LEVIN, FISHBEIN, SEDRAN & BERMAN

Counsellors at Law and Proctors in Admiralty

ARNOLD LEVIN
MICHAEL D. FISHBEIN
HOWARD J. SEDRAN
LAURENCE S. BERMAN
FRED S. LONGER
DONALD E. HAVILAND, JR.
DANIEL C. LEVIN
TERRIANNE BENEDETTO
CHARLES E. SCHAFFER
AUSTIN B. COHEN
SCOTT LEVENSTEN
JUDY SHOPP

510 WALNUT STREET
SUITE 500
PHILADELPHIA, PA 19106-3697

TELEPHONE (215) 592-1500
FACSIMILE (215) 592-4663

September 28, 2001

VIA DHL OVERNIGHT DELIVERY

Dockets Management Branch
MAILSTOP HFA-305
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

Re: Docket 01N-0196: Comment

Dear Sir/Madam:

On August 14, 2001, FDA announced its intent to withdraw approval of New Drug Applications and Abbreviated New Drug Applications for drugs containing phenylpropanolamine "because of the association of phenylpropanolamine with increased risk of stroke." *See* 66 Fed. Reg. 42665 (Aug. 14, 2001) and FDA Docket 01N-0196. At that time, FDA reviewed the scientific evidence regarding phenylpropanolamine and stated:

> FDA believes that the data from the Yale study demonstrating an association between phenylpropanolamine and hemorrhagic stroke, taken together with spontaneous reports and reports in the published medical literature, provide evidence that nasal decongestant and weight control drug products containing phenylpropanolamine are no longer shown to be safe. Because hemorrhagic strokes often lead to catastrophic, irreversible outcomes and the factors that may predispose some individuals to develop this adverse event are not fully known, individuals at risk cannot be adequately warned. The agency tentatively concludes that the benefits of the intended uses of this ingredient do not outweigh the potential risk.

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Id. Further, FDA stated that:

> Accordingly, the Director of the Center for Drug Evaluation and Research (CDER) concludes with respect to the NDA and ANDA products containing phenylpropanolamine listed in section II of this document that phenylpropanolamine is no longer shown to be safe for use under the conditions that formed the basis upon which the applications were initially approved.

Id. FDA gave applicants and other interested parties an opportunity to request a hearing to show why approval of the NDAs or ANDAs should not be withdrawn and held that any such requests must be filed on or before September 13, 2001 and that any applicant requesting a hearing must file on or before October 13, 2001, all data, information, and analyses relied on to demonstrate that there is a genuine issue of material fact to justify a hearing.

It is our understanding that the Director of Regulatory Affairs for Novartis Consumer Health, Inc. and outside counsel for American Home Products Corporation and Schering-Plough Healthcare Products have written to FDA regarding its Notice of Opportunity for a hearing. None of those companies has requested a hearing or provided any data, information or analyses to demonstrate that there is a genuine issue of material fact justifying a hearing. Instead, their letters merely rehash all of their prior objections to and disagreements with the Yale Study and all request that if FDA's proposed action becomes final that the agency include a "disclaimer" stating that:

> The agency wishes to emphasize that the inclusion of a drug product on the list does not mean that the drug product was marketed negligently, was defective, or was marketed in breach of any warranty. Even after exhaustive clinical studies, safety problems may not become apparent until a drug product has been in commercial distribution for a significant amount of time, so the fact that a drug was removed or withdrawn from the market does not mean that the drug was improperly placed in commercial distribution.

In addition, American Home Products' counsel has requested that the FDA Commissioner formally state that statements made in the Notice for Opportunity of a Hearing and any final order "are not intended to - and should not - be used as evidence in product liability cases".

This comment is submitted in response to the requests by Novartis, American Home Products and Schering-Plough regarding their proposed "disclaimer". The disclaimer sought is incorrect on the facts, implies that the agency is taking sides in litigation to which it is not a party and is outside the scope of FDA's jurisdiction and authority. We therefore request that the agency not adopt any such disclaimer, now or in the future. At the very least, if FDA is at all inclined to grant the drug companies' request it should postpone such action until after injured consumers have had an opportunity to conduct full discovery of the drug companies regarding their negligence, breach of any warranties or responsibility under strict liability in their ongoing lawsuits and can present such evidence in a hearing.

This law firm, and many others, represent plaintiffs involved in product liability litigation against pharmaceutical companies in both state and federal courts relating to the use of drug products containing PPA. The plaintiffs ingested PPA drug products and as a result are now dead or severely incapacitated. They are legally entitled to compensatory damages under numerous state strict liability and tort laws because PPA drug products were and are unsafe. We know these products are unsafe because of the Yale study, the general consensus of medical experts, and because FDA itself has concluded they are unsafe. *See id.* at 42666 and references thereto. The disclaimer sought by these drug companies falsely suggests that, although FDA believes PPA to be unsafe under the specific standards set forth in Section 505 of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 355, FDA does not mean to imply that the drug is actually unsafe in fact. Such a disclaimer would reduce FDA's finding of fact and law to a matter of mere technicality. FDA knows this is not the case. PPA is unsafe, under the FDCA definition or under any other definition.

FDA has been asked to adopt a disclaimer like one included in FDA's Federal Register notice of March 8, 1999. See 64 Fed. Reg. 10944 (Mar. 8, 1999). There, the agency was issuing a lengthy list of drug products withdrawn because they are unsafe or ineffective, as required under Section 127 of the FDA Modernization Act of 1997. Although FDA had been asked in that instance to restrain its choice of words, the agency understood that its responsibilities under the FDCA and the language it used could not be altered simply because of the possibility of some unintended impact in private litigation. The agency noted:

> the addition of language designed to minimize the potential effect of the list in litigation is unnecessary to fulfill its intended purpose.

