Drugs

Maryland: County Executive Douglas Duncan

Department of Health and Human Services

Public Health Service
Food and Drug
Administration
Rockville MD 20857

November 8, 2005

Douglas M. Duncan
County Executive
Office of the County Executive
Rockville, Maryland 20850

Dear Mr. Duncan:

I have been asked to respond to your October 10 letter to Secretary Leavitt for a waiver under the Medicare Prescription Drug Improvement and Modernization Act (MMA) to allow residents of Montgomery County, Maryland and its government employees to import prescription medications from Canada. We have thoroughly reviewed your request and for the reasons stated below, we must deny your request for a waiver.

FDA is very concerned about the safety risks associated with the importation of prescription drugs from foreign countries. In our experience, many drugs obtained from foreign sources that are represented as U.S. approved prescription drugs are of unknown origin and quality. In examining imported drugs sent through the mail, FDA has identified counterfeit drugs, so-called "foreign versions" of FDA-approved drugs improperly labeled drugs, drugs that failed to meet special storage conditions, and drugs requiring physician monitoring. Such findings illustrate the types of risks posed by the illegal importation of prescription drugs. The December 2004 HHS Task Force on Drug Importation has found that the unregulated importation of prescription drugs poses serious health risks. The agency cannot provide adequate assurance that the drug products delivered to consumers in the United States from any foreign country, including Canada, are the same as products we approved. In fact, many drugs tha U.S. consumers purchase from Canada and believe were made in Canada in fact originate from other countries such as India and Costa Rica.

These safety concerns are reflected in Congress' enactment of the new drug and import provisions of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. § 301 *et. seq*., which strictly limit the types of drugs that may be sold within and imported into the United States and who may import them. Congress enacted these provisions to create a relatively "closed" drug distribution system, which helps ensure that the domestic drug supply is safe and effective.

General Legal Framework

Virtually all prescription drugs imported for personal use into the United States from Canada violate the Act because they are unapproved new drugs (21 U.S.C. § 355), labeled incorrectly (21 U.S.C. §§ 352, 353)), or dispensed without a valid prescription (21 U.S.C. § 353(b)(1)). Importing a drug into the United States that is unapproved and/or does not comply with the labeling requirements and dispensing requirements in the Act is a prohibited act under 21 U.S.C. §§ 331(d), and/or (a) that may be enjoined or prosecuted. *See also* 21 U.S.C. §332(a), 333(a).

FDA approvals are manufacturer-specific, product-specific, manufacturing site-specific, and include many requirements relating to the product, such as formulation, source and specifications of active

ingredients, processing methods, manufacturing controls, packaging location, container/closure system and appearance. (21 C.F.R. § 314.50) Frequently, drugs sold outside of the United States are not manufactured or packaged 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 and shipped to Canada may not meet all of the specific requirements of the FDA approval, and thus it is unapproved (21 U.S.C. § 355). The version also may be misbranded because it may lack certain information that is required under 21 U.S.C. §§ 352 or 353(b) but is not required in the foreign country, or it may be labeled in a language other than English (21 C.F.R. § 201.15(c)).

Furthermore, if a prescription drug is originally manufactured in this country and exported, the law unequivocally provides that only the United States manufacturer may import the drug back into the United States (21 U.S.C. §381(d)(1)). This is true even if the drug complies in all other respects with the Act. Importing a drug into the United States in violation of section 381(d)(1) is a prohibited act under Section 331(t) of the Act.

In light of the above, it is virtually certain that a foreign wholesaler or pharmacy would fail to comply with these applicable requirements, and therefore virtually every importation of such drugs would violate federal law.

Consistent with this analysis, on November 6, 2003, following an evidentiary hearing, U.S. District Cour Judge Claire V. Eagan entered an order of preliminary injunction to prevent RxDepot, Inc. from causing the importation of unapproved and misbranded drugs into the United States from Canada. See*United States v. Rx Depot, Inc.*, 290 F. Supp. 2d 1238 (N.D. Okla. 2003). On August 20, 2004, Judge Eagan entered a consent decree of permanent injunction in which Rx Depot, Inc. agreed to obey permanently the import prohibitions ordered earlier by Judge Eagan.

