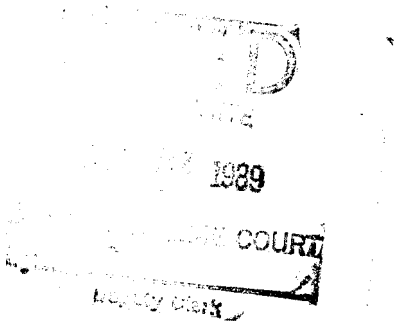
OA 9-5-89

SUPREME COURT OF FLORIDA

CASE NO. 73,596



THE UPJOHN COMPANY,

Petitioner,

vs.

ANNE MARIE MACMURDO, a/k/a
ANNE MARIE STAFFORD,

Respondent.

PETITIONER'S REPLY BRIEF

JOHN A. REED, JR.
Fla. Bar No. 065522

R. KIMBARK LEE
Fla. Bar No. 437278
Lowndes, Drosdick, Doster, Kantor
& Reed, Professional Association
215 North Eola Drive
Post Office Box 2809
Orlando, Florida 32802
(407) 843-4600
Attorneys for Appellant

TABLE OF CONTENTS

TABLE OF CITATIONS

Note: References in this brief to the transcript will utilize the abbreviation "T" followed by the appropriate page and line designations. References to deposition excerpts will be identified by the name of the deponent, "D" (indicating Deposition), and the appropriate page of the deposition with a line designation, if one is available. References to the record on appeal will be identified by "R" followed by the appropriate page number(s). References to the Appendix accompanying Upjohn's initial brief will be abbreviated "App."

I. Summary of The Upjohn Company's Reply

The Respondent, Anne MacMurdo, has misconceived the standard to be applied in connection with motions for directed verdict and for judgment not withstanding the verdict. In ruling on such motions, the court considers all the evidence and determines, therefrom, whether or not a jury, acting reasonably, could differ as to the existence of material facts or inferences on which liability turns. Westchester Exxon v. Valdes, et al., 524 So.2d 452, 455 (Fla. 3d DCA 1988). In applying this standard, it is a part of the judicial function to determine the reasonableness of material inferences to be drawn from the evidence. Brock v. Merrell Dow Pharmaceuticals, Inc., 874 F.2d 307, 309 (5th Cir. 1989).

The fallacy of MacMurdo's approach to the issues lies in her effort to suggest favorable inferences based only on selected parts of the relevant evidence. This brief, therefore, will be devoted primarily to the clarification and amplification of what The Upjohn Company, as Petitioner, believes to be inaccurate or incomplete factual references in MacMurdo's brief.

11. Reply to MacMurdo's Statement of the Case and Facts

At page 4 of MacMurdo's brief, she states that Dr. Levy did not testify that he was aware that Depo-Provera was not recommended by Upjohn for contraception. Dr. Levy testified he was aware that the only indication for Depo-Provera stated in the package insert was the treatment of endometrial carcinoma (Levy, D. 28/3-19; R. 1084). Thereafter, Dr. Levy testified that the

term "indication" in a package insert was understood by him to mean the recommended use of the drug (Levy, D. **38/22-24;** R. **1094).** The obvious conclusion to be drawn from this testimony is that Dr. Levy knew the only recommended use of Depo-Provera was for treatment of endometrial carcinoma.

At page 5 of her brief, MacMurdo claims that Dr. Levy " **...** does not consider the package insert to be a direction to him from Upjohn not to use the drug for contraception." Dr. Levy did not testify to that effect and the assertion is not a reasonable inference to draw from the testimony of Dr. Levy. Please see Levy D. **27/3-28/19** (R. **1083-1084).**

At page 5 of her brief, MacMurdo informs the Court that Dr. Benjamin testified that if Upjohn really intended to discourage doctors from using Depo-Provera as a contraceptive, it could have simply stated on the package insert that it was not recommended for that use. The Respondent cites to the transcript at pages **312** and **313.** That testimony will not support the Respondent's implication. Dr. Benjamin actually said:

> THE WITNESS: Well, one simple thing that can be done is to just incorporate the wording that's right there in a black box, that's called the black box warning. That's just to highlight it.
>
> That wouldn't change the wording, and additional wording might go to say that it wasn't recommended for that purpose, in addition, to whatever else was said, and those are two right off the top of my head.
>
> (T. 313/10-19)

Neither of those suggestions had any probative significance for the simple reason that Drs. Levy and Shapiro knew that Depo-Provera was not recommended for use as a contraceptive.

