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Roche

Pharmaceuticals

April 4, 2000

Mr. Bradford W. Williams, Director
Divison of Labeling and Non-Prescription Drug Compliance
Food and Drug Administration
Center for Drug Evaluation and Research
7520 Standish Place
Rockville, MD 20855

Dear Mr. Williams:

Re: Improper Dispensing of Accutane® (isotretinoin) Capsules via the Internet

It is our understanding that your Division is responsible for monitoring Internet prescribing activities. We are writing to advise you of a foreign Internet pharmacy that is dispensing Accutane in the United States in a manner which may jeopardize patient safety. The website pharmacy in question, Alant's Pharmacy in South Africa (http://www.alants.co.za/com), allows patients to bypass all of the prescreening, testing, and prescription requirements associated with Accutane simply by completing an on-line questionnaire.

As you know, Accutane is a prescription medication reserved for patients with severe recalcitrant nodular acne. The package insert includes boxed warnings about the drug's teratogenic potential. Female patients of childbearing potential must complete an informed consent form and are urged to enroll in a pregnancy tracking survey. In addition, an FDA-approved Accutane Pregnancy Prevention Program Kit is also provided by Roche to prescribers to assist them in evaluating appropriate female candidates and excluding pregnancy.

In view of the foregoing, we urge you to take whatever action you deem appropriate to ensure that the pharmacy's dispensing of Accutane to patients in the United States complies with relevant U.S. laws and regulations.

Please let us know if we can be of any further assistance.

Very truly yours.

HOFFMANN-LA ROCHE, INC.

Betty C. Holland

Betty C. Holland, M.S.
Program Director
Drug Regulatory Affairs
(973) 562-5549 (phone)
(973) 562-3700/3554 (fax)

BCH/gb
HLR No. 2000-874

cc: Jonathan Wilkin, M.D., Director
Division of Dermatologic and Dental Drug Products

Hoffmann-La Roche Inc. 340 Kingsland Street
Nutley, New Jersey 07110-1199

Roche

June 26, 2000

Mr. Bradford W. Williams, Director
Division of Labeling and Non-Prescription Drug Compliance
Food and Drug Administration
Center for Drug Evaluation and Research
7520 Standish Place
Rockville, MD 20855

Dear Mr. Williams:

Re: Improper Dispensing of Accutane® (Isotretinoin) Capsules via the Internet

It is our understanding that your Division is responsible for monitoring Internet prescribing activities. We are writing to advise you of a foreign Internet pharmacy that appears to be dispensing Accutane in the United States in a manner that may jeopardize patient safety. The website pharmacy in question, MedicaPharma in Thailand (http://www.medicapharma.com/Contacts/contacts.html), allows patients to bypass all of the prescreening, testing, and prescription requirements associated with Accutane simply by completing an on-line questionnaire.

As you know, Accutane is a prescription medication reserved for patients with severe recalcitrant nodular acne. The package insert includes boxed warnings about the drug's teratogenic potential. Female patients of childbearing potential must complete an informed consent form and are urged to enroll in a pregnancy tracking survey. In addition, an FDA-approved Accutane Pregnancy Prevention Program Kit is also provided by Roche to prescribers to assist them in evaluating appropriate female candidates and excluding pregnancy.

In view of the foregoing, we urge you to take whatever action you deem appropriate to ensure that the pharmacy's dispensing of Accutane to patients in the United States complies with relevant U.S. laws and regulations.

Please let us know if we can be of any further assistance.

Sincerely.

HOFFMANN-LA ROCHE INC.

Betty C. Holland

Betty C. Holland, M.S.
Program Director
Drug Regulatory Affairs
(973) 562-5549 - (phone)
(973) 562-3700/3554 - (fax)

BCH/js
HLR No. 2000-1611

cc: Jonathan Wilkin, M.D., Director
Division of Dermatologic and Dental Drug Products

Roche

August 2, 2000

Mr. Bradford W. Williams, Director
Division of Labeling and Non-Prescription Drug Compliance
Food and Drug Administration
Center for Drug Evaluation and Research
7520 Standish Place
Rockville, MD 20855

Dear Mr. Williams:

Re: Improper Dispensing of Accutane® (isotretinoin) Capsules via the Internet

It is our understanding that your Division is responsible for monitoring Internet prescribing activities. We are writing to advise you of a website for foreign Internet pharmacies that appears to be dispensing Accutane in the United States in a manner that may jeopardize patient safety. The website for the pharmacies in question, Mexican Pharmacies Guide By Email (http://www.foreigndrugs.com) allows patients to bypass all of the prescreening, testing, and prescription requirements associated with Accutane, as no prescription is required.

As you know, Accutane is a prescription medication reserved for patients with severe recalcitrant nodular acne. The package insert includes boxed warnings about the drug's teratogenic potential. Female patients of childbearing potential must complete an informed consent form and are urged to enroll in a pregnancy tracking survey. In addition, an FDA-approved Accutane Pregnancy Prevention Program Kit is also provided by Roche to prescribers to assist them in evaluating appropriate female candidates and excluding pregnancy.

