might be highly vulnerable to breakdown or sabotage.

Senator Henry M. Jackson (D-Wash.), chairman of the Committee on Energy and Natural Resources, plans to hold hearings on the House-passed bill next session. Last year, the committee had the earlier House bill on its agenda but ran out of time and never acted on it. But, according to a Republican staffer on the committee, there was probably enough opposition from a mix of environmentally oriented and fiscally conscious senators to have killed the bill had it ever been brought to a vote. The makeup of the committee has since changed somewhat, but there again seems a strong likelihood that the majority will want to go slow on the SPS, given the environmental unknowns and trillion-dollar scale.—LUTHER J. CARTER

Large Drug Firms Fight Generic Substitution

But small firms point to misleading ads for brand name drugs as evidence that the fight is not fair

Three years ago, the patent expired on Librium, the popular antidepressant made by Hoffmann-La Roche. Immediately, several small firms began marketing their own brands of chlordiazepoxide, which is the generic name for Librium. But even though its generic competitors cost no more than half as much, Librium still dominates the market. It was ranked 23rd on a 1978 list of the 200 most prescribed drugs, whereas the generics did not even make the list. And even though pharmacists in many states can substitute generic drugs when brand names are prescribed, results of a recent survey indicate that most prescriptions are dispensed as written.

What happened with Librium is the norm, says George Schwartz of the National Association of Pharmaceutical Manufacturers, an organization of small firms that make generic drugs. Schwartz claims, and a number of officials at the Food and Drug Administration (FDA) agree, that the large drug companies are successfully using scare tactics to keep doctors prescribing, pharmacists dispensing, and patients requesting the more expensive brand name drugs when there are cheaper generic versions available.

The large companies disagree. They say they have good reasons to disparage small manufacturers and that they are merely pointing out their own good records and reliability when they advertise. More important, however, they question the wisdom of generic substitution, saying that widespread substitution could so lower the profits of the large companies that it could play havoc with their research and development of new drugs.

In recent years, state legislatures and the federal government have actively promoted generic substitution as part of a drive to lower the costs of health care. Thirty-seven states and the District of Columbia have passed laws allowing pharmacists to dispense lower-priced generic drugs when brand name drugs are prescribed, except when doctors instruct them not to substitute.

The states were encouraged to pass these laws by the Federal Trade Commission (FTC), which drew up a model substitution law. The FTC even went so far as to do research on whether doctors are more likely to prohibit substitution if they have to check a box saying "do not substitute" or if they have to explicitly write "do not substitute" on their prescriptions. Since the FTC found that doctors are more likely to prohibit substitution if they merely have to check a box, the agency recommended that states require doctors to write "do not substitute" if they want their prescriptions dispensed as written. To further encourage substitution, the FDA drew up a list of drugs that, in the agency's opinion, are equivalent.

The Department of Health and Human Resources has also gotten into the business of promoting substitution. Under the Medicare and Medicaid programs, pharmacists are reimbursed only for the lowest-priced drug that is widely available and, in the government's opinion, equivalent to the brand name drug.

As a result of these laws and federal programs, pharmacists have suddenly become key people in determining whether generics will be substituted. So drug companies have begun turning their attention to pharmacists and apparently have convinced many of them that generic substitution is too risky to be worthwhile unless the generics are made by the large drug companies. Quite a few generics are made by the large companies, but these so-called branded generics are more expensive than those made by the small firms.

A major theme in this advertising to pharmacists is "product liability." Countless ads have as their theme the assertion that pharmacists could be sued if they dispensed a faulty product. The large companies point out in these ads that they have product liability insurance to cover pharmacists' legal costs in case of suits.

One company, Pfizer, even made a film for pharmacists to hammer home the message that serious legal problems could result from generic substitution. The Pfizer film was made at a convention of pharmacists during a session when several legal experts spoke on product liability. The film starts out on a light note but quickly becomes ominous in tone. Periodically, the camera pans the stony-faced audience of pharmacists, one of whom actually has tears in his eyes. The pharmacists are told they may be sued for substituting products that, unbeknownst to them, may not be therapeutically equivalent to the drugs the doctors prescribed. And even if the pharmacists win the suits, they are told, the time they would have to spend with lawyers and in court could be ruinous.

