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Hearings on H.R.s 3199-3201

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Chairman Bilirakis and members of the Subcommittee, thank you for the opportunity to present testimony on this legislation.

As many of you know, our organization has continually been, for 25 years this November, the most outspoken critic of the Food and Drug Administration (FDA). On more than 50 occasions we have submitted petitions, occasionally resulting in lawsuits against the agency, to ban or force warning labels on dangerous drugs or medical devices or to require the agency to uphold its legal obligations concerning other regulated products such as food dyes and raw (unpasteurized) milk. Although we have not succeeded in getting the FDA to act on some of these products, for most we have. Examples include the bans of the arthritis drugs Oraflex and Tandearil, the painkiller Suprol, the diabetes drug phenformin, Pfizer's Bjork-Shiley heart valve which caused hundreds of deaths, and warning labels on aspirin for Reye's syndrome and on tampons for toxic shock. Although some in industry would not agree, our work is constructive criticism of the agency in the form of petitions and, when necessary, lawsuits. In sharp contrast is the legislation being considered here, which falls into the category of destructive criticism of the FDA and which would cripple its ability to adequately protect Americans from dangerous drugs,

medical devices and other products that the Agency regulates.

In this testimony, I will concentrate on H.R. 3199, concerning drugs and biological products. The need for this legislation--intended to speed up the drug approval process--is highly questionable in light of three facts:

1. There is no dispute that drug user fees have safely speeded up the approval process--especially for important drugs--by providing more funds to hire additional reviewers.
2. As a result of drug user fees and a much faster track for those few drugs that are important therapeutic advances over existing drugs, the FDA has--in recent years--been approving important drugs as quickly or more quickly than other countries.
3. Since these important breakthrough drugs--the ones patients and their doctors are most concerned about--are already getting approved and marketed in the U.S. in an expedited manner, the main "beneficiaries" of any legislative changes to force further speed-up of the drug approval process would be me-too drugs, which make up 70-80% of drug approval applications. Me-too drugs are not important therapeutic advances over existing drugs but manufacturers are quite eager to get quick approval so as to cash in on multi-billion dollar U.S. markets.

In countries such as the United Kingdom, France, Germany, and others whose drug approval process is weaker and faster than ours for these less-than important drugs, the toll on health and lives is clear.

In a statement to the *Washington Post* reported in the April 30, 1996 issue, Congressman James Greenwood, the floor manager of this legislation, referred to the purported benefits of allowing drug companies to choose to have third-party (outside of the FDA) review of new drug applications instead of FDA review. He accurately summarized the current attitude of the FDA--founded on stricter laws and regulations--about the approval process for me-too drugs. He said the proposed third-party review option would eliminate "nit-picking" by federal bureaucrats "saying 'not yet, not yet, not yet' for years and years and years." The reason why I believe his remarks apply almost exclusively to me-too drugs is that for important drugs, as mentioned above, the FDA has already expedited review as safely as is possible.

I would like to briefly review the rewards to Americans of such "nitpicking" by summarizing a study I did last year entitled "Differences in the Number of Drug Safety Withdrawals: United States, United Kingdom, Germany, France 1970-1992." In this study, we looked at all drugs approved for the first time in one of these four countries from 1970 on and later withdrawn (before the end of 1992) because of dangers to patients.

There were 56 drugs which fell into this category. Of the 56, 31 were withdrawn in France, 30 in Germany, 23 in the United Kingdom and only 9 in the United States. In the case of three of the U.S. drugs--Oraflex, Selacryn and Merital--their manufacturers later pleaded guilty of criminal charges in withholding safety information from the FDA, information which would likely have prevented approval of the drugs had the FDA been aware of it.

Not one of these drugs was an important breakthrough drug. Thus, Americans were spared exposure to 45 drugs which caused thousands of serious injuries or deaths in Europeans whose weaker drug regulatory procedures allowed the drugs on the market there but were kept off the U.S. market.

