DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NOV ** 6 2003

Via Facsimile and U.S. Mail
G. Anthony Howard
President
CanaRx Services, Inc.
P.O. Box 21086
Tecumseh, ON N8N 4S1
Canada

Via Facsimile and Federal Express
Joseph K. Todd, Jr.
Regional Manager
CanaRx Services, Inc.
510 S. Harkless Dr.
Syracuse, IN 46567

Re: CanaRx Services, Inc. ("CanaRx")

Dear Messrs. Howard and Todd:

We have reviewed CanaRx's response to the warning letter that it recently received from the U.S. Food and Drug Administration ("FDA"). While we have considered the points in the response and we acknowledge CanaRx's changes to its operations as a result of our warning letter, we find that the response is deficient in a number of respects. Following is a discussion of some of those deficiencies.

I. CanaRx's Practices Violate U.S. Law.

A. Violations of the Federal Food, Drug, and Cosmetic Act

As a basic matter, CanaRx has not explained how its practices satisfy the Federal Food, Drug, and Cosmetic Act ("Act") provisions intended to assure drug safety. CanaRx claims that all drugs obtained through it "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 . . . ." and that "[A]ll [drugs] 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." Notwithstanding these assertions, Canadian and other foreign versions of FDA-

approved drugs are generally considered unapproved in the United States. This is so because FDA approvals are manufacturer-specific, product-specific, and include many requirements relating to the product, such as manufacturing location, formulation, source and specifications of active ingredients, processing methods, manufacturing controls, container/closure system, and appearance. 21 C.F.R. § 314.50. Frequently, drugs sold outside of the United States are not manufactured by a firm that has FDA approval for that drug. Moreover, even if the manufacturer has FDA approval for a drug, the version produced for foreign markets usually does not meet all of the requirements of the U.S. approval, and thus it is considered to be unapproved. 21 U.S.C. § 355. Even if a drug bound for a foreign market is produced in the same plant as a similar drug approved for the U.S. market, FDA is not able to track that drug in foreign commerce before it enters this country. Consequently, it is difficult for the Agency to determine that a drug appearing at a U.S. border is, in fact, the one produced in the FDA-inspected plant, pursuant to FDA approval.

In addition, CanaRx does not seem to have any comprehensive oversight mechanisms in place to assure that its claims of safety and efficacy are accurate. The response letter indicates that CanaRx does not fill prescriptions or send drugs to its customers. Indeed, according to the letter, at no time does the company have possession of the drugs that its customers receive. Rather, CanaRx forwards its customers' prescriptions to Canadian pharmacies, which are then responsible for filling them and shipping the drugs. Absent any control over these drugs, it is unclear how CanaRx would know what its customers actually receive. CanaRx has no way of ensuring that the drugs are not adulterated or misbranded in violation of the Act. Thus, CanaR operations raise the concerns that FDA has identified in connection with drugs from foreign sources - that U.S. citizens may be receiving the wrong drugs, drugs with the incorrect strength, drugs that are dangerous when combined with other drugs, and drugs that lack proper directions for use. These risks are exacerbated by the fact that CanaRx is not a licensed pharmacy and apparently is not otherwise subject to regulatory standards or regulatory oversight, either in Canada or the United States (if, in fact, the company no longer has a physical presence in the United States).

Even if the drugs that CanaRx helps to import were to possess the qualities that it ascribes to them, they would still be illegal. For FDA-approved drugs manufactured in the United States, 21 U.S.C. § 381(d)(1) clearly limits their importation to these drugs' original manufacturer. Congress determined that the safety and quality of the drugs could not otherwise be assured. Importing drugs into the United States in violation of Section 381(d)(1) violates 21 U.S.C. § 331(t). Drugs obtained through CanaRx that are manufactured abroad also generally violate the Act. Even if the manufacturer has FDA approval for a particular drug, the version produced for foreign markets usually does not meet all of the requirements for U.S. approval. For example, there may be deviations regarding the drug's formulation, active ingredients, or packaging. Such deviations would make the drug an unapproved drug. 21 U.S.C.

§ 355. The drug may also be misbranded because it lacks certain information required by 21 U.S.C. § 352, but which is not required in the foreign country. Or, the drug may be labeled in a language other than English (21 C.F.R. § 201.15(c)) or dispensed without a valid prescription. 21 U.S.C. § 353(b)(1).