Peter Rheinstein, a lawyer and director of the Division of Drug Advertising at the FDA, finds this film a bit overblown. To his knowledge, there has never been a lawsuit involving drug substitution. Bruce Brennan, lawyer for the Pharmaceutical Manufacturers Association (PMA), an organization of the large drug firms, agrees that there have been few or no lawsuits but believes that this is because the substitution laws are too new. Thus it may be too soon for these legal consequences to be manifest. "Sometime soon there will be a body of case law on this," Brennan says. "It is legiti-

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mate, it is not a scare tactic for companies to suggest to pharmacists that they will indemnify them."

But small companies have product liability insurance too, says Schwartz. "If a pharmacist has any doubts, he can simply ask his supplier for a copy of his insurance certificate," Schwartz explains. Milton Bass, lawyer for the association of small companies, sees the insurance issue as just a way for large companies to scare pharmacists into not substituting.

There is some evidence that the large companies' advertising of their product liability insurance is having an effect. *American Druggist*, a monthly magazine for pharmacists, recently published results of its survey of pharmacists in 11 states that have had substitution laws for at least 2 years. These pharmacists said they are substituting on only 20 percent of the occasions when it is legal to do so. When asked why they do not substitute more often, the pharmacists replied that the major reason is to avoid confusing consumers. But they said the second most important reason is their concern over product liability.

More blatant examples of scare tactics are certain advertisements and promotional materials sent out to pharmacists and physicians. The large companies have begun comparing their products to generic drugs in what are at times extremely misleading ways.

One example of such a misleading comparison, says Joseph Belson, director of the FDA's division of drug product quality, is Pfizer's promotional material for Antivert (meclizine HCl). In material sent out to doctors, Pfizer claimed that 10 out of 17 lots of generic meclizine HCl it had tested were below the minimum potency for the drug. But Pfizer had actually had 65 samples tested, only 11 of which were not within standard potency limits, according to the laboratory that tested them. Furthermore, the laboratory contracted to test the generic drugs had no experience in this particular assay and seemed to do a bad job with it.

In September, the FDA sent a warning letter saying to Pfizer, "FDA's investigation of the contract laboratory you used reveals serious discrepancies in their laboratory procedures and practices that raise serious concerns about their accuracy and validity. In addition, it appears that Pfizer very selectively used these data to discredit the quality of competitive generic products." The FDA requested that Pfizer immediately withdraw the Antivert promotional material and warned the company not to try any similar tricks in the future. Pfizer says there are problems with some of the generics it tested, but that it withdrew the ad and is reexamining its data.

A similar problem arose about 1 year ago with G. D. Searle's advertisement for Pro-Banthine tablets. The advertisement compared Searle's product to what seemed to be 12 separate generic lots. But when the FDA asked Searle for more information, it found that three of the products were from the same lot, three of the generic samples should not have been included because they were different products than the Searle tablets, and two of the assays were run with too few tablets for the results to be valid. By the time the FDA made its inquiry, Searle had withdrawn its advertisement, but the agency wrote to Searle saying, "the ad could be considered misleading." Searle spokesman Samuel Huff says "we did not think the general point of the ad was misleading."

The message that generics are of inferior quality is also delivered in another kind of promotional material, which Belson calls sub rosa. It consists of photocopies of letters and documents that drug company detail men show to doctors and pharmacists to convince them of the merits of the company's products. Although this material could be perfectly legitimate, Belson suspects that much of it is not. Since the material is never published, it is seldom seen by the FDA. In one recent case, however, some of this material came to light when a Pfizer detail man let Charles Schau, a pharmacist with ABC HMO Pharmacy in Mesa, Arizona, photocopy it. The result was a lawsuit.