In view of the foregoing, we urge you to take whatever action you deem appropriate to ensure that the pharmacy's dispensing of Accutane to patients in the United States complies with relevant U.S. laws and regulations.

Please let us know if we can be of any further assistance.

Sincerely.

HOFFMANN-LA ROCHE INC.

Betty C. Holland

Betty C. Holland, M.S.
Program Director
Drug Regulatory Affairs
(973) 562-5549 - (phone)
(973) 562-3700/3554 - (fax)

BCH/JS
HLR No. 2000-1895

cc: Jonathan Wilkin, M.D., Director
Division of Dermatologic and Dental Drug Products

Hoffmann-La Roche Inc. 340 Kingsland Street
Nutley, New Jersey 07110-1199

Roche Online Pharmacy Audit – US Sites/Accutane®

Site Name/URL	Backing Pharmacy	Country of Origin	Contact Info
http://online-pharmacy.discounts24-7.com/index_fw.htm		N/A	N/A
www.accutane-acne-treatments-medication.com		USA?	Fax to (786) 551-6174 (Florida) Registrant: Eric Kaiser Registered through: Go Daddy Software (http://www.godaddy.com) Domain Name: ACCUTANE-ACNE-TREATMENTS-MEDICATION.COM
.2bbrands.com/drugstore		USA/ Mexico	2bBrands P.O. Box 0798 Manhattan Beach, CA 90266
healthpluspharmacy.com		USA?	Fax: (646) 349-2584 Administrative Contact, Technical Contact: LUSK, N T (NXL80) ntl39@hotmail.com LUSK,N T P.O. Box 01000A23 freeport, na na BS
Rxusa.com		USA	RxUSA Administrative Office 38-38 13 STREET LONG ISLAND CITY, N.Y. 11101 FAX: (718)-392-9250 (866) 501-0003 Phone: (718) 472-1835
Discountmeds4u.com		USA	CHARISMA MEZA 1424 W. Price Rd #321 Brownsville,Tx.78520-8672 DISCOUNTMEDS4U@Aol.com
endlessmeds.com/		USA	Endlessmeds.com P.O.Box 781 Liberty Park Road Hallstead, PA 18822 USA Local Calls (In State) Phone # (570) 879-2310 Out of State Toll Free# 1-888-739-6005
http://pharmacyseek.homestead.com/		USA	Administrative Contact: Homestead.com Inc. (DO434-ORG) Homestead.com Inc. 3375 EDISON WAY MENLO PARK, CA 94025-1811 US (650) 549-3100 fax: - - (650) 364-7329

Roche Online Pharmacy Audit – International Pharmacies/Accutane®

Site Name/URL	Backing Pharmacy	Country of Origin	US Affiliate	Contact Info
www.canadameds.com	Point Douglas Pharmacy	Canada		Canadameds.com 881 Main Street Winnipeg, Manitoba Canada, R2W 3P2 License # 12801 Phone: 1-877-542-3330 Fax: 1-877-994-2121
medicapharma.com		Thailand		Vut, Suthapintu (SK8105) M & CO CO. Ltd. 2591 Ladprao101 Bangkapi Bangkok 10240 TH 011 662 946 7699
medsmex.com		Mexico		Medicine Mexico PMB 330 4233 SE 182nd Ave. Gresham, OR 97030 US 503-665-0787 Fax 1-503-650-9616
Canadapharmacy.com		Canada		Sikka, Sikka, Monty monty@canadapharmacy.com World-Wide Exports Inc. Sumas, WA 98295-0188 US 604-532-9311 P.O. Box 93 Sumas, WA 98295 **Phone** 1-800-891-0844 **Fax** 1-800-883-6005
1drugstore-online.com		Singapore		David Lee 429 Rochor Road Startech Holding Limited. 188452 SINGAPORE edrugmart@yahoo.com Fax to (775) 414-9344 (U.S. Number) or (0870) 139-8938 (U.K.Number)
overseaspharmacyconnection.com/		West Indies/US		Site: CLM Cyber Info Services - PO Box 13123, Alexandria, LA 71315 Information, Cyber (18897776l)

