#755

Public Citizen

January 28, 1975

Commissioner Alexander Schmidt
Food and Drug Administration
200 C Street S.W., Rm. 6815
Washington, D.C. 20204

Dear Commissioner Schmidt:

We ask you to declare the Dalkon Shield and all other intrauterine contraceptive devices "drugs" and to thus require full safety testing before more deaths and injuries occur. Already, the Dalkon Shield has been implicated in 14 deaths and 223 pregnancy-related injuries. Had FDA required proper tests, these women may not have been dead and others may not have suffered critical illnesses.

Long before the Dalkon Shield case, the history of medicine demonstrated that the dangers of medical treatments, drugs and devices cannot be identified and prevented without adequate controlled tests beforehand.

IUDs ARE "DRUGS" UNDER THE LAW

The Food and Drug Act grants FDA the authority to require full safety and efficacy tests on all new drugs.* "Drugs" are defined as:

> articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease... and...articles intended to affect the structure or any function of the body.... 21 U.S.C. 321 (g).

Although most are currently classified as devices, intrauterine devices are "drugs" since they are implanted in the body in order to prevent the natural occurrence of birth. In U.S. v. An Article of Drug...Bacto-Unidisk, 394 U.S. 784, 799 (1969), the Supreme Court stated:

> the legislative history, read in light of the statute's remedial purpose, directs us to read the classification "drug" broadly, and to confine the device exception as nearly as is possible to the types of items Congress

* Drugs which are already "generally recognized as safe and effective" do not require submission of tests to FDA.

> suggested in the debates, such as electric belts, quack diagnostic scales and therapeutic lamps, as well as bathroom weight scales, shoulder braces, air conditioning units and crutches.

FDA has already declared soft contact lenses, bone implants, some diagnostic equipment, eyeglasses, "weight-reducing" cigarettes, gauze bandages, suture devices, and antibiotic sensitivity tests to be "drugs."

Further, FDA has declared two IUD's to be "drugs," the Copper T and the Copper 7, on the grounds that copper leached from the device into the uterus. FDA guidelines exempt the following IUDs from "drugs" safety testing:

> (1) Intrauterine devices fabricated solely from inactive materials (e.g., inactive plastics or metals).
> (2) Intrauterine devices with substances added to improve the physical characteristics if such substances do not contribute to contraception through chemical action on or within the body and are not dependent upon being metabolized for the achievement of the contraceptive purpose.
> (3) Intrauterine devices that contain a component such as barium, added exclusively for the purpose of visualization by X-ray. 21 C.F.R. s. 310.502

On the basis of this policy, FDA has not required safety tests on other IUDs, even though it has the legal authority to do so, on the theory that other IUDs are composed of substances which do not interact with the body. FDA has never required proof that an IUD was inert in the body. Numerous scientific articles document inflammation of the tissues by an IUD, easily chemically induced. For ex., see Tatum, "Intrauterine Contraception," Am. J. Obstet. and Gynec. 112: 1000, 1010 (April 1972). The Dalkon Shield in fact leaches copper into the uterus. Utah Biochemical Test Laboratories, under FDA contract, September 1974.

DANGERS OF THE DALKON SHIELD IUD

The chief known danger is infected pregnancies with the Dalkon Shield in place, causing miscarriage, severe illness and sometimes death. The Public Health Service's Center for Disease Control June 29, 1974 reported a survey of doctors which showed five deaths and 3,502 hospitalizations from IUDs in the first six months of 1973. 53.9% of pregnancy-related

hospitalizations involved the Dalkon Shield IUD. "IUD Safety: Report of a Nationwide Physician Survey" Morbidity and Mortality, vol. 23, no. 26. The deaths were distributed among Lippes Loops (2), Saf-T-Coils (2) and the Dalkon Shield (1). The same month, Dr. Donald Christian published a report of four deaths associated with the Dalkon Shield. "Maternal Deaths Associated with an Intrauterine Device," Am. J. Obstet. Gynec., vol. 119, no. 4, 441. A fifth death with a Lippes Loop was reported. (Also reported were 6 severe illnesses from Dalkon Shield pregnancies, 1 Lippes Loop). In each case, a woman had died from an overwhelming infection in the second trimester of pregnancy after a spontaneous abortion from an infected uterus.

Particularly alarming about the Dalkon Shield deaths is the fact that the infection moved throughout the body very rapidly, and with no localized symptoms to alert the woman, or her doctor, to what might be wrong. For instance, in one of the cases, the woman merely had flu symptoms before she became acute; in another, the woman had a sore throat and earache.