Rx Depot was a domestic "storefront pharmacy" that was engaged in the business of helping individuals procure prescription medications from pharmacies in Canada. Rx Depot would accept prescriptions from U.S. customers and then transmit these prescriptions and the customers' credit card numbers to a cooperating pharmacy in Canada. The Canadian pharmacy would then fill the prescriptions, bill the customers' credit cards, and mail the prescription drugs directly to the U.S. citizens.
Judge Eagan held that, although Rx Depot never took possession of the imported drugs, its facilitation of the transactions caused the importation of unapproved new drugs into the United States in violation of sections 355 & 181(d)(1) of the Act. The Court explained that "unapproved prescription drugs and drugs imported from foreign countries by someone other than the U. S. manufacturer do not have the same assurance of safety and efficacy as drugs regulated by the FDA." *Id.* The Court also observed that "because the drugs are not subject to FDA oversight and are not continuously under the custody of a U.S. manufacturer or authorized distributor, their quality is less predictable than drugs obtained in the United States." *Id.*

The facts in the Rx Depot case are also instructive. FDA investigators made two undercover purchases of drugs from Rx Depot. Judge Eagan found that in one case the investigator had ordered FDA-approve Serzone (to treat depression) but received instead an unapproved version of that product (APO-Nefazodone). The investigator was allowed to purchase 100 pills (but received only 99 pills), even though his prescription only called for dispensing of only 60 pills; the labeling accompanying his order did not, as did his prescription, limit the duration of treatment to 30 days (a potential safety concern); nor did the labeling warn the purchaser of all side effects that were listed in US-approved labeling. The second undercover purchase resulted in shipment of a drug illegally reimported into the US. See *Rx Depot, supra*, at 1242-43 (findings 22-31).

Another federal court reached a similar conclusion in *Vermont v. Leavitt*, 2005 U.S. Dist. LEXIS 20864 (D. Vt. 2005). The case arose from a Citizen Petition that the Vermont Agency of Administration ("VAA" submitted to FDA in December 2003. The VAA requested that the agency allow the Vermont State Employee Medical Benefit Plan to establish a program for the individual importation of prescription drugs from Canada. FDA denied the Petition explaining, among other things, that drugs imported into Vermont under the proposed program would violate sections 355 and 381(d) of the Act. The VAA and the State of Vermont subsequently filed a lawsuit in August 2004 challenging FDA's denial on several grounds.

On September 19, 2005, the federal district court ruled in favor of the government and dismissed the state's complaint. The court's opinion specifically addressed the legality of the state's proposed

importation plan. Citing *Rx Depot*, the court concluded, "[t]here is no question that Vermont's proposed program would violate the FDCA." *Id*. at 13. The court explained that, "as Vermont's proposed plan would be highly likely to include drugs manufactured in the United States, it would lead to violations of section [301(t)]." *Id*. In addition, the court explained that the plan would likely lead to violations of section 331(a) because "[m]any Canadian drugs will have packaging and labeling that is not approved by FDA" and "many Canadian drugs have not been manufactured according to GMP (even if these drugs are pharmacologically identical to drugs approved by FDA)." *Id*.

On March 31, 2005, in yet another case, a couple from Chicago claimed that the provisions of the Act that restrict the importation and reimportation of prescription drugs violated their Constitutional substantive due process rights. The United States District Court for the District of Columbia found: "The FDA's interest in ensuring the safety of prescription medications is a legitimate governmental interest. The statutory scheme of which plaintiffs complain reasonably furthers this legitimate interest by shielding the public from reimported drugs that may be adulterated or otherwise unsafe." *Andrews v. HHS*, No. 04-0307, 2005 U.S. Dist. LEXIS 5710, at *8-*9 (D.D.C. Mar. 31, 2005).

Action by the Council

On November 1, Mr. Tom McGinnis, R.Ph., Director of Pharmacy Affairs at FDA, testified before the Montgomery County Council in opposition to the County's proposal to adopt the import legislation. During that hearing, several council members stated that the proposed importation plan was legal. As noted above, this is clearly not the case. Moreover, we have learned that the County has solicited and received *three* legal opinions unequivocally stating that the proposed legislation would violate federal law. One of these opinions was issued by your Office of the County Attorney in 2004; two other opinions, issued to the County Board of Education, come to the same conclusion. See August 30, 2005 letter from Reese & Carney, LLP, to the Board of Education of Montgomery County, and August 16, 2005 letter from DLA Piper Rudnick Gray Carey, to the Board of Education. The latter opinion concluded "It is our opinion that a credible argument asserting the legality of such a drug re-importation program, voluntary or otherwise, cannot be made." Thus, there can be no serious question regarding the legality of the County's measure.