Roche Online Pharmacy Audit – International Pharmacies/Accutane®

Site Name/URL	Backing Pharmacy	Country of Origin	US Affiliate	Contact Info
				drugstorelinks@cs.com Clyde Moore Web Design P.O. Box 679 Charlestown, Nevis 99999 KN 876-842-7-8976 318-445-8765
planetdrugsdirect.com	Gilbert Family Trust	New Zealand		Gilbert Family Trust Box 105-290 Auckland Central, Not Applicable - - New Zealand
Crossborderpharmacy.com		Canada		Cross Border Pharmacy 2912 Memorial Drive SE - Suite 100 Calgary, Alberta, Canada T2A-7R9 Phone: 1-888-626-0696 Fax: 1-888-635-0535 info@crossborderpharmacy.com
www.rx2world.com		Australia		lusk nfa st lucia 4067 AUSTRALIA enquiries@rx2world.com
pharmamex.com		Mexico		Not Available
www.adv-care.com also: www.canadadrugstore.org also: www.pharmacyonthenet.com also: www.canadian-pharmacy.com	TCE Group Inc.	Canada		TCE Group Inc. Amr Bannis 50 Heathcote Ave. Toronto, ON M2L1Z1 CA Phone: 416 444 6242 Fax..: 416 444 7824 Email: abannis@tcegroup.com
pharmagroup.com		Belize/USA?		Fax 1-530-686-8391 Administrative Contact: PHARMA GROUP (A8196-OR) PHARMA GROUP P.O. Box 1879 Belize City, - - BZ +1 (888) 318-9841 fax: +1 (888) 318-9841 Technical Contact: Hostmaster (HO1350-ORG) iNNERHOST, Inc. 2300 NW 89th Place, Dept H

Roche Online Pharmacy Audit – International Pharmacies/Accutane®

Site Name/URL	Backing Pharmacy	Country of Origin	US Affiliate	Contact Info
				Miami, FL 33172 USA 305-717-6600 Fax- 786-845-1694
www.mcknights-canadian-pharmacies.com		Canada		116-B Sherbrook Street Winnepeg, Manitoba R3C 2B4 Toll Free: 1-800-841-8598 Fax: 1-866-662-3689 info@canadadiscountrx.com
Canadarx.com	N/A	Canada		N/A
Halfoffmeds.com	US pharmacy that negotiates prices with Canadian affiliates.	Canada/US	Health Care Options, LLC.	chatrick clark 951 Arden Street Longwood, FL 32750 US 4078306224 4078306636 [fax] chatrick@cfl.rr.com Health Care Options LLC. 860 East Semoran Blvd. Casselberry, FL. 32707 Phone: 407-339-1085
Pharmacy-online.ca	Minit Drugs	Canada		Minit Drugs #206, 400 Crowfoot Cres. NW Calgary, Alberta T3G 5H6, Canada (403) 693-3100 Fax (403) 693-4117 general@pharmacy-online.ca
Mapleleafmeds.com		Canada/US	Conover Ins. Co based in Yakima, WA	Conover Insurance Inc. PO Box 10088 Yakima, WA 98909 USA 800-794-8552
access-meds.com		South Africa		Herman Jansen van Vuuren P.O.Box 20122 Newcastle, 2940 ZA (South Africa) +27 82 893 7435
discountmedsonline.com		West Indies		Registered Office is located at Grand Anse, P.O. Box 1107, St. George's, Grenada, West Indies Discountmeds Online Corp

Roche Online Pharmacy Audit – International Pharmacies/Accutane®

Site Name/URL	Backing Pharmacy	Country of Origin	US Affiliate	Contact Info
				(ZGCLBDJRCO) mark@usamedicine.com Discountmeds Online Corp po box 1005 Grand Anse, St. Georges GD 585 359 1020
valuepharmaceuticals.com	Liberty Lifestyle Pty. Ltd.	Australia		Liberty Lifestyle Pty Ltd Managing Director PO Box 103 Concord West Sydney, NSW 2138 AU Phone: +61287650749 Fax..: 15306788731 Email: enquiries@valuepharmaceuticals.com
e-pharmacy.net		Australia		Chris Ciardi Suite 9, 14 Norton St NL Leichhardt 2040 NSW AUSTRALIA chrisc@maxi.net.au 61 2 9572 6411 61 2 9572 6288
epharmacyunited.com		Bahamas		Cooper, Peter (PCO142) regos@EPHARMACYUNITED.COM 8 Nortons Road PO Box 42515 Freeport BS +1 (801) 905-8552 +1 (801) 905-8552
medicineshoppecanada.com	The Medicine Shoppe	Canada		Medicine Shoppe Pharmacy #9 31205 Old Yale Road Abbotsford BC, Canada V2T 5E5 Ph: 604-854-5800 Toll Free: 1-866-596-4364
uniglobalpharmacies.com		Hong Kong		UniGlobal Pharmacies Rm A, 2/F, Power Pacific Centre, 216-218 Hennessy Road Wanchai, – – HK

Roche Online Pharmacy Audit – International Pharmacies/Accutane®

Site Name/URL	Backing Pharmacy	Country of Origin	US Affiliate	Contact Info
				442076917531 442076917531 [fax] ugpharmacies@yahoo.com
nationalpharmacygroup.com		Mexico		Pharmacy Group, National customerservice@nationalpharmacygroup.com 1531 guadalupe rd mexico city, MX 89357 MX 8008865403
1meds.com		Taiwan	Zip code is in Spring- dale, AR	drugcyber@yahoo.com#0 owner: Steven King email: drugcyber@yahoo.com#0 address: 21 Marion St city: Shorewood postal-code: 72762 country: TW

Electronic Mail Message

GTRCN

Date: 09/07/2001 9:54:11 AM
From: Anne Trontell 301-827-3174 FAX (TRONTELLA@A1)
Subject: Re: internet Accutane pharmacies

Kathy,

I don't know enough about the magnitude of legitimate internet sales (as opposed to patient self-referred or foreign sites) to comment on the likely impact of this. Perhaps you should check what tracking is being done by Compliance about internet sales.