At page 8 of her merits brief, MacMurdo advises the Court that when she returned to Dr. Levy in December 1974 (actually it was January 7, 1975), with symptoms of continuous bleeding for four months, Dr. Levy was at a disadvantage because Upjohn knew something that he did not. At page 9 of her brief, MacMurdo proceeds to advise the Court that Dr. Levy testified he did not consider that Depo-Provera might have been causing the dysfunctional bleeding she experienced because it was supposed to have the opposite effect. MacMurdo cites to Dr. Levy's deposition at pages 57 and 58. On the basis of this treatment of the record, MacMurdo argues at page 23 of her brief that Dr. Levy misdiagnosed Anne MacMurdo's prolonged excessive bleeding and performed a hysterectomy because he was given no warning from Upjohn that Depo-Provera could produce such side effects.

MacMurdo has sought to generate a favorable inference by citing the Court to only a part of the pertinent testimony. The Respondent wishes the Court to infer that the package insert, if read, was inadequate to put Dr. Levy on notice that the symptoms displayed by Anne MacMurdo in January 1975 could result from the use of Depo-Provera. This is not a reasonable inference in light of the other testimony of Dr. Levy as follows:

> Q. So it's possible then, is it not, that the drug Depo-Provera, once analyzed by yourself in reading that insert, could have alerted you to a change in the menstrual flow that she was having; couldn't it..?
>
> * * *
>
> A. I'm not sure I understand the question. In other words, it could have alerted me at what point?
>
> Q. Well, doctor, when she came to you in January of '75.

A. I see. In other words, if I had this in front of me in January of '75?

Q. Correct.

A. This is dated August 1977.

Q. Correct

A. If I had a piece of paper that had a package insert from Upjohn in front of me when she was complaining of abnormal bleeding and I would have been reading this, you're saying would I have thought that possibly her problem was due to the drug?

Q. Correct.

A. I think that's possible.

* * *

Q. With a reasonable medical probability, had you been aware of an adverse reaction coming from the drug of Depo-Provera in the change of a menstrual flow, would that have indicated that the drug Depo-Provera could have been causing the problem...?

A. I'd say yes.*

(Levy D. 59/11-61/24; R. 1115-1117; emphasis added)

Thus, Levy's testimony, when read as a whole, will not support an inference that the package insert, if read, was insufficient to inform him that Depo-Provera might have occasioned MacMurdo's abnormal bleeding.

---

* It is apparent from Dr. Levy's deposition testimony that he was referring to the **"ADVERSE REACTIONS"** section of a 1977 Depo-Provera package insert which cites change in menstrual flow and breakthrough bleeding as possible side effects of Depo-Provera. It should be noted, however, that the package insert in effect when he prescribed the Depo-Provera in May 1974 and when he performed the hysterectomy was in evidence as Plaintiff's Exhibit 8 and contained an identical reference to change in menstrual flow and breakthrough bleeding in its **"ADVERSE REACTIONS"** section. Please see App. 1 to Upjohn's initial brief.

Regarding Dr. Shapiro, MacMurdo states at page 9 of her brief that he testified nothing in the package insert would have put him on notice that Depo-Provera could cause excessive bleeding. This is not a fair rendition of the relevant testimony. Dr. Shapiro clearly acknowledged that in 1974 he was aware of the possibility that Depo-Provera could cause excessive bleeding. This appears from his testimony at page 504 of the transcript and quoted at page 5 of Upjohn's merits brief. Furthermore, the other testimony of Dr. Shapiro bearing on the subject, but not cited by the Respondent is as follows:

> Q. Can you imagine the circumstances in which if a woman gets Depo-Provera and has heavy bleeding, that getting of Depo-Provera causes her to have a hysterectomy unless she wants it for sterilization?
>
> A. The scenario usually with Depo-Provera is absence of menstrual bleeding. The other type of side effect, as I mentioned, is really a -- maybe an intermittent, prolonged stage, but nothing in terms of that I have seen or been acquainted with, but <u>of course on theoretical grounds it can occur in terms of heavy menstrual flow</u>.
>
> (T. 521/18-522/3; emphasis added).