It is no defense to these violations for CanaRx to claim that it is not the actual importer of the drugs. The Act proscribes the introduction into interstate commerce of adulterated and misbranded drugs, "and the *causing* thereof . . ." 21 U.S.C. § 331 (emphasis added). In the course of its operations, CanaRx solicits orders from U.S. consumers, forwards those orders to Canadian doctors and pharmacies, and ensures that the orders are shipped to the customers seeking them. Further, CanaRx created this distribution system, promotes it, and profits from its operation. Plainly, given this significant level of involvement, it is apparent that CanaRx is *causing* the introduction of adulterated and misbranded drugs into interstate commerce. We also disagree with CanaRx's assertion that the term "cause" must be narrowly defined. *See United States v. Bacto-Unidisk*, 394 U.S. 784 (1969).

B. The Personal Importation Policy

FDA's personal importation policy guides the agency's enforcement discretion with respect to imports by individuals of drugs for their personal use. Under certain *defined* circumstances, as a matter of enforcement discretion, FDA allows consumers to import otherwise illegal drugs. Under this policy, FDA may permit individuals and their physicians to bring into the United States small quantities of drugs sold abroad for a patient's treatment of a serious condition for which effective treatment may not be available domestically. FDA has followed this approach with products that do not present an unreasonable risk and for which there is no known commercialization and promotion to U.S. residents.

While the personal importation policy describes the agency's enforcement priorities, it does not change the law. And the policy does not legalize importation of foreign versions of drugs that are not part of this country's comprehensive system for assuring a drug's safety from the point of manufacture, through distribution, and on to the pharmacy and patients. Moreover, personal importation is very different from the case with CanaRx, in which the foreign versions of drugs are being diverted from standard, well-regulated channels to U.S. citizens for a substantial profit. CanaRx's large-scale commercial import operation differs from the personal importation of drugs physically purchased in a well-regulated pharmacy.

CanaRx's response letter asserts that the personal importation policy is "arbitrary and capricious and not in accordance with the law." The letter further argues that the policy should have been developed through notice-and-comment rule making. We are unpersuaded by these points. As discussed above, the policy is a function of FDA's enforcement discretion. As an established line of decisions makes clear, federal agencies have extremely broad latitude in making enforcement

decisions. *See, e.g., Heckler v. Chaney*, 470 U.S. 821 (1985) (the exercise of enforcement authority is presumptively committed to agency discretion by law). The response letter also complains that the personal importation policy bears little resemblance to "FDA's actual, longstanding policy, under which U.S. Customs allows the personal importation of virtually any drug." To date, FDA has focused its limited enforcement resources on potentially dangerous drugs and those who, like CanaRx, commercialize the practice of importing illegal drugs without regulatory oversight. Thus, as a matter of enforcement discretion, FDA has generally not seized foreign pharmaceuticals from U.S. citizens carrying them into the country for their personal use. Instead, FDA has attempted to educate those citizens about the safety risks associated with consuming foreign drugs. Nevertheless, the law remains unchanged and FDA retains the authority to bring an enforcement action whenever a provision of the Act is violated.

C. Trade Agreements and the Medicine Equity and Drug Safety Act

In challenging the Act's drug-import restrictions, CanaRx's response letter cites certain trade agreements, including the North American Free Trade Agreement ("NAFTA"). The letter asserts in particular that FDA's "reimportation ban" is at odds with Article 712 of the NAFTA, which requires that sanitary and phytosanitary measures be based on "scientific principles or an appropriate risk assessment." We disagree with this contention. FDA's action is fully consistent with the relevant provisions of the NAFTA and other trade agreements. The provisions relating to sanitary and phytosanitary measures that CanaRx cites, for example, do not apply to FDA-regulated drugs

The response letter also addresses the Medicine Equity and Drug Safety Act of 2000 ("MEDS Act") and questions why the Secretary of Health and Human Services ("HHS") has not made the written certification to Congress that is necessary to trigger the law under 21 U.S.C. § 384(l). Section 384(l) is intended to safeguard the public health. Under that provision, the Secretary cannot make the necessary certification unless he can demonstrate to Congress that implementation of the MEDS Act "will (1) pose no additional risk to the public's health and safety; and (2) result in a significant reduction in the cost of covered products to the American consumer." 21 U.S.C. § 384(l).