Id. at 10944. Likewise, with respect to PPA, FDA should not choose words or add disclaimers with the purpose of impacting private litigation one way or the other, inasmuch as it has long been agency policy not to take sides in private litigation.

Notwithstanding its purported impartial position, the agency added to its March 8, 1999 notice, and is asked to repeat here, a statement which the agency is not authorized by law to make about litigation which is entirely outside its jurisdiction. Specifically, FDA has been requested to state that:

> The agency wishes to emphasize that the inclusion of a drug product on the list does not mean that the drug product was marketed negligently, was defective, or was marketed in breach of any warranty.

Such a statement was inappropriate in March of 1999 as a blanket statement regarding dozens of drugs and would also be improper with respect to a specific drug like PPA because it implies that the drug was in fact not marketed negligently, was not defective, or was not marketed in breach of any warranty. To our knowledge, FDA has not conducted any factual investigation of the marketing practices of the various drug companies which manufactured and distributed PPA products and it therefore has no basis for determining whether such companies were negligent or breached any warranties made to consumers. Moreover, under many states' laws a product is "defective" and "unreasonably dangerous" if its risks outweigh its benefits; which is precisely the conclusion made by FDA's Office of Post-Marketing Drug Risk Assessment, the Non-Prescription Drug Advisory Committee and now, apparently, FDA itself. In addition, there is nothing in the FDCA or other statutes which expressly or implicitly grants FDA the authority to make determinations regarding the liability of drug manufacturers in civil litigation or the admissibility of evidence in such litigation. *Motus v. Pfizer*, 127 F. Supp. 2d 1085 (C.D. Cal. 2000); *see also Hill v. Searle Labs*, 884 F.2d 1064, 1068 (8th Cir.1989) (no evidence that, in enacting the FDCA, Congress intended to preempt common law causes of action). Indeed, in none of the letters by Novartis, American Home Products or Schering-Plough do their counsel cite any legal authority for the proposition that FDA may limit or comment upon the liability of drug manufacturers in civil litigation with their injured consumers or attempt to determine what evidence is or is not admissible in such litigation.

As there is no private cause of action under the FDCA, it is a matter for the courts overseeing federal and state product liability litigation, and the causes of action which arise under the various laws of the 50 States, to determine what is relevant and admissible evidence in such cases - not FDA. FDA's decision to withdraw its approval of any drug may or may not be evidence that the drug was unsafe. Some state courts have held that FDA's administrative actions are relevant to state law causes of action. *See Hatfield v. Sandoz-Wander, Inc.*, 124 Ill. App.3d 780 (1984) (FDA issues may be relevant in a failure to warn case); *Carlin v. Superior Court (Upjohn Co.)*, 13 Cal. 4th 1104 (1996) (same). FDA should enforce its statutes and regulations impartially and maintain silence on all other issues as Congress intended.

As noted previously, Novartis, American Home Products and Schering-Plough have also asked FDA to adopt a statement that:

> Even after exhaustive clinical studies, safety problems may not become apparent until a drug product has been in commercial distribution for a significant amount of time, so the fact that a drug was removed or withdrawn from the market does not mean that the drug was improperly placed in commercial distribution.

As a general principle, it may be true (although unproven in this instance) that some safety problems do not become apparent until a drug product has been exhaustively studied and commercially distributed for a significant amount of time, and that some highly effective and irreplaceable drug products should not be withdrawn earlier. In the March 8, 1999 notice, where FDA was adopting a lengthy list of drug products, it was clear that FDA's statements were not specifically applicable to any one of the products on the list. To adopt that same language about one specific drug product, however, would suggest facts, and in this case facts relating to PPA, that are false or misleading.

In 1976, when the DESI panel originally recommended that PPA be classified as "generally recognized as safe" it acknowledged that each of the studies it had reviewed was flawed in some way. Several years later, as the use of PPA increased, cases of hemorrhagic stroke were reported in the medical literature and to FDA. Indeed, FDA has expressed concern about the risk of hemorrhagic stroke with the use of PPA products since the early 1980s. *See* FDA Dockets 76N-052N and 81N-0022. Yet, after numerous reports of hemorrhagic stroke, several petitions by citizens groups to have PPA banned in the 1980's and several congressional hearings regarding the safety of PPA there were no "exhaustive clinical studies" of PPA to assess its safety and efficacy, particularly with respect to the risk of hemorrhagic stroke until the recent Yale Study.

The disclaimer sought for PPA would only be appropriate if FDA had thoroughly investigated all PPA products, as well as the companies that marketed them, all of the actions of the companies and clinical investigators and FDA employees who have dealt with PPA, and can represent to the American public that no safety problems with PPA drug products were known or knowable at any time before November 3, 2000 when FDA requested that PPA products be taken off the market. Such a guarantee is of course impossible; FDA can be rightly proud of what it does to protect the American public, but FDA not have the authority or resources to conduct such an investigation or make any such representation. Any suggestion by FDA to the contrary would only be a fruitless attempt to shield the drug companies from civil liability.

For these reasons, we request that the FDA not adopt the disclaimer requested and maintain its impartiality on matters that are outside the agency's jurisdiction and legal authority.

Very truly yours,

MICHAEL D. FISHBEIN

MDF:mcl

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