My impression is that internet sales were largely by patients who bypassed an in-person doctor visit and/or bought the drug at a cheaper price abroad. I do recall Janet saying at one point in time that we couldn't manage this problem. I tend to agree. We cannot engineer a voluntary system to catch all scofflaws. Only if there is a susbtantial and legitimate (eg. in person doctor dx and Rx) internet presence for acquiring Accutane would I think we need to specifically engineer Slone and DMD. Perhaps HLR can tell us what they know.

Anne

>Hi Anne, Marilyn, and Jonca
>
>Are we going to address the issue of internet pharmacy sales of Accutane
>before the roll-out? If we don't, I fear we may make the problem (fetal >exposures) worse if unethical prescribers simply tell their patients to go
>to internet so they don't have to bother with SMART.
>
>Specifically, will internet pharmacies receive the same mailings as >store-front pharmacies? What is the experience with Clozaril (do the >internet pharmacies cooperate)? Does the DMD metric include a look at >compliance by internet pharmacies? Will the Slone Survey ask patients if
>they used internet pharmacy and if so, did they have to mail in the special
>sticker? Once the labeling is official, can Compliance do anything about
>internet pharmacies whose website policy is inconsistent with the labeling
>or is that considered "practice of pharmacy" analogous to off-label practice
>of medicine? Can we require HLR to track and report how much drug they ship
>to internet pharmacies? If they knowingly ship to ones that require no >prescription at all, is HLR in violation of any law?
>
>K

① How is FDA & Roche dealing with the issues of Internet Pharmacies?

② How much is out there?

③ What is FDA doing about it? Have we issued guidance specifically about Accutane? What is HHS doing about this?

④ Is there any way to have the kind of Doctor-patient relationship that FDA & Roche has envisioned?

⑤ How are these sites getting these drugs? Diversion?

Electronic Mail Message

Date: 09/07/2001 10:18:13 AM
From: Marilyn Pitts (PITTSM)
Subject: Internet Pharmacies

Kathy,

I don't know much about internet pharmacies, and the rules that govern. But I would suspect that once the labeling is changed to reflect the revised PPP program, that the internet pharmacies are held accountable to the same standards of processing. However, I don't know how much oversight is given. I suspect that the operations with a concurrent brick and mortar business (such as CVS, etc) will seek to comply. Additionally,I think we should approach this as the rules for everyone, and let the operations figure out how they are going to comply, or choose not to offer the product if they cannot comply.

U.S. House of Representatives
Committee on Commerce
Room 2125, Rayburn House Office Building
Washington, DC 20515–6115

September 29, 2000

The Honorable Jane E. Henney, M.D.
Commissioner
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Dear Dr. Henney:

Recently, Committee staff traveled to Laredo, Texas, to meet with U.S. Customs Service and U.S. Food and Drug Administration (FDA) officials, in order to discuss a range of issues relating to U.S. citizens traveling to Mexico to purchase pharmaceuticals. Specifically, staff was interested in knowing (1) the sources and quality of the drugs being purchased at border pharmacies; (2) the types of pharmaceuticals being declared at the U.S.- Mexican border; and (3) what FDA and U.S. Customs' interpretations are regarding current policies that allow for some drug importation for personal use.

Thousands of U.S. residents cross into Laredo each week and many use such excursions to purchase pharmaceutical products from the numerous conspicuous pharmacies that exist on the Mexican side of the border. During this visit, the U.S. Customs Service provided staff a copy of the most recent policy regarding personal-use reimportation guidance. As outlined in a June 29, 2000, memorandum, this policy allows a U.S. resident to bring into the U.S. potentially significant quantities of controlled substances without any requirement that the citizen possess a valid prescription, or any proof that the citizen is under the care of a licensed practitioner. As taken from the June 29 memorandum, current policy reads as follows:

> "In summary, the controlled substances must be declared to Customs upon arrival, be for that individual's personal use, and be in their original container. If all these conditions are met, a United States resident may import the type and amount of the controlled substance (except those in Schedule I or other prohibited substances) as specified on the prescription.... If the controlled substances are declared, but the United States resident does not possess a valid prescription issued by a practitioner as defined above, the United States resident may bring in only an amount not to exceed 50 dosage units. Remember

that the 50 dosage units amount applies to each type of controlled substance being imported. In other words, if the resident is importing 3 different types of controlled substances, the resident may import up to 50 units for each type for a total of 150 dosage units...."

