drug, and the patient would have to seek a new prescription after that time. We impose this restriction to avoid any risk (or even just consumer concern) that might be implicated by repackaging after the product leaves the manufacturer.

Insulin Shipment

The warning letter alleges that CanaRx “does not reliably use good shipping practices to assure drug safety and effectiveness.” The basis for this appears to be an FDA sting operation, in which (as the warning letter states) an investigator filled multiple prescriptions through CanaRx, including one for insulin. The warning letter asserts that insulin “generally should be stored under refrigerated conditions,” and claims that the CanaRx shipment of insulin “was not shipped in a manner that ensures adherence with storage conditions specified in FDA approved labeling, potentially compromising its safety and effectiveness.” This allegation concerned us, because of the possible implications for patient safety. Because the warning letter lacks any of the details

that are necessary for CanaRx to respond substantively, I called FDA Associate Commissioner William Hubbard to obtain additional information. Mr. Hubbard told me only that the shipment in question was made to an address in the midwest U.S., and that it took five days to arrive at its destination. He did not provide any more details or tell me whether the safety or effectiveness of the insulin had, in fact, been compromised.

Without more information, it remains difficult for me to respond to this specific allegation, but I can tell you that the situation described to me is flatly inconsistent with CanaRx policies and procedures, and bears no relation to any information we have regarding our insulin shipments. After receiving the warning letter, we contacted every U.S. consumer to whom we had shipped insulin. With one exception (not in the midwest), each customer reported no problems with his or her insulin shipment. One customer told us the insulin had arrived at room temperature, and we immediately sent him another shipment by overnight express, at no cost, and asked him to return the first shipment to us, at our expense. We also checked U.S. Postal Service shipping records (previously, shipments of insulin were sent by Express Mail), and determined that the initial shipment to that customer had been picked up within 48 hours of having been shipped.

Although insulin may be refrigerated and often is stored in refrigeration, it is not required to be handled that way and may be stored for up to 28 days at room temperature. Our policies are consistent with that; we require insulin to be refrigerated before shipment, then shipped with cold packs in insulated packaging for delivery within 24 hours.^[1] To our knowledge, that practice is consistent with – or exceeds – the practices of many entities that provide mail-order insulin within the U.S. In fact, the one customer whose insulin arrived at room temperature told us he was not concerned, and that he had on occasion received insulin shipments at room temperature from other (presumably domestic U.S.) suppliers.

It is inaccurate and unfair to make a blanket assertion as to the inadequacy of CanaRx's shipping practices on the basis of a single episode, particularly one that is contrary to our policies and that we cannot corroborate. Further, even if the incident occurred as described by FDA, this rare occasion does not create a risk any greater than that posed by everyday domestic U.S. shipments of mail- or Internet-ordered insulin. We know of no prescription processed by CanaRx that has been the subject of any adverse event.

Website Statements

FDA also takes exception to certain statements at www.canarx.com as incorrectly describing the agency's personal importation policy and misleading U.S. consumers as to the safety of prescriptions processed by CanaRx and filled by Canadian pharmacies. We disagree with the agency on these points.

It is true that the personal importation policy is described in chapter 9 of the *FDA Regulatory Procedures Manual* as an exercise of enforcement discretion limited to certain defined situations. But that description bears little resemblance to FDA's actual, longstanding policy, under which U.S. Customs allows the personal importation of virtually any drug. Additionally, given the limits CanaRx has imposed on itself – processing prescriptions only for

FDA-approved drugs, and in quantities that do not require opening a sealed container, for example – we do not believe statements about the drugs provided are false or misleading.

The literal claims are not false or misleading. For instance, FDA objects to the statement that “there is no difference” between drugs purchased from U.S. pharmacies and those dispensed by Canadian pharmacies in response to prescriptions processed by CanaRx. The agency identifies a number of ways in which “prescription drugs purchased from foreign countries” are “different” from drugs purchased in the U.S., including that foreign purchased drugs “generally are not FDA-approved, do not meet FDA standards, and are not the same as the drugs purchased in the United States.” However true FDA’s characterization may be with regard to foreign drugs generally (which CanaRx does not necessarily concede), it certainly is not true with regard to the specific drugs for which CanaRx processes prescriptions.

Similarly, even if, as FDA contends, “[f]oreign dispensers of drugs to American citizens may provide patients with incorrect medications, incorrect strengths, medicines that should not be used in people with certain conditions or with other medications, or medications without proper directions for use,” FDA’s own enforcement actions and public pronouncements amply demonstrate that those same risks exist with regard to domestic U.S. dispensers. Moreover, we are unaware of any such incident involving a prescription processed by CanaRx and, given the nature of the limited CanaRx formulary, we do not believe the risk is any greater than with regard to drugs dispensed domestically.

Any reasonably implied representations are not false or misleading. The statements do not imply (nor would reasonable consumers infer) the claims regarding safety that FDA asserts, but even if such implied claims are assumed, they are not false or misleading. Again, given the limited drugs for which CanaRx processes prescriptions, the other safeguards we take, and the oversight Health Canada provides regarding drugs within our country, we believe the drugs are as safe as those dispensed in the U.S.[\[2\]](#)

Nonetheless, we are in the process of reviewing all statements on the website, and have made revisions intended to address the agency’s expressed concerns.