As the response letter notes, in a January 2001 letter to Senator James Jeffords, HHS Secretary Tommy Thompson explained why he could not make the Section 384(l) certification. His reasons included the danger that, if implemented, the MEDS Act, would "pose a greater public health risk than we face today," and would result in "a loss of confidence by Americans in the safety of our drug supply." Notably, Secretary Thompson's findings re-affirmed the decision that then-Secretary Donna Shalala made in 2000 when she also concluded that the standards set forth in Section 804(l) were not met.

CanaRx counters that special consideration should be given to its operations and to Canadian operators like it. This argument ignores the requirements of the Food, Drug, and Cosmetic Act, which is intended to assure the safety of the drugs used by Americans. Moreover, the MEDS Act does not limit drug imports to Canada, but would potentially open American borders to drug shipments from all of the nations set forth in 21 U.S.C. § 382(b). This poses an unacceptable health risk to U.S. citizens.

II. CanaRx's Operational Changes Do Not Make Its Otherwise Illegal Practices Legal.

As we noted at the outset of this letter, we acknowledge that CanaRx has changed its business practices. But these changes do not affect our judgment of the overall safety or legality of those practices. Nor do the changes mitigate the concerns expressed in our September 2003 warning letter. For example, taking as true CanaRx's assertion that prescriptions processed through it are reviewed by Canadian doctors and filled by Canadian pharmacists, it is nevertheless the case that the drugs then shipped to the United States are generally illegal. As troubling, it appears that neither CanaRx nor the pharmacies that it employs can verify the source of those drugs. Nor are they at all knowledgeable about the manufacture, packing, and labeling of the drugs. This raises FDA's specific concerns about all illegally imported drugs: that they are unapproved, do not meet FDA standards, and are otherwise less safe than drugs purchased in the United States.

We are likewise unpersuaded by CanaRx's assertion that it limits the quantity of drugs for which it will fill prescriptions. CanaRx states that it typically processes prescriptions only for quantities of drugs that can be provided in the sealed containers sent to the pharmacy filling the prescription. This raises the question of how the company handles prescriptions calling for amounts less than the amounts in the sealed containers. We have no way of knowing whether CanaRx would refuse the prescription, disregard the quantity identified in the prescription, or deviate from its policy of not opening sealed containers. In any event, the importation of drugs under these circumstances is illegal and threatens consumer safety.

Finally, CanaRx's operational changes do not alleviate our concern that the company is misleading U.S. consumers. Claims that drugs supplied by Canadian pharmacies are FDA approved and that "there is no difference" between them and drugs purchased in the United States simply are not true. Unlike FDA-approved drugs purchased in this country, the drugs that CanaRx markets are generally illegal when imported, and their importation circumvents measures designed to protect U.S. citizens. Consequently, FDA remains fundamentally concerned about CanaRx's misleading claims, which could pose significant health risks to consumers.

* * *

For the reasons explained above, CanaRx has not mitigated FDA's concerns about the legality of, and the risks associated with, its business. These risks are exacerbated by CanaRx's business model, in which its employees review medical histories, cause prescriptions to be written, determine the amount of medication to be dispensed, and supervise the shipment of that medication. Although CanaRx's recent efforts to move business practices outside of the United States may limit FDA's jurisdiction over certain aspects of its operations, we take seriously the violations and potential safety risks that CanaRx continues to cause, and we are reviewing our enforcement options. We are also forwarding information about these violations to the appropriate Canadian authorities for their review.

Sincerely,

David J. Horowitz, Esq.
Director
Office of Compliance
Center for Drug Evaluation and Research
Food and Drug Administration

cc: CanaRx
Registrant
302 Russel Woods Drive
Lakeshore, ON N8N 4K5
Canada

Melanie Brim, Director
Michigan Board of Pharmacy
Michigan State Department of Consumer & Industry services
611 West Ottawa Street
Lansing, MI 48909-8170
Fax (517)373-2179

Greg Ujiye
Pharmacy Practice Programs
Ontario College of Pharmacists
483 Huron St.
Toronto, ON M5R 2R4
Canada
Fax (416)847-8292

Daniele Dionne
Inspectorate Health Canada
Health Products and Food Branch
11 Holland Avenue
Ottawa, Ontario K1A 0K9
Canada
Fax (613) 957-2991