As part of this visit, Committee staff also met with Dr. Marvin Shepherd of the College of Pharmacy at the University of Texas. In 1996, Dr. Shepherd completed a study entitled, *"Examination of the Type of Pharmaceutical Products Being Declared by U.S. Residents Upon Returning to the U.S. From Mexico at the Laredo, Texas, Border Crossing."* That analysis focused on the types of pharmaceuticals being reimported by U.S. citizens from one specific location on the border by examining declaration forms. Given the apparent laxity of the reimportation policy as applied to potentially dangerous drugs, some of the findings in this study raise troubling questions. Several excerpts from the executive summary of Dr. Shepherd's analysis are as follows:

"A total of 5,624 declarations were analyzed.... The average age of people who completed the declaration forms was 34.5 years. Males were found to be younger than females (33.2 years versus 34.8 years). The median age for males was 33 years, and for females it was 35 years. People over 50 years of age only represented 9.3 percent of the sample and people under the age of 40 represented over half the people declaring drug products. Thus these findings do NOT support the assumption that the majority of people who purchase pharmaceutical products in Mexico and declare the products at the U.S. Customs port of entry are elderly."

The report then goes on to note following:

"There was an average of 2.48 drug products listed on each claim form. The top 15 drug products listed by number of people declaring a product was as follows: 1. Valium, 2. Rohypnol, 3. Tafil, 4. Tenuate Dospan, 5. Neopercodan, 6. Diminex, 7. Asenlix, 8. Tylex, 9. Darvon, 10. Nubain, 11. Qual, 12. Halcion, 13. Ritalin, 14. Ativan, and 15. Somalgesic. Valium was claimed by 69.8 percent of the people and another benzodiazepine, Rohypnol was declared by 42.6 percent of the people. All the products in the top 15, except Solmalgesic, are classified in the U.S. as "controlled" substances. These results show that the most popular drugs being declared are sedative/hypnotics, antianxiety agents, stimulants and narcotic analgesics."

"Less than two percent of the declared products were for the treatment of cardiovascular problems and only 42 claims out of the 5,624 claims were for an antiulcer agent. Only 96 declaration forms had an antibiotic or antifungal agency listed. Thus, it can be seen that drugs being brought across the border and being declared were not for people who

suffer from chronic health conditions such as hypertension, ulcers or cardiovascular problems."

Finally, the report indicates that at least at the time of the study,

> "... on average, 11,000 Valium tablets were being declared a day; this extrapolates to approximately four million Valium tablets per year. For Rohypnol, over four thousand tablets were found to be declared each day and this extrapolates to 1.5 million tablets a year coming into the U.S. These two examples point out that large numbers of pharmaceutical products are being allowed into the U.S. And, when one realizes that many of these products have tremendous abuse potential and some are not even approved by the FDA for use in the U.S., the seriousness of the issue becomes more pronounced."

Because this study was published in 1996, certain of the above findings may be different today than when the study was first released. For example, Rohypnol is now a prohibited substance, and thus would not be allowed into the U.S. Nonetheless, as present policy now allows an individual to bring 50 dosage units of many other controlled substances across the border, it is unclear whether the quantity of the controlled substances being transported into the U.S. has fallen, remains the same, or has even increased.

For example, presently, an individual could legally bring in 300 doses of various controlled substances, as long as these were divided into 6 separate drug-types. And as neither the FDA nor the Customs Service appears to track the frequency by which persons are bringing such drugs into the U.S., one could imagine that several trips a week could be made by certain individuals and thus the number could be higher. Most of the controlled substances listed above are available in the U.S. and are relatively inexpensive, so one must question exactly what this policy is designed to achieve. Do individuals really need 50 Valium tablets between the period of when they first reenter the U.S. and the time they see their doctor? What would the logic be for a traveler needing 150 pills of various controlled substances?

I also remain somewhat confused by how the FDA's personal use policy can operate simultaneously with the U.S. Customs Service directive. Which policy actually governs? Under the Food, Drug, and Cosmetic Act, individuals are not allowed to re-import pharmaceuticals into the U.S., unless certain strict conditions are met. That guidance, as posted on FDA's Website, states that FDA should not consider taking enforcement actions against importation for personal use,

> "when 1) the intended use [of the drug] is unapproved and for a serious condition for which effective treatment may not be available domestically either through commercial or clinical means; 2) there is no known commercialization or promotion to persons residing in the U.S. by those involved in the distribution of the product at issue; 3) the product is considered not to represent an unreasonable risk; and 4) the individual seeking to import

the product affirms in writing that it is for the patient's own use (generally not more than a three month supply) and provides the name and address of the doctor licensed in the U.S. responsible for his or her treatment with the product or provides evidence that the product is for the continuation of a treatment begun in a foreign country."