> "It appears that the infection becomes generalized at about the same time as or before there are any localizing signs, and therefore the margin of safety that time ordinarily provides in treating such infections is not present." at 443.

FDA has found a total of 13 Dalkon Shield deaths from infected miscarriages, and 223 infected miscarriages, the majority in mid-trimester and life-threatening.*

Exactly why the Dalkon Shield causes these effects is not known. The device has barbs on each side, and is basically shaped like a flat crab. Christian has speculated:

> ...there may be something about the design of the shield type device that allows vascular dissemination of infection that might otherwise be locally contained. Ibid. at 443.

Another scientist has speculated that the Dalkon Shield is hazardous becuase it has a multi-threaded tail reaching from the implanted device through the cervix, a tail which has been shown to harbor bacteria which single-thread IUD tails do not. Tatum, "Microbial Migration in the Thread Attached to an IUD as a Possible Factor in Infectious Complications," Third Internat'l Conf. on Intrauterine Contraception, Program Abstracts, Dec. 1974. The Dalkon Shield

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* One death from a non-pregnant infection is reported, as are non-life-threatening side effects.

was designed with the multi-strain tail because it is more difficult to remove than other IUDs. Perlmutter, "Experience with the Dalkon Shield as a Contraceptive Device," Obstet. and Gynecol. 43, 3, 445 (March 1974). Davis in Contemp. Ob-Gyn 4, 55 (Sept. 1974).

A third possibility is the large surface area of the Dalkon Shield which "acts as a foreign body, predisposing the placental site to acute inflammation and necrosis." Hurt, "Septic Pregnancy Associated with Dalkon Shield Intrauterine Device," Obstet. and Gynecol. 44, 4, 494 (Oct. 1974).

That the multi-thread tail alone is responsible for the special dangers of the Dalkon Shield is unlikely. All IUDs apparently introduce bacteria into the uterus upon insertion, but with other IUDs, the uterus can cope with the bacteria and return to its normal, sterile condition. Mishell et al, "The Intrauterine Device: A Bacteriologic Study of the Endometrial Cavity," Am. J. Obst. and Gynecol. 96, 1, 119 (Sept. 1966).

Efficacy. The Dalkon Shield has been used for contraception since 1970, largely on the basis of a study by Davis in which the pregnancy rate was less than half that of other IUDs -- 1.1 pregnancy per 100 woman years of use. Obstet. and Gynecol. 36, 350 (1970). Davis, co-developer of the Dalkon Shield, failed to mention that the women in his study were advised to use contraceptive foam on days 10-17 of the menstrual cycle. Schwartz, Fam. Planning Persp. 6, 4, 201 (Fall 1974). Later studies showed a pregnancy rate equal to or higher than other IUDs, such as: (a) 4.7 pregnancies/100 woman years of use; Jones, Brit. Med. J. 21 Jul. 1973, 153; (b) 6 pregnancies/100 woman years of use; Horowitz, Contracep. 7, 1, 1 (Jan. 1973); and (c) 10.1 pregnancies/100 woman years of use; Perlmutter, Obstet. and Gynecol. 43, 3, 443 (Mar. 1974). Since other IUDs have a pregnancy rate of about 2.7/100 woman years of use, the Dalkon Shield has no efficacy advantage over other IUDs and is apparently considerably less effective. Tietze, Stud. Fam. Planning 55, 1 (1970).

OTHER IUDs

Deaths and infected pregnancies have been reported for other IUDs. FDA knows of 50 infected miscarriages and 6 deaths from pregnancies associated with the Lippes Loop, 14 infected miscarriages and 1 death from the Saf-T-Coil. See Vessey et al, "Outcome of Pregnancy in Women Using an Intrauterine Device," Lancet Mar. 23, 1974, 495; Stevens et al, "The Outcome of Pregnancy after Failure of an Intrauterine Contraceptive Device: J. of Obstet. and Gynecol. 81, 282 (Apr. 1974).

Dalkon Shield injuries, however, are disproportionately high. Of 291 infected miscarriages linked to IUDs, 223 are Dalkon Shield cases. Of 21 known IUD deaths in pregnancy, 13 are Dalkon Shield. A 1968 survey conducted by the Food and Drug Administration found only 10 deaths associated with all U.S. I.U.D. use over the years, of which two were associated with pregnancy (both second trimester). FDA Advisory Committee on Obstetrics and Gynecology, Report on Intrauterine Contraceptive Devices, 1968, 43.

