GOVERNMENT REGULATION

DRUG EXPORT: BRINGING IT ALL BACK HOME?

NEW YORK—The Federal government's current ban on exporting unapproved drugs has forced many pharmaceutical and biotechnology companies to export their technology instead—and thereby risk losing it. When a product is approved overseas before it is approved at home, these companies have little choice but to take advantage of foreign markets by exporting the technology.

As Charles H. Blum, the assistant U.S. Trade Representative, has testified: "...The trend toward increased R&D abroad, combined with foreign manufacturing, is alarming. America is losing its competitive advantage in an important sector of high technology precisely at a time when we are becoming more dependent on exports. We are witnessing: the transfer of technology out of the United States, lost employment opportunities for U.S. workers, lost capital investment in the United States, and lost opportunity to improve the balance of trade. The drug export prohibition is a significant reason for these trends."

Thus, concern over the loss of technology, jobs, and profits has prompted new legislation to lift the Food, Drug and Cosmetic Act's ban on drug exports.

Bill S.1848, introduced to the Senate by Orrin G. Hatch (R-UT) and Edward M. Kennedy (D-MA) in November 1985, is the more liberal of the two bills addressing this issue, and has the support of the pharmaceutical and biotechnology industries. (A similar bill, H.R. 3495, was introduced in the House by Edward Madigan (R-IL).) Bill H.R. 3962, introduced in the House in December 1985 by Henry A. Waxman (D-CA), adopts a very conservative approach.

The provisions of the Hatch bill establish the following conditions for exporting an unapproved drug:

- the drug must meet foreign specifications;
- sale of the drug does not conflict with the importer's laws;
- the drug is labeled for export;
- the drug has not been offered for sale or sold in the United States; and
- the FDA has not denied, suspended, or withdrawn approval of the drug.

The countries to which these drugs can be exported must have sophisticated drug approval systems comparable to the FDA's. The bill suggests approving 15 developed nations, though the Secretary of Health and Human Services (HHS) would actually draft the list.

The Hatch bill includes a secondary tier of countries to which unapproved drugs can be sent. Any drug shipped to a secondary country must be the subject of a New Drug Application (NDA), an Investigational New Drug Application (IND), or a master file containing the safety information required for an IND. Any drugs shipped to countries on the second list must have been approved by a country on the first list. There is even a third tier of countries; these may receive drugs to treat a disease that exists in the importing country, but not in the United States. The Secretary of HHS has the power to add countries to any of the three lists.

Opponents say this bill establishes a double standard for drug quality, and implies that the United States is willing to dump inferior products abroad. Proponents counter-argue that the safeguards built into the bill would prevent this. According to Jeffrey C. Warren, assistant vice president of public affairs for the Pharmaceutical Manufacturers Association (PMA), since the bill requires that some other country must have approved the drug before we export it, the drug obviously must have successfully passed clinical trials in that country. Moreover, each country makes its drug approval decisions according to its own medical, social, and economic needs, and its own risk-benefit calculations.

The Waxman bill, which also lifts the ban on drug export, contains the following provisions:

- an NDA must have been submitted;
- antibiotics—which have to now been exempt from the export ban—will now be regulated as drugs;
- the importing country must approve the drug;
- the drug cannot have been disapproved by any country authorized to receive it;
- the NDA has not been withdrawn or disapproved by the Secretary;
- application for approval has not been denied in the importing country either; and
- the application is subject to comment after publication in the *Federal Register*.

Waxman's list of suggested approved countries is half as long as Hatch's. New countries may be added by Congressional action.

The Waxman bill requires that any exported drug must have successfully completed clinical trials in the United States, a process that takes five or six years. PMA's Warren says that the average NDA approval time is currently 32 months. Thus the Waxman bill would only allow an "overseas advantage"of less than three years. The Hatch bill, on the other hand, would allow about four years. He says that companies need this much time to realize any economic advantages.

Lifting the drug export ban will finally give pharmaceutical and biotechnology companies an important option: they will be able to choose between exporting an unapproved drug and locating manufacturing facilities overseas. Hubert J. P. Schoemaker, the president of Centocor (Malvern, PA), says that this option would not have affected the company's decision to locate its $25-million R&D operation in Holland. Centocor's business philosophy is to locate operations near the area where the product will eventually be marketed. In fact, Centocor will soon open a facility in the Far East.

Genentech's business philosophy, however, is to manufacture products at home and then export them. Stephan Lawton—a partner in the law firm of Pierson, Ball, and Dowd—represents Genentech on the drug export issue. He says that Genentech does not want to have to license its technology. Lawton says that the company believes it has a two-to-three year scientific edge, but this may erode quickly if it has to share the technology to capitalize on foreign markets. For instance, Genentech has licensed a West German company, Boehringer Ingleheim, to market gamma interferon and tissue plasminogen activator for Western Europe. But who will make the products? Lawton says that, if the Hatch bill is passed, Genentech will; otherwise, it will have to license the technology. While West German approval for the two products is imminent, the FDA has not yet acted on them.

The lag time in getting drugs to market in the United States has become a chronic problem: Warren states that, in the 20 year period from 1961 to 1980, only 114 drug products were first introduced in the U.S., while 1,384 were first introduced elsewhere. At the same time, the U.S. led the world in new drug discovery. Until the FDA drug approval process is streamlined, lifting the ban on unapproved drug exports will at least restore this country's competitive edge in the international market.

—Jennifer Van Brunt