Because virtually all of the drugs cited in the above study have "approved" versions of their formulation available in the U.S., it is unclear how an individual can transport such controlled substances into the U.S. under FDA's own policy. Does the guidance, as issued by the U.S. Customs Service, simply nullify FDA's guidance? If so, how does the U.S. Customs Service take into consideration the fact that many of these substances are apparently arriving at the border in misbranded or mislabled containers, which makes such drugs in violation of the FD&C Act? Also, does the U.S. Customs guidance consider the fact that the agency has no evidence or guarantee that many of the above products are made in facilities that meet current good manufacturing practices? What is also unclear is why one directive, issued by the Customs Service, allows a traveler to bring in potentially dangerous substances without a prescription, and yet the other policy, as outlined by FDA, requires that some proof be given that the importer is under the care of a licensed practitioner or provides evidence that the product is for the continuation of a treatment begun in a foreign country. Why the difference? Which agency's policy takes precedence at the U.S. - Mexican border?

I am concerned that, in their present form, these practices may be facilitating the easy entry of substances that cause serious harm when not taken under the supervision of a licensed practitioner. Moreover, I am troubled by the general confusion and differing interpretations staff has found in the implementation of U.S. policy on the importation of pharmaceuticals for personal use. I would therefore ask you to address the following questions:

(1) Please explain the personal use guidance policy that is now being followed at the Mexico-U.S. border. It is unclear whether FDA's policy is the standard or whether the policy as outlined in the June 29 Customs Service memorandum (or a combination of the two) is the policy now in place at the border. Please also explain the origin of this policy (whichever one is used) and how it comports with the various import prohibitions under the Food, Drug and Cosmetic Act. Also, does FDA believe the June 29 Customs Service guidance is consistent with the original intent of FDA's personal use import guidance? Please explain.

(2) Has FDA conducted a study similar to that of Dr. Shepherd's that attempts to determine (1) the average age of persons visiting Mexico to purchase prescription drugs, and (2) types of drugs being declared at the U.S. border for reentry under the above-cited U.S. Customs policy? If so, please provide such findings.

(3) Of the 15 drugs outlined in Dr. Shepherd's study, please provide a brief description of (a) the drug's typical pharmacological use (for what conditions it is generally prescribed); (b) whether a generic version of the drug exists today; (c) the average cost of the drug in the U.S. (please provide the average brand name price and the price for the generic version if one exists); and (d) whether 50 dosage units of the drug would be considered a "three month supply" under FDA's application of its own personal use guidance policy.

(4) Does FDA believe that the present policy, as outlined by the June 29, 2000, memorandum, creates a significant opportunity for controlled substance abuse by U.S. residents? Has FDA conducted any analysis to attempt to measure the abuse potential of this policy? Please discuss any analysis FDA has undertaken in this regard.

(5) Does FDA believe that the findings of Dr. Shepherd's study, which focuses on the Laredo, Texas, border crossing, have application to other border communities in Texas, or in other border states such as California, Arizona, and New Mexico? Does FDA have any basis to make such a judgment?

(6) Are there any age restrictions on those individuals allowed to bring controlled substances into the U.S. without a prescription? Under the June 29 memorandum cited above, there does not appear to be a specific age limitation involving importation. Committee staff was told that many college students travel to Mexico to purchase drugs for "recreational use." Please indicate what the policy is regarding age limits and in which guidance documents this is set forth.

(7) It is my understanding that, under Texas law, controlled substances cannot be brought into the State without a valid prescription. Nevertheless, Customs' guidance policy says that, as a general rule, Customs Officers "will not initiate reports of violations to state authorities." Does FDA have any formal effort to coordinate such policies with Texas officials? If so, please describe them.

(8) What is the quality of the drugs being purchased in Mexico and brought back into the United States? Are they of the same quality drugs manufactured in the United States? Do they pose any risks to the U.S. consumer? If so, please explain any analysis FDA may have undertaken in this regard and what risks, if any, may be posed.

(9) It does not appear that FDA or the Customs Service has any formal mechanism to track the frequency or the volume of drugs being imported by any individual. Please explain how the Customs Service and FDA assess whether present personal use guidance policies are being abused by the frequency in which drugs are being imported by U.S. residents.

Thank you for your cooperation with this request. I ask for your response to these questions by no later than Monday, October 30, 2000. If you need any further information, please have your staff contact Mr. Christopher Knauer of the Commerce Committee Democratic staff at (202) 226-3400.

Sincerely,

JOHN D. DINGELL
RANKING MEMBER

cc: The Honorable Tom Bliley
Chairman, Committee on Commerce

"Knauer, Chris"
<Chris.Knauer@mail .house.gov>
12/05/02 01:27 PM

To: "DOROTHY. W. REILLY (E-mail)" <DOROTHY.W.REILLY@customs.treas.gov>
cc: "Stupak, Bart" <Yooper@mail.house.gov>, "Slobodin, Alan" <Alan.Slobodin@mail.house.gov>
Subject:

Dot,

As part of our investigation into a range of safety issues relating to Accutane, we have noticed that this drug now appears widely available through internet pharmacies (we also think the drug may be available from the many Mexican 'farmacias' that now dot the border and from certain Canadian sources).