Pfizer had compared the company's Marax Syrup to the generic hydroxyzine syrup made by Barre-National, a small firm in Baltimore. It claimed that Barre's product had 39 percent more of the active ingredient than was stated on its label. "Without a doubt, these results indicate *extraordinarily inferior quality*," Pfizer stated. It could lead to dangerous overdoses in a drug given primarily to children with asthma.

When Schau saw these claims by Pfizer, he filed a drug problem report with the FDA, commenting in his report that when he spoke to the Pfizer detail man, "I asked him if he had submitted a report to the USP and he said that it wouldn't do any good since the FDA didn't have the staff or the time to deal with such matters. I assured him that this *was not true* and that I had received good follow-up on any drug problems I reported. He still refused to file a report. This study may be a hoax, although I have a hard time believing that Roerig [a Pfizer division] would open itself to legal suit." Schau told *Science* that "periodically, the companies have little campaigns like this."

In fact, Barre-National's product was perfectly acceptable. Joseph Callahan of Pfizer explains that Pfizer tested Barre-National's syrup with a standard test but that a preservative in the Barre product interfered with the assay. Max Mendelsohn, president of Barre-National, does not think Pfizer is so innocent as it claims to be. He successfully sued Pfizer "to establish the baselessness of Pfizer's claim." Says Mendelsohn, "The main thing that was damaged was our name. It cost a lot in legal fees but we knew we were 100 percent right and that there was no way Pfizer could win. We weren't about to just sit back and let Pfizer do this to us."

The large drug companies, through their organization PMA, say that they cannot condone misleading claims but that these are a problem in only a small fraction of advertisements. The companies say, however, that it is not a scare tactic to tell people that generics made by small firms may be of poor quality.

The large companies claim that small companies who do no research and development are more likely to produce inferior drug products. To back up this claim, they refer to a study prepared by Eli Lilly & Co. and released in June 1978. Lilly used the FDA's own data to argue that research-intensive firms have fewer recalls and court actions initiated against them than do firms that do no research. Lilly defined research-intensive firms as the 23 companies that spend more than $10 million a year on research and development. According to Lilly, the nonresearch-intensive firms have 7 times more recalls, 43 times more FDA-initiated court actions against them, and $1^1/_2$ times more drug product problem reports than the research-intensive ones. "The FDA was embarrassed by the Lilly study," says Nicholas Ruggieri, a gov-

Pharmacists said they are substituting on only 20 percent of the occasions when it is legal to do so.

ernment relations specialist at the PMA.

James Morrison of the FDA tells a somewhat different story. "The Lilly study is so flawed that it is not indicative of anything. The FDA's answer is to point out the flaws." According to Morrison, some major flaws are that the Lilly study includes recalls that have nothing to do with the quality of drug products, such as drugs recalled because they were marketed without FDA approval, and that it makes no attempt to compare the quality of competing drugs. "What you really want to know is what is the quality of Librium, for example, as compared to the generics that can be substituted for it. But the Lilly study just throws all the drugs into a big pot," he says. Lilly responds by saying it never intended to compare the quality of supposedly equivalent drugs. Its aim was to compare the records of different companies.

Lilly disagrees with all of the FDA's objections and insists its conclusions are valid. The FDA, spurred by the Lilly study, is conducting a study of its own, designed to compare the quality of supposedly equivalent drugs. The FDA is still analyzing its data, Morrison says, but so far there appear to be no striking differences between research-intensive and other firms.

J. Richard Crout, director of the Bureau of Drugs, comments, "The small drug industry is tagged by some firms that have had a disproportionate amount of regulatory incidents in the past decade. The large drug industry has focused on those pockets of vulnerability and has made more of them than is correct." He points out that the large firms keep referring to a few occasions when generic drugs were not equivalent to the brand name drugs for which they were substituted. The problem, Crout says, is being represented as "much more widespread and much more severe than it really is."