It is difficult to estimate the incidence of serious IUD complications because no one knows exactly how many IUDs of each kind have been, or are in use. The CDC report estimated that there were 3.2 million women using an IUD in early 1973. FDA estimates that a total of 8 million IUDs have been distributed in the U.S., 1965-1974. Robins has distributed a total of 2.2 million Dalkon Shields for U.S. use over five years -- slightly over 1/4 of total IUD distribution. Their share of present use is probably about 1/3. Dalkon Shield deaths and injuries are a much greater proportion of total IUD deaths and injuries than the Dalkon Shield market share.

FDA ACTIONS

June 27, 1974, the Dalkon Shield manufacturer, Robins, suspended distribution of the device at the request of FDA. July 2, 1974, Louis M. Hellman, HEW Deputy Ass't Secretary for Population Affairs advised U.S. Regional Health Administrators to "discontinue any new insertions of the Dalkon Shield." Shortly thereafter, FDA also advised doctors not to prescribe the Dalkon Shield until the safety issues could be resolved.

After several months of deliberation, an FDA advisory committee recommended Oct. 30, 1974, "that the moratorium on commercial distribution of the Dalkon Shield remain in effect pending accumulation of definitive data."

FDA nevertheless re-permitted Dalkon Shield marketing Dec. 20, 1974, stating that the manufacturer had agreed to conduct further studies and maintain a registry system of doctors who insert the device. The manufacturer decided to remarket the device with a single strand tail. FDA did not require premarket assurances of safety, as it requires for "drugs," such as thorough animal tests and well-designed, controlled clinical trials. It required no guarantees of informed consent. It required no other legal protections necessary for "drugs," such as use of qualified investigators and compulsory reporting of adverse effects. See 21 C.F.R. 312. FDA apparently assumed, without proof, that the multi-

threaded tail on the old device has been responsible for the excess injuries.

December 23, 1974 Dr. Emanuel A. Friedman, a member of the FDA advisory committee, resigned in protest against FDA's decision to allow re-marketing without safety data. Two other members of the committee, Dr. Richard P. Dickey and Dr. Louise B. Tyrer, sent strong letters of protest. FDA advisory committees are normally entirely compliant with FDA officials' wishes, and these strong protests are unprecedented.

SUMMARY

The Dalkon Shield should not be marketed before it is proven safe. Questions have been raised about its efficacy, and about its safety in pregnancy. Proper animal studies--required of new drugs--have not been conducted. Even though the device remains implanted for years, no long-term animal studies have been done.

In 1970, a high FDA official recommended that women be granted greater safety protection on IUDs. This memo was written long before the Dalkon Shield cases were reported.

Miss MARY MCENIRY (BD-3), SEPTEMBER 11, 1970.
Assistant to Director for Regulatory Affairs.

INTRAUTERINE CONTRACEPTIVE DEVICES

We feel that the IUDs should be considered as "drugs," as an extension of the AMP decision. We have long been concerned over the high incidence of adverse reactions, the lack of records and reports and of informational material to the patient. A recent letter to Dr. Edwards from a concerned physician who attempted to obtain information from several sources on the number of IUDs inserted, the number in current use, mortality and morbidity revealed that data are extremely sketchy or nonexistent. I also think that we need appropriate animal studies on the possible adverse histologic effect on the uterus of long-term insertion of the foreign body represented by the loop.

In addition, our OB-Gyn Advisory Committee noted that the highest incidence of severe adverse reactions occurs with the closed loop and we would then be in a position, with NDAs for all, to weigh benefit/risks for the various designs.

Dr. Simmons agrees that we should go ahead with this. Mr. Goodrich feels that we can call the IUDs "drugs."

I think that 6 months would be a reasonable time for the companies to submit in NDAs the data that they can gather on their products and to commence controlled studies under INDs. (INDs should be submitted in 3 months.) If we allowed a longer period for the NDA (e.g., one year, and we assume that many if not all the NDAs would be not approvable for some reason on the first submission, then we would only be prolonging the time when we could control the IUD marketing with respect to safety and efficacy.

MARION J. FINKEL, M.D., *Deputy Director,*
Bureau of Drugs.

Before there are further victims of FDA negligence, we ask for proper consumer protection on IUds.

Yours truly,
Anita Johnson
Anita Johnson, esq.