(1) First Email

In a recent meeting with FDA officials, we asked FDA what they were doing to prevent this drug from illegally entering the U.S., particularly via online pharmacies (Roche has made a survey of the many internet sites that are purportedly selling the drug). FDA officials at that meeting said that they believed that they had "sent out" an "import alert" on accutane, and thought that it had gone to Customs. Obviously, it is the Customs inspectors [and not the FDA] that actually inspects (and opens) packages entering the U.S. through the many international mail-branch facilities, so Customs would be the key agency in need of receiving such an alert. Customs is also the agency that inspects the multitude of pharmaceutical products people bring into the U.S. each day from Mexico and Canada.

Can you find out for the Committee (1) what specifically did FDA ask Customs to do regarding Accutane entering the U.S. from offshore internet sites and border crossings, and (2) when was this request from FDA first made? Also, has Customs been provided written import alerts from FDA, and

Knauer, Chris

From: DOROTHY.W.REILLY@customs.treas.gov
Sent: Friday, December 06, 2002 3:19 PM
To: Knauer, Chris
Subject: Re:

Chris, I directed your inquiry to the Director of the "Other Government Agency" branch. FDA (among other agencies) gives Customs import alerts that require Customs to take a specific enforcement action at the ports. USCS does an impact study (Where is it coming in? How much is coming in?) and develops instructions for the field. After sign off by the respective agencies, these instructions (seize, detain, call FDA etc.) are the sent electronicly to the Directors, Field Operations (DFO's) and disseminated to the field.
I was informed that at this time, there is no import alert for Accutane.
Dot

(2) Response from Customs

Knauer, Chris

From: DOROTHY.W.REILLY@customs.treas.gov
Sent: Monday, December 09, 2002 9:15 AM
To: Knauer, Chris
Subject: Re: Import Alerts on Accutane

FDA had informally mentioned this issue to OGA during our weekly bio-terrorism meeting (Tuesday, December 3). They mentioned the alert but had no details. Since that time, they said they were going to forward a copy of the alert to us. They have not done so. Customs has has reached out to FDA for information. As of this writing, Customs has no formal plan of action to deal with this situation. FDA must provide the necessary guidance for OGA to develop and implement the interagency enforcement strategy.

(3)

U.S. Food and Drug Administration
FDA News

Department of Health and Human Services

FOR IMMEDIATE RELEASE
P02-52
December 9, 2002

Media Inquiries: 301-827-6242
Consumer Inquiries: 888-INFO-FDA

FDA STRENGTHENS CONTROLS, ISSUES CONSUMER ALERT ON IMPORTING CERTAIN PRESCRIPTION DRUGS

As part of its ongoing efforts to reduce preventable adverse events from the products it regulates, the Food and Drug Administration (FDA) today announced that it is strengthening the controls designed to protect patients by restricting imports of certain prescription drugs that can be used safely only with specified controls in place.

FDA's action involves adding the drugs to an existing FDA Import Alert, which alerts FDA field personnel to the possible importation of these drugs, provides guidance as to their detention and refusal of admission into the United States, and also advises United States Customs personnel to refer any attempted importation to the local FDA field office.

The drugs added to the Import Alert are as follows:

- Accutane (isotretinoin) - indicated for the treatment of severe recalcitrant nodular acne
- Actiq (fentanyl citrate) - indicated for the management of severe cancer pain in patients who are tolerant to opioid therapy
- Clozaril (clozapine) - indicated for the management of severe schizophrenia in patients who fail to respond to standard drug treatments for schizophrenia
- Lotronex (alosetron hydrochloride) - indicated for the treatment of severe irritable bowel syndrome in women
- Mifiprex (mifepristone or RU-486) - indicated for the medical termination of early intrauterine pregnancy
- Thalomid (thalidomide) - indicated for the acute treatment of the cutaneous manifestations of moderate to severe erythema nodosum leprosum
- Tikosyn (dofetilide) - indicated for the maintenance of normal sinus rhythm in patients with certain cardiac arrhythmias
- Tracleer (bosentan)- indicated for the treatment of severe pulmonary arterial hypertension
- Trovan (trovafloxacin mesylate or alatrofloxacin mesylate injection) - an antibiotic administered in in-patient health care settings for the treatment of severe, life-threatening infections
- Xyrem (sodium oxybate)- indicated for the treatment of cataplexy in patients with narcolepsy

In a related action, FDA today alerted consumers not to buy these drugs over the internet, because drugs obtained via websites usually are not accompanied by these safety controls.

FDA is concerned about the safety risks posed by use of any of these products without the specified controls in place.

The revised Import Alert and the consumer advisory are available online at http://www.fda.gov/ora/fiars/ora_import_ia6641.html and http://www.fda.gov/oc/buyonline/consumeralert120902.html respectively.

Although these drugs have important benefits for many patients, they have serious known risks and so are available in the U.S. only under specially created safety controls. These safety controls are bypassed when these drugs are purchased from foreign sources, placing patients who use these imported drugs at higher risk. Therefore, because of this higher risk to patients, FDA took action to further curtail the products' availability from foreign sources. The drugs purchased from foreign sources are generally not FDA-approved.