At page 10 of MacMurdo's brief she uses a reference to the testimony of Dr. Benjamin to bolster her incorrect factual assertions with regard to the knowledge of Drs. Levy and Shapiro. Dr. Benjamin, without predicate, testified that neither Levy nor Shapiro was aware Depo-Provera could cause excessive bleeding (T. 423/16-23). His testimony in this respect was completely incompetent and can hardly raise a <u>reasonable inference</u> that Levy and Shapiro were misled by the package insert, <u>in the absence of testimony from Levy and Shapiro to that effect</u>.

At page 11 of her brief, MacMurdo states:

> The evidence at trial was that "breakthrough bleeding" ... means there is some continued irregular spotting after the normal five day bleeding period has ended (T. **425-426**). It is a completely different condition than excessive and prolonged heavy inter-menstrual bleeding (T. **426**).

This again is not a fair rendition of the testimony. Dr. Benjamin's exact testimony was as follows:

> A. My understanding of the term break through bleeding, it's usually to who are taking oral contraceptives that contain either estrogen or estrogen progesterone combinations.
>
> Break through bleeding is when a woman is taking one of those oral contraceptives and instead of having a five day period, and then having a - say **23** day non-bleeding period, she also bleeds or spots on after her normal menstrual period of five days has completed....
>
> * * *
>
> Q. Is that different than what the phenomenon we are talking about from the studies of the 11 to **30** day bleeding.
>
> A. Yes. It's a different type of bleeding.
>
> (T. **425/19-426/17;** emphasis added).

While it is true that Dr. Benjamin was led by Plaintiff's counsel into the statement that breakthrough bleeding was somehow "different" from the bleeding referred to in the Schwallie article, there is absolutely no basis in that or any other evidence to suggest that a competent physician (including Dr. Levy) who read the package insert would not have been alerted to the possibility that Depo-Provera could have caused MacMurdo's irregular bleeding which Dr. Levy in January **1975** classified as "... painful menstruation and dysfunctional bleeding which is abnormal bleeding" (Levy D. 41/23; R. 1096). The trial judge specifically recognized that Benjamin, not being a physician, was

not qualified to assess the impact of the package insert on the thought processes of a physician (T. 310/24; 330/3-16). Dr. McConnell, who testified on behalf of Upjohn, testified without contradiction that breakthrough bleeding is bleeding outside the normal menstrual cycle (T. 724/25-725/2).

At page 11 of MacMurdo's brief, she states because Dr. Levy did not understand Depo-Provera could produce prolonged intermenstrual bleeding, " ... he misinterpreted Plaintiff's symptoms and he recommended a hysterectomy, to which Plaintiff consented..." (emphasis added). One will look in vain for evidence in support of that conclusion. During MacMurdo's cross-examination of Dr. Shapiro, Dr. Shapiro read into the record a letter from Dr. Levy dictated March 10, 1975 (T. 488/20). In that letter, Dr. Levy indicates that: "Due to the fact that she still wanted to have elective sterilization, we elected to do a vaginal hysterectomy. This was carried out on January 9, 1975..." (T. 489/11). Dr. Levy repeatedly testified that he did not recommend the sterilization as a method of correcting the bleeding (Levy D. 46/11; 47/9; R. 1101-1102). Although MacMurdo was asked about Levy's recommendation on direct examination, she never testified that Levy recommended the hysterectomy as a means of stopping her bleeding. Her oblique reply simply avoided the issue (T. 560/11; T. 607/14).

Finally, at page 16 of the Respondent's brief, she states that the use of drugs was brought into the trial "just to prejudice the jury against the Plaintiff over irrelevant matters.'' In point of fact, MacMurdo's trial attorney introduced

the subject of drugs and suicide in his opening statement (T. 118/2-9).