Crout believes that the real issue bothering the large companies is not drug quality but profits. The PMA agrees to the extent of saying that economics is its strong point in arguing against generic substitution. Although the large drug industry still is highly profitable, its profits have been steadily decreasing over the past decade. The companies say that even with the protection of the patent laws, they can no longer make enough money on their drugs to support research and development.

The PMA says that there are two major reasons for this decline in profits. First, more and more drug patents are expiring, but new drugs are not being discovered as quickly as they were 10 or 20 years ago. So the companies have proportionately fewer patented drugs.

The second reason is that even patented drugs no longer have anywhere near 17 years of patent protection. This is because FDA regulations have slowed the process of getting approval to market a drug to the point where it now takes an average of 8 years from the time a patent is approved to the time a drug is marketed. (In contrast, this period is only 18 months in the electronics industry, according to PMA economist Samuel Mitchell.) As recently as 1960, it took no more than a year or so to get FDA approval to market a new drug. As a result, the effective patent life of drugs has declined from nearly 17 years in the 1950's to 9 years today.

Mitchell sees the continuing decline in drug company profits as ruining the firms' research and development programs. The PMA, he says, would like to see the FDA prune its regulations that delay the marketing of new drugs. Also, it would like the patent laws changed for the drug industry so that the period of patent protection starts when a drug is approved for marketing. And the PMA is against generic substitution because it further lowers the companies' profits. "The key issue from the consumer's viewpoint is, What is more in the public interest: cheaper drugs now or fewer drugs in the future?" Mitchell asks.

Morrison argues that this is not a fair question because drug companies can always raise their prices for patented drugs to make up for the money they lose on drugs whose patents have expired. Mitchell responds by saying that drug companies cannot raise prices without losing money, that their patented drugs are carefully and optimally priced. The drug market is highly competitive, even for patented drugs, he says. If, for example, a patented antihypertension drug or a patented antibiotic is priced too high, there are plenty of alternatives that can be bought instead. William Comanor, director of the Bureau of Economics at the FTC also says that patented drugs are already priced as high as they can be.

The large drug firms have sympathy from Crout for their economic problems. But Crout is disturbed by the companies' focusing on the quality of generics rather than the economic issues in trying to maintain their profits. He thinks the firms are fighting a losing battle when they fight generic substitution. "Ultimately," says Crout, "I don't think the large drug industry will be convincing. The hollowness of its approach will be revealed."—GINA BARI KOLATA

Macht durch Weisheit

"Americans' incompetence in foreign languages is nothing short of scandalous, and it is becoming worse," says a report issued by the President's Commission on Foreign Language and International Studies. "Nothing less is at issue than the nation's security," contends the commission, which links America's weakening position in trade and international relations to "our gross national inadequacy" in foreign language skills and knowledge about foreign cultures.

The report, entitled "Strength through wisdom," indicates that Americans' sophistication about matters foreign has been in a steep decline for more than a decade. Foreign languages have practically disappeared from primary and secondary schools and few colleges now require language facility for entrance or obtaining degrees. Money, both public and private, for foreign studies has dried up: for example, the Ford Foundation support for training and research has dropped from $27 million a year in the 1960's to $3 million to $4 million a year. The State Department is only in compliance two-thirds of the time when it comes to filling Foreign Service positions requiring foreign language competence, and compliance is closer to one-third in filling positions requiring difficult languages such as Arabic. The percentage of undergraduates enrolled in international studies programs has dropped by one-half in the past decade, and it is rare for graduate students in fields outside the humanities or social sciences to get international training—this despite the fact that demand for people with multiple expertise, such as economics and an area specialty, is on the rise. Exchange programs are on the wane: the Fulbright program budget has dropped by 55 percent since 1967. U.S. research facilities abroad are clinging to their lives by a thread. And so on.

The commission has made a multitude of recommendations which would add up to increased federal expenditures of about $180 million a year. It calls for the establishment of regional centers and summer institutes for foreign language instruction as well as 20 new international high schools. It wants reinstatement of for-

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