What has been referred to as nit-picking--the FDA's asking more questions about questionable drugs which do not remotely offer a breakthrough in treatment--turns out to be quite healthy for the American public. Replacing this process by outside third-party review, chosen by the drug company because it believes it will get the drug to market more certainly and more quickly, poses significant dangers.

Having reviewed evidence of the toll on Europeans of quicker drug approval for me-too drugs, I would like to put these differences in the context of current differences in the drug approval processes of the U.S. and these (and other) European countries and then to review some parts of this legislation which would lower U.S. standards in a way which would make the drug approval process here much more like those in Europe, thereby endangering Americans' health and safety.

Prior to 1962, when there was no rigorous U.S. standard for efficacy, there was no difference between the U.S. and these European countries in the number of drugs which were approved and had to be later banned because of health dangers. But once the 1962 efficacy laws were in place and operating, the differences became quite apparent.

Although there have also been some changes in the laws in European countries since 1962, the U.S. still has more rigorous standards than the rest of the

world. As far as the use of third parties--outside of the government--to review new drug applications, Europe, again, has been using groups such as this for some time and it is this, along with the lower efficacy standards, which most differentiates the U.S. from these countries.

H.R. 3199 has two provisions which seek to weaken our laws and regulations so as to make them more like those in Europe.

Sec. 5: **Weakening of the Efficacy Standard and therefore of Safety**

This section would allow effectiveness to be established by results of "one or more" clinical investigations, which could be interpreted to set the default at one, as opposed to the current system in which two or more is the norm but one is allowed in unusual circumstances.

Other parts of this section which seriously undermine FDA standards for effective drugs include the fact that the FDA could waive the requirement of well-controlled investigations, thereby creating a situation where known risks would have to be measured against unknown benefits. In addition, for new uses of approved drugs, the legislation would allow approval without evidence from well-controlled studies if the new use is common among clinicians experienced in the field and is based on reliable clinical experience and confirmatory information. This might be called the DES provision, because under its terms, this cancer-causing drug which ultimately turned out to be ineffective for the unapproved use of preventing miscarriage would have been approved.

Another part of this section which seriously weakens the efficacy standard is

that effectiveness determination shall not include relative effectiveness. Thus, if there are data that for two equally safe (or unsafe) drugs, one is clearly more effective, the FDA would be barred from using this information as a basis for saying no to the approval of the less effective drug.

Sec. 7: **Marketing Approval**

This section would allow the applicant to submit an NDA to the FDA or to an accredited third-party reviewer. If the NDA is submitted to an accredited outside reviewer, the reviewer must submit the report and recommendation to the FDA prior to 60 days before the end of the statutory deadline for NDA review (usually 180 days, so this report would be due by day 120).

The outside reviewer's approval recommendation would be deemed approval by the FDA unless the FDA finds reasonable probability that the drug is not safe or effective. And the FDA must evaluate the external reviewer's recommendation within 60 days of receiving it. If the FDA does not accept a recommendation of approval, it must provide a detailed explanation of the basis for its disagreement. This section is written to suggest that the House believes the external recommendation will always be an approval.

A whole new private sector industry/bureaucracy, probably quite profitable, will be created by this legislation. Most drug companies will want to choose this "fast" route and it will be in the third-party reviewers' interests to recommend approval in order to get future business from the drug company. There is little question that unsafe and/or ineffective products which current FDA review keeps off

the market would reach American patients under this dangerously expedited private pathway, necessarily fraught with conflict of interest.

In conclusion, passage of this legislation would be a dangerous step backward for our health and safety, although it might represent a bonanza for those companies whose me-too products would thereby get approved as a result of the various ways in which the legislation would cripple FDA's ability to carefully scrutinize new drug applications. As you consider voting for this legislation, either in the subcommittee or if the measure comes to the floor for a vote, remember that if this legislation becomes law and your name is listed as one of those voting for its approval, you will be personally responsible for the inevitable consequences of its passage.

Were H.R. 3199 to become law, it would unleash the approval of a torrent of me-too drugs now being kept off the U.S. market, many of which will eventually have to be banned because they are too dangerous, after they kill and injure thousands of Americans now protected from such drugs.