Controls on these prescription drugs include limiting their distribution to specific facilities (such as hospitals); limiting their distribution to physicians with special training or expertise; or requiring certain medical procedures (such as pregnancy testing or blood testing) with their use.

Commissioner of Food and Drugs Mark B. McClellan, M.D., has set as a major FDA priority the reduction of
preventable adverse events. "The FDA is committed to taking action, through educational activities and other means where necessary, to improve patient safety," said Dr. McClellan. "Use of these FDA-approved products without adequate controls or monitoring, and using versions of these products not approved by FDA, increases the risk of serious adverse events for patients who might otherwise benefit from the drugs' use."

According to a 1999 report by the Institute of Medicine, medical errors in hospitals alone cause annually 40,000-98,000 deaths. The IOM has estimated that preventable adverse events cost the United States economy $17 billion a year.

Detailed information for consumers and patients who would like to learn more about how to buy prescription drugs safely may be found in FDA's guide, "Buying prescription Medicines Online: A Consumer Safety Guide," available online at http://www.fda.gov/cder/drug/consumer/buyonline/guide.htm

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IMPORTANT CONSUMER SAFETY ALERT

You should not buy the drugs listed below over the Internet.

You bypass important safeguards to protect your health (and others) if you buy these drugs over the Internet.

These drugs have special safety restrictions on how they are distributed to the public. Also, drugs purchased from foreign Internet sources are not the FDA-approved versions of the drugs, and are not subject to FDA-regulated manufacturing controls or FDA inspection of manufacturing facilities. To learn more about buying drugs safely over the Internet, please read "Buying Prescription Medicines Online: A Consumer Safety Guide" available at <http://www.fda.gov/cder/drug/consumer/buyonline/guide.htm>.

Accutane (isotretinoin)

Actiq (fentanyl citrate)

Clozaril (clozapine)

Lotronex (alosetron hydrochloride)

Mifiprex (mifepristone or RU-486)

Thalomid (thalidomide)

Tikosyn (dofetilide)

Tracleer (bosentan)

Trovan (trovafloxacin mesylate or alatrofloxacin mesylate injection)

Xyrem (sodium oxybate)

See also FDA Talk Paper: FDA Strengthens Controls, Issues Consumer Alert on Importing Certain Prescription Drugs

FDA Places Curbs on Risky Drugs

By Chris Adams

WASHINGTON—Seeking to curb unmonitored use of particularly risky drugs, the Food and Drug Administration put import restrictions on them and warned consumers not to buy them on the Internet.

The 10 drugs are available on the market, but only after patients and doctors jump through certain hoops to get them. Acne drug Accutane, from drug maker Roche Holding, for example, carries with it tight restrictions on use—including mandated pregnancy tests for potential users and a requirement that doctors read and sign special guidelines about appropriate use. The restrictions are to keep the drug away from pregnant women since it can cause birth defects and fetal death.

To make sure drugs are going through proper channels, the FDA added Accutane and nine other drugs to an existing import alert, warning FDA and Customs Service workers to watch for and prevent importation of the drugs. Buying the drugs from overseas sources increases the likelihood they were obtained without patients participating in "risk management" programs, the FDA said.

Similarly, patients who obtain these drugs via the Internet aren't likely to have taken the necessary tests or to have received important information about side effects from doctors. While the FDA is concerned about all Internet sales of drugs—which often occur without a physician exam—the agency is especially worried about these 10 medications.

In recent years, risk-management programs increasingly have been used by the FDA to allow particularly risky drugs to stay on the market. Purchases on the Internet can undermine the effectiveness of such programs.

"I've heard from people who have seen the ads on the Internet and are worried patients will get the drugs without ever having gone through a doctor," said Janet Woodcock, a top FDA drug official. "We're trying to keep things as safe as possible but still provide access to the drugs."

In addition to Accutane, the FDA's actions applied to: Actiq (fentanyl citrate), used for pain; Clozaril (clozapine), for severe schizophrenia; Lotronex (alosetron hydrochloride), for the treatment of severe irritable-bowel syndrome in women; Mifeprex (mifepristone or RU-486), for abortion; Thalomid (thalidomide), for skin sores; Tikosyn (dofetilide), for cardiac conditions; Tracleer (bosentan), for treatment of hypertension; Trovan (trovafloxacin mesylate or alatrofloxacin mesylate injection), an antibiotic; and Xyrem (sodium oxybate), for the treatment of episodes of muscle weakness in patients with narcolepsy.

Roche recently conducted a survey and found eight U.S. Internet sites and 26 outside the U.S. that were offering Accutane directly to the customer. The Swiss company said it is in "full support" of the FDA's actions. Accutane also will be the subject of a congressional hearing tomorrow, which was called to explore other potential side effects of the drug, including depression and suicide.

Rep. Jim Greenwood (R., Pa.), of the House Energy and Commerce investigations subcommittee, said he was pleased that the FDA, in announcing the import alert and the other warnings, seemed to be cracking down. "This is one step toward closing the door" on the black market in the drugs, he said.