Legal Issues

To be sure, CanaRx disagrees with FDA’s general proposition that the prescriptions processed by CanaRx and filled by Canadian pharmacies pose a greater risk than prescriptions filled by U.S. pharmacies. As discussed above, FDA makes any number of broad statements about the risks of “foreign drugs,” many of which involve scenarios that do not relate to the limited activity in which CanaRx engages. At the same time, however, I recognize that FDA has taken the position that, regardless of whether or not there is any enhanced risk, CanaRx is violating the Food, Drug, and Cosmetic Act (FDCA or the Act), basically because the drugs in question are either U.S.-manufactured drugs that only the manufacturer may import back to the U.S., or unapproved new drugs.

As a threshold matter, CanaRx does not believe its actions violate the FDCA. In the first instance, as discussed above, CanaRx will not process prescriptions for drugs that are

unapproved new drugs. Some of the drugs for which CanaRx processes prescriptions are approved drugs manufactured at foreign facilities inspected and approved by FDA, and which may be imported under the FDCA. The other drugs for which CanaRx processes prescriptions are U.S.-manufactured, and I understand that FDA would assert they are subject to the Act's "reimportation ban." But CanaRx clearly does not import these drugs, nor do we "cause" their importation. The Act leaves undefined precisely who can be said to "cause" their importation. Because there can be criminal penalties for violating the Act,[\[3\]](#) and Congress has not indicated that the term's ordinary meaning does not apply, "cause" must be narrowly defined, and should not reach CanaRx's activities.

Additionally, we believe the actions being threatened against CanaRx, as well as the reimportation ban more generally, are inconsistent with U.S. obligations under a number of international trade agreements. For example, because the reimportation ban, at least as applied in this context, is not based on scientific principles or an appropriate risk assessment, it does not meet the requirements enumerated in Article 712 of the North American Free Trade Agreement (NAFTA) with respect to sanitary and phytosanitary measures. As a result, the actions may constitute a disguised restriction on trade within the meaning of that Article. Furthermore, because less trade-restrictive means exist for addressing any legitimate health or safety concerns, the ban also may constitute an unnecessary obstacle to trade under NAFTA Articles 712 and 904. FDA's actions also may be inconsistent with U.S. obligations under NAFTA Article 301 to grant "national treatment" to the goods of Canada. NAFTA Chapter 11 provides a private right of action for the abrogation of such international obligations.[\[4\]](#)

We also believe the personal importation policy, as enforced by FDA, is unlawful for a number of reasons, including that it is arbitrary and capricious and not in accordance with the law. Among other things, the policy is not well-crafted to meet its presumed goal of protecting U.S. consumers' health and safety. By permitting importation by individuals while limiting enforcement to those FDA considers to be engaged in "commercial" conduct, the agency threatens to eliminate from the process entities, such as CanaRx, that are actually in the best position to help safeguard patients. Had FDA formulated its policy through notice-and-comment rulemaking, it would have had the opportunity to receive public input and consider issues that likely would have led to a more rational, defensible policy.

Furthermore, the policy flouts Congressional findings that led to the adoption of the Medicine Equity and Drug Safety Act of 2000 (MEDS Act). To date, FDA has not complied with the requirements of the MEDS Act, which calls for regulations to permit importation of prescription drugs in certain circumstances. FDA's determination that it would be "impossible to ensure that the MEDS Act would result in no loss of protection for the drugs supplied to the American people," as reported in HHS Secretary Thompson's July 9, 2001, letter to Senator Jeffords, does not comport with the facts, particularly with regard to the drugs with which CanaRx is involved. The extent to which FDA actually reviewed those facts is not evident from the public record. Moreover, the fact that importation from *some* sources may pose an additional risk does not excuse the total failure to seriously consider (let alone develop) regulations that provide for importation from sources or under circumstances where that risk would not be present – particularly where Congress has expressed the need for U.S. consumers to have more affordable access to prescription drugs.

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The warning letter implicates a number of significant issues of great importance to FDA, CanaRx, and U.S. consumers. To the extent legitimate concerns about the health and safety of U.S. consumers are at issue, we hope the agency recognizes the steps we have taken to address those concerns. If the agency has continuing concerns, please contact me.

Sincerely,

G. Anthony Howard

[1] As noted above, some previous insulin shipments were sent by U.S. Postal Service Express Mail, for delivery within 48 hours. Although the incident described in the warning letter does not match any shipment we reviewed (and, in any case, would represent an anomaly), we have revised CanaRx policies to require insulin and other such drugs to be shipped by the pharmacy via overnight delivery.

[2] If, as discussed below, FDA had issued the regulations called for by the MEDS Act, there would be specific means to demonstrate the safety of drugs imported by prescriptions processed by CanaRx.

[3] As you no doubt are aware, violative importation in general is a misdemeanor or felony, and reimportation of a U.S.-manufactured drug by anyone other than the manufacturer is a felony.

[4] FDA's actions also may violate similar obligations imposed upon the United States by virtue of agreements under the authority of the World Trade Organization, including the Agreement on the Application of Sanitary and Phytosanitary Measures, the Agreement on Technical Barriers to Trade, and the Agreement on Trade-Related Investment Measures.