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October 7, 1971

Commissioner of Food and Drugs
Department of Health, Education and Welfare
Washington, D. C. 20204

Dear Sir:

I am herewith transmitting a petition relative to the Food and Drug Administration's actions based on the agency's acceptance of and extrapolations from the conclusions of the University Group Diabetes Program.

I would appreciate a prompt reply to this petition and would hope that in any case, one could be received within 30 days.

I anticipate that the petition will be printed in the Federal Register in the usual course. Kindly address your reply to me at the above address.

Very truly yours,

Neil L. Chayet

NLC:m

Document #20

PETITION

OF

COORDINATING COMMITTEE OF

THE COMMITTEE ON THE CARE OF THE DIABETIC

TO

COMMISSIONER OF FOOD AND DRUGS

From the office of:

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Document #20

Commissioner of Food and Drugs
Department of Health, Education, and Welfare
Washington, D. C. 20204

Dear Sir:

This petition is submitted with respect to (1) the issuance of recommendations contained in the October, 1970 FDA Current Drug Information Bulletin entitled, "Diabetes Prescribing Information" and (2) the recommended changing of the INDICATIONS AND WARNINGS section of the labelling of all sulfonylureas as stated in the June 23, 1971, FDA Drug Bulletin.

Attached hereto, in quintuplicate and constituting a part of this petition are the following:

A. The FDA Current Drug Information, October, 1970 (marked Appendix A).

B. Relevant excerpts from FDA Drug Bulletin dated June 23, 1971 (marked Appendix B).

C. Written communications of Robert F. Bradley, M.D. and the Committee on the Care of the Diabetic to the FDA. (marked Appendix C).

D. A statement of the grounds upon which your petitioner relies for the action requested herein (marked Appendix D).

The recommendations which are the subject of this petition have been made by the Food and Drug Administration (FDA) as a result of the report of the University Group Diabetes Program (UGDP). This report has been the subject of intense controversy since its conclusions were made known both because of the unprofessional manner in which the conclusions originally became known, in the lay press, as well as the irreparable flaws of its methodology, and the major inconsistencies in the conclusions. The report, which suggested that tolbutamide is no more effective than diet alone in the treatment of mild adult-onset diabetes, is insupportable in the light of impartial scientific inquiry, and the Food and Drug Administration, by embracing its conclusions, has intruded into the practice of medicine, placing the physician who continues to prescribe tolbutamide for the treatment of maturity-onset diabetes in jeopardy and causing great concern on the part of more than a million diabetics and their physicians who have regularly used this drug.

5 to statements of A NIH AMA Medical letter

This petition is grounded in three fundamental principles:

1. Regardless of the validity of the UGDP study, it is the contention of your petitioners that the Food and Drug Administration's legal mandate is solely the regulation of drugs as to safety and efficacy and not the control of medical or scientific practices; furthermore, the FDA should not engage in the establishment of an official governmental policy in respect to the practice of science or medicine. We believe this to be as true for the treatment of diabetes as it would be in relation to such procedures as cardiac surgery or kidney and heart transplants.

2. The government should particularly refrain from taking a partisan position and establishing a "government line" in an area of medicine and science in which extensive controversy and debate exists among qualified scientists and/or physicians. In the present situation such a position has been taken despite the absence of corroborating studies which have reproduced the UGDP findings, an essential criteria in the establishment of scientific principles. Even if the UGDP study were

beyond reproach, which the statement marked "Appendix D" will show it is not, the FDA should not adopt the singular position of one group if contradicting positions are advocated by other qualified scientists and physicians. With respect to the UGDP findings, strong controverting data and extensive comment, disagreement and experience among a large body of extremely well qualified scientists exists and is a matter of scientific record. Furthermore, in this situation the FDA has ruptured its own rule of fair balance in failing to present the other side of the issue in its mailings and statements, even as it has itself taken sides in the issue.

3. The single study upon which the FDA bases its action has been criticized on professional, scientific, clinical, statistical, and other grounds. Furthermore, FDA action did not properly reflect the criticisms and recommendations of its own medical advisory panel on the subject. In effect, despite repeated requests for over a period of a year from many different sources, the basic data of the study remain unavailable

to the scientific community and the recent report on phenformin[1] presents an inadequate amount of protocol material to enable adequate scientific evaluation. The 6/23/1971 FDA Current Information Bulletin nevertheless made the general statement that "although this study considered only one sulfonylurea, tolbutamide, it raises serious questions as to the ultimate place of all antidiabetic agents in the treatmentof diabetes mellitus."