Despite the foregoing precedents and opinions, several Council members expressed the view that the importation plan would not be illegal until a court has so found. I am sure that you as an elected official responsible for assuring law enforcement by County officials and residents, can readily see that such a view, if widely adopted, could result in a tide of lawbreaking that would overwhelm the courts.

Several Council members also expressed the view that the plan would not place County citizens at risk because, to their knowledge, there have not been any reported injuries associated with Canadian drugs. Even ignoring the facts found in the *RxDepot* case, in FDA's experience the absence of reported injuries is a treacherous basis on which to assume product safety or effectiveness. It is well established that only a small fraction (from 1-10%) of adverse reactions are reported to physicians and/or FDA. This is true for a number of reasons. First, patients may not attribute or even be aware of the reaction to the product unless it occurs shortly after drug ingestion and/or the adverse experience is distinctly different than symptoms of the underlying condition. Chronic adverse effects may only occur after a product has been used for weeks or months. Second, patients may not report the experience to their doctors, even when they believe it is caused by the drug: when patients do report their suspicions to their doctors, there is no assurance that the busy doctors will forward the information to FDA. Third, if a product is sub-potent (for example, it has been improperly made or stored), its diminished effectiveness may not be attributed to the sub-therapeutic dose. The doctor may react to this diminished or lack of therapeutic effect by increasing the dose or switching the person to a different drug, without realizing that the patient has received a sub-potent, imported drug.

Conclusion

You request that FDA grant a waiver under the MMA to facilitate the importation of prescription drugs from Canada. The MMA retains the requirement, originally included in the Medicine Equity and Drug Safety Act of 2000, that FDA may make effective a program for the importation of drugs by pharmacists and wholesalers only if the Secretary of Health and Human Services (HHS) (Secretary) first certifies that implementing the program would (1) pose no additional risk to the public health and safety and (2) result in a significant reduction in the cost of drugs to the American consumer. Both former Secretary Thompson and Secretary Shalala concluded (separately) in the past that such products may pose

additional risks to safety and therefore declined to make the certification necessary to authorize importation.

The certification requirement in the MMA does not authorize a specific waiver for a discrete state pilot program. This was confirmed recently in *Vermont v. Leavitt*. As noted above, the state of Vermont suec FDA on several grounds when the agency denied the state's December 2003 petition. One of Vermont's allegations was that the certification requirement applied only to some of the importation provisions in the MMA. Thus, Vermont argued, its program was actually legal under the MMA despite the fact that there had been no certification from the Secretary of HHS. The court rejected this argument. "Overall," said the court, "the only sensible way to read the statute is to assume that Congress intended the certification provision to apply to the whole of section 384." *Vermont, supra.* at 16.

Granting a waiver that permits the importation of prescription drugs from Canada will not only result in violations of federal law, but will also put Montgomery County residents and its employees at risk. FDA approves a drug based on scientific data submitted by the drug sponsor to demonstrate that the drug is safe and effective. We cannot provide adequate assurance to your constituents that the drug products delivered to them from foreign countries are the same products approved by FDA.

FDA is well aware that the high cost of some prescription drugs is a serious public health issue, and we have taken several steps in recent months to help reduce the cost of drugs in the United States without opening our borders to the risks of foreign unapproved pharmaceuticals. These steps include changing our regulations to reduce litigation that unnecessarily delays access to more affordable generic drugs, and doubling the annual number of generic drug approvals over the last five years.

We understand your desire to provide safe and effective prescription drugs at lower cost to the citizens and government employees of Montgomery County. We are doing all we can to lower the cost of drugs in the United States without exposing consumers to unapproved pharmaceuticals. However, for the reasons stated above, we must deny your waiver request.

If you need additional information, please feel free to contact me.

Sincerely,

Randall W. Lutter, Ph.D.
Acting Associate Commissioner for Policy
and Planning

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