111. Reply to MacMurdo's Argument under First Issue

Under the First Issue, the Respondent reargues the jurisdictional question. This argument is improper in light of this Court's order of May 11, 1989, directing the parties to file "merits briefs" and conflicts with the intent of Fla. R. App. P. 9.330(d). In any event, there can be no questions that the opinion of the Fourth District Court of Appeal which is before this Court conflicts with the opinion of this Court in Felix v. Hoffmann-LaRoche, Inc., 540 So.2d 102 (Fla. 1989). The Fourth District Court of Appeal's opinion clings to the notion it had theretofore expressed that "... in all events the adequacy of the warning is for the jury to decide...." Upjohn v. MacMurdo, 536 So.2d 337, 339 (Fla. 4th DCA 1988). The harmful effect of such a rubric is that its application denies an appealing party the right to a thorough judicial analysis of the legal sufficiency of the evidence.

At the bottom of page 23, MacMurdo advises the Court that Dr. Levy " ... misdiagnosed her prolonged and excessive bleeding and performed a hysterectomy because he was given no warning from Upjohn that this drug can produce such side effects." As previously demonstrated, there is no factual support for the conclusion that Dr. Levy was in any way misled or left uninformed by the package insert. Furthermore, there is no evidence in this record (and none is cited by the Respondent) that Dr. Levy misdiagnosed the cause of MacMurdo's bleeding. Insofar as the

record is concerned, there is simply no evidence that Dr. Levy concerned himself with the cause of MacMurdo's bleeding, although he clearly understood there were methods short of a hysterectomy for treatment of the bleeding (Levy D. **86**; R. **1142**).

At page **25** of her brief, MacMurdo tells this Court that not only did the jury find adequate evidence on the issue of negligent warning, but three separate appellate panels did likewise. This is not correct. Please see footnote 1 to the opinion under review.

MacMurdo argues at page **27** of her brief that the jury's finding of negligent warning could have been based on the fact that The Upjohn Company did not place in its package insert information to the effect that **25-35%** of the females studied experienced bleeding after the first two injections. What MacMurdo does not point out is that the study which was reported on by Dr. Schwallie was conducted between **1965** and **1972** on the use of 150 mg injections of Depo-Provera at **90** day intervals for contraception. The study was conducted in accordance with FDA regulation (T. 623/6-626/12). It indicated that a percentage of the women in the study group experienced bleeding or spotting after the first injection, but the incidence of such bleeding decreased markedly after the second and subsequent injections. The bleeding was irregular and unpredictable from individual to individual and within the same individual, but such bleeding was more frequently in the nature of spotting or light bleeding than heavy menstrual flow. Please see App. 5 to Upjohn's merits brief.

It is inconceivable that The Upjohn Company should be held negligent for not including the findings of that study in the package insert for Depo-Provera when the FDA specifically declined to approve Depo-Provera for use as a contraceptive (T. 623/4-630/15; particularly 630/15). The information MacMurdo claims Upjohn should have published would obviously be viewed as an implied invitation to physicians to use Depo-Provera for contraceptive purposes. The information would have rendered the product misbranded and subjected the manufacturer to the severe sanctions of federal law. 21 U.S.C.A. §§352(a) and 331. See also App. 9.

The Appellate Division of the New Jersey Superior Court has just issued an opinion containing a lengthy discussion of the problem created when liability is sought to be imposed under state tort law for a failure to warn under circumstances in which federal law would preclude the warning. The court adopted a theory of "conflict preemption" which precluded state tort law liability. Feldman v. Lederle Laboratories, ___ A. 2d ___ (N.J. App. Div. 1989). Because of its recent origin, a copy of this case is provided as an appendix to this brief.

If the jury verdict is allowed to stand, The Upjohn Company will be penalized for failing to provide information on the contraceptive use of Depo-Provera in the face of evidence adduced by MacMurdo herself that the United States Food and Drug Administration would never have approved the publication of such information (T. 623/4-630/18). Such a result is not unlike that condemned in Taylor v. General Motors Corp., 875 F.2d 816 (11th

Cir. 1989), wherein the Court of Appeals concluded that an automobile manufacturer could not be held liable under theories of negligence or strict liability for adopting a design standard specifically permitted by federal law. In the present case, the format and the text of the product label were approved by the FDA after a long and arduous administrative process described by MacMurdo's own witness, Dr. Benjamin (T. 294/17-296/14; T. 384/2-19; T. 389/4-11).