This petition for a reversal and clarification of the FDA's positions as stated above is thus grounded not only on the basis of the fundamental principle of the separation of science and state, but also on the fact that legitimate scientific controversy exists and the UGDP study has been controverted by a large and leading body of specialists in the field as being more than just erroneous. In point of fact, the FDA has sought in this situation to regulate therapy on the basis of an experiment which is based on faulty methodology, which has disregarded many essential recommendations related to the true therapeutic application of the agents under study, and in doing so has extrapolated without valid statistical basis,

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[1] "Effects of hypoglycemic agents on vascular complications in patients with adult-onset diabetes," JAMA, August 9, 1971.

thus flying directly in the face of the caveat of the authors of the UGDP study themselves, to wit:

> It should be noted that any conclusion reached in this study pertains only to the type of patient studied and to the specific hypoglycemic agents and dosage schedules used. Extrapolation of findings obtained in the UGDP to other dosage schedules of the same drug or to other chemically related hypoglycemic agents not included in this study must be made on a judgmental and nonstatistical basis. [2]

In addition, it was recently reported that Dr. Christian R. Klimt, the statistical coordinator of the UGDP study, stated that a similar trial of diabetic oral agents, which he will be conducting in Yugoslavia under FDA auspices, will employ a flexible dosage regimen and be confined to a symptomatic diabetic population.[3] The use of fixed dosage and asymptomatic patients are two of the serious limiting factors in the UGDP study (see Appendix D). This action by the statistical coordinator indicates the merit of the most serious criticism which has been levelled at the UGDP report.

It has also been reported that the protocol in regard to the double blind technique may not have been followed in every participating clinic for all patients (see Appendix D, Part 2).

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[2] "University Group Diabetes Program," Diabetes 19, Supp. 2, 1970

[3] Drug Trade News, August 23, 1971

Lastly, it should be noted that the conclusions of the study have been specifically rejected by the Canadian Food and Drug Directorate, the Canadian Diabetes Association, the British Committee on Drug Safety, the British Diabetes Association, the German Ministry of Health, the German Diabetic Society, and the Swedish government.

Failure to grant petitioner's requests will result in a continuance and aggravation of damage which has already been perpetrated by the dissemination of these recommendations already made and the suggested labelling changes. As a result of actions taken by the Food and Drug Administration, an undetermined number of patients stopped taking medication on their own or were taken off the medication by their alarmed physicians and subsequently became symptomatic.

Failure to grant these requests will cause further irreparable harm to more than a million patients, particularly to their relationship with their physicians and to their personal psychic stability so essential in a disease such as diabetes.

Failure to grant the request will perpetuate the unjustified damage done to a large number of physicians and research scientists in the field of diabetes with respect to their standing in the public view as well as in the medical and scientific communities.

The Food and Drug Administration has taken a partisan position in an area of valid and continuing medical and scientific discussion and debate. This is a serious error both in principle and in fact.

The Food and Drug Administration indentification with a controversial study which has been subject to extensive criticism is particularly unfortunate.

It must clearly be recognized that the government has no role as a partisan in valid continuing scientific controversy.

Your petitioners, in reliance on the statement contained in Appendix D of this petition, respectfully request that the following steps be taken immediately:

(1) That the recommendations contained in the October 1970 Food and Drug Administration Current Drug Information Bulletin, entitled "Diabetes Prescribing Information" be immediately rescinded and that notice of such rescission be distributed in exactly the same manner as the Bulletin was distributed.

(2) That the recommendations which would change the INDICATIONS AND WARNINGS section of the labelling of all sulfonylureas as stated in the June 23, 1971 Food and Drug Administration Drug Bulletin be rescinded and that notice of same be distributed in exactly the same manner as the Bulletin was distributed.

(3) That the Food and Drug Administration use its best efforts to restore the confidence of patients in their physicians who use tolbutamide and the sufonylureas generally.

(4) That pending corroboratory studies the Food and Drug Administration refrain from making any further recommendations related to hypoglycemic substances based on the University Group Diabetes Program and that any actions related to the UGDP studies

deficiencies and the controversial nature of its implications. And that any references be made in the context of fair balance as above stated.

(5) That the Food and Drug Administration repudiate all other recommendations, statements, mailings or communications of any kind which have been distributed to the medical and scientific communities, to the lay press, or to the general public based on the UGDP study and that the Food and Drug Administration use its best efforts to widely disseminate such repudiation.

(6) That the Food and Drug Administration make available to your petitioners and other qualified researchers the baseline data of the University Group Diabetes Program; such baseline data shall include the total patient record of each patient included in the study.

(7) That in accord with its policy of fair balance, the Food and Drug Administration dissenimate with equal effort, emphasis and frequency, the results of all other studies reported by qualified researchers as well as clinical opinions of outstanding diabetologists which disagree with or controvert UGDP study and the conclusions extrapolated therefrom.

(8) That your petitioners be provided with full and complete answers to the following questions:

(a) By virtue of what statute, regulation, rule, or other legal authority does the Food and Drug Administration establish therapeutic regimens by stating preferences - i.e., first, diet; second, insulin and third, oral agents - in its Bulletins marked Appendix A and Appendix B of this petition?

(b) Why did the Food and Drug Administration ignore the views of the majority of its own Advisory Committee on Diabetes, a committee that was composed of four diabetologists, two biostatisticians and a biochemist? That majority was not willing to accept the conclusions of the UGDP report.

(9) That any other relief be granted that the Food and Drug Administration may deem meet and proper to fulfill the spirit and letter of this petition.

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respectfully submitted,

Coordinating Committee
of the
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of the Diabetic
By:

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