IV. Reply to MacMurdo's Argument Under Issues Two through Five

MacMurdo argues under Issues Two through Four that the issues raised therein were not considered by the Fourth DCA and, therefore, should not be considered in this appeal. The points raised by The Upjohn Company in Issues Two through Four were fully briefed and presented to the Fourth DCA. Therefore, it is completely appropriate for this Court to consider those points in connection with the present appeal. Once this Court takes jurisdiction because of a conflict as to one question, it normally resolves all questions properly presented. Bould v. Touchette, 349 So.2d 1181, 1183 (Fla. 1977), reh. denied, 1977.

In footnote 5 on page 34 of MacMurdo's brief, she suggests that the argument made by The Upjohn Company under the Third Issue relating to the policy aspect of foreseeability was not properly presented to the trial court. On the contrary, the argument made by trial counsel for Upjohn at page 665 of the transcript beginning at line 18 and running through page 666, line 20, clearly should be deemed sufficient to have alerted the

trial judge to the twin problems of proximate causation. Please see Curtis Publishing Co. v. Fraser, 209 F.2d 1, 6 (5th Cir. 1954).

At page 37 of her brief, MacMurdo argues that the medical malpractice of Dr. Levy was foreseeable as a matter of law by The Upjohn Company. The case cited in support of this contention, Stuart v. The Hertz Corp., 351 So.2d 703 (Fla. 1977), is so distinct from the present situation as to be uninstructive. Furthermore, that case seems to involve the cause-in-fact aspect of proximate cause. The proximate cause issue Upjohn discusses under its Third Issue does not involve the cause-in-fact aspect of proximate causation. In dealing with Upjohn's Fourth Issue, MacMurdo argues at page 39 of her brief that Upjohn is somehow estopped to seek alternative relief in the form of a new trial on a limited aspect of the damage claim. What conceivable reason there could be to support that type of estoppel argument is unapparent from MacMurdo's citation to Shamel v. Schechter, 371 So.2d 109 (Fla. 4th DCA 1978). In Shamel, the appellant apparently attempted to present to the appellate court factual and legal theories that were not presented in the trial court. In the present case, the trial court was clearly afforded an opportunity to rule that Depo-Provera was not a legal cause of the hysterectomy and fashion appropriate relief. Please see paragraph 19 of The Upjohn Company's Alternative Motion for New Trial, R. 2586-2590.

With regard to the contentions MacMurdo directs to Upjohn's Fifth Issue, Upjohn has heretofore pointed out MacMurdo's under-

lying factual inaccuracies and will simply rely on its merits brief for further rebuttal.

V. Conclusion

There is no testimony from the physicians who prescribed Depo-Provera for Anne MacMurdo in **1974** that they were somehow misled in their treatment of her by the FDA-approved product labeling distributed by The Upjohn Company with Depo-Provera. Similarly, there is no evidence from any other medical expert that the Depo-Provera labeling was inaccurate or ambiguous. MacMurdo's only medical expert found the labeling to be quite clear (Roshan D. **54/25**). The record is barren of competent evidence to support the jury's finding that Upjohn was negligent in connection with such labeling. The Upjohn Company is, for the reasons stated herein and in its main brief, entitled to appropriate relief in this Court.

Dated this 18th day of August, **198**

Respectfully submitted,

John A. Reed

JOHN A. REED, JR.
Fla. Bar No. **065522**

R. Kimbark Lee

R. KIMBARK LEE
Fla. Bar No. **437278**
Lowndes, Drosdick, Doster, Kantor & Reed, Professional Association
215 North Eola Drive
Post Office Box **2809**
Orlando, Florida **32802**
(407) 843-4600
Attorneys for Appellant

CERTIFICATE OF SERVICE

I HEREBY CERTIFY that a true and correct copy of the foregoing was furnished by U.S. Mail to DOMINIC L. BRANDY, ESQ., 115 S.E. 13th St., Ft. Lauderdale, FL 33316, and RICHARD A. KUPFER, ESQ., Cone, Wagner, Nugent, et al., P.O. Box 3466, West Palm Beach, FL 33402, Co-counsel for Respondent; DAVID M. COVEY, ESQ., 59 Maiden Lane, 41st floor, New York, NY 10038, and ~~G. WILLIAM BISSETT, ESQ.,~~ 501 N.E. First Avenue, Miami, FL 33132, Co-counsel for Petitioner, this 18th day of August, 1989.

John A. Reed, Jr.
Attorney