FDCC 71-1

Manufacturing Chemists' Association, Inc.

MINUTES OF MEETING

FOOD, DRUG, AND COSMETIC CHEMICALS COMMITTEE

MCA Conference Room Washington, D.C.

January 25, 1967

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Members Present

W. E. McCormick, Chairman	B. F. Goodrich Company
V. H. Knoop, Vice Chairman	Mallinckrodt Chemical Works
R. N. Bell	Stauffer Chemical Co.
C. P. Carpenter	Union Carbide Corp.
Frank Di Prima (for J. M. Stocker)	Merck & Co.
James Hulse (for C. F. Hagan)	Chas. Pfizer & Co.
J. A. Korth (for J. T. Seawell)	Corn Products Co.
W. H. Meyer	Procter & Gamble Co.
Robert Miller (for J. G. Kuniholm)	Hercules Inc.
K. E. Mulford	Atlas Chemical Industries, Inc.
O. H. Peterson	Salsbury Laboratories
A. M. Schnitzer (for R. P. Howard)	Phillips Petroleum Co.
H. C. Spencer	Dow Chemical Co.
G. J. Stopps (for T. W. Hanavan)	E. I. du Pont de Nemours & Co.
G. P. Vincent	Olin Mathieson Chemical Corp.
Samuel Zuckerman	H. Kohnstamm & Co.
A. R. Marusi, Board Liaison	Borden Company
M. M. Hoover, Secretary	MCA Staff

Guests Present

G. W. Fiero	Humble Oil and Refining Co.
John Kelly	Pharmaceutical Manufacturers Assn.
R. J. Kunz	Borden Co.
H. N. Reiman	Stauffer Chemical Co.
J. H. Yeager	Mallinckrodt Chemical Works

Members Absent

T. R. Aalto	Tenneco Chemicals, Inc.
F. R. Barron, Jr.	American Cyanamid Co.
C. F. Hagan	Chas. Pfizer and Co.
T. W. Hanavan	E. I. du Pont de Nemours & Co.

Members Absent....continued

R. P. Howard	Phillips Petroleum Co.
J. G. Kuniholm	Hercules Inc.
B. T. McMillan	Allied Chemical Corp.
L. A. Miller	Monsanto Co.
H. L. Schulman	Washine Chemical Corp.
J. T. Seawell	Corn Products Co.
D. A. Seligman	Hoffmann- La Roche Inc.
J. M. Stocker	Merck and Co.
R. G. Troup	J. T. Baker Chemical Co.
N. G. White	Shell Chemical Co.

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1. Minutes of the Last Meeting

The minutes of the October 11, 1966 meeting were approved as distributed with the exception of the identification in Item 7 of Dr. Stopps. He is with E. I. du Pont de Nemours and Company.

2. Membership

The secretary reported that MCA has been advised by Corn Products Company that J. T. Seawell has been transferred to otner areas of operation.

3. Liaison with MCA Environmental Health Advisory Committee

The chairman announced that he will appoint an FDCC Committee representative to EHAC to replace Mr. Hagan.

4. Cosmetics Legislation

It was decided that the FDCC Committee should express to the Toilet Goods Association our interest in their activities in this area, and request that they keep us advised in the event they wish our support. The secretary was asked to make the contact.

Mr. Miller reported that SPI has been and will be quite active in following the legislation.

5. Animal Care Legislation

Dr. Stopps' report on Animal Care Legislation is attached to these minutes as Exhibit A.

Referred to in Dr. Stopps' report are the animal care law passed in August 1966 (together with the comments of the Joint House - Senate Conference Committee) and the proposed laboratory animal welfare rules as printed in the December 15, 1966 Federal Register. These were

distributed to the FDCC Committee at the January 25 meeting.

Dr. Stopps stated that: "Most industrial laboratories would not find the intent of the law to be very different from their own guide lines for the conduct of testing and research procedures using animals. It is obviously in our own interest to have healthy, well-housed animals, and worthwhile research requires good record keeping--all of which are the stated aims of the law. Some discussion arises at the point when the methods by which these aims are to be achieved are published."

6. Medical Devices Legislation

Mr. Kelly's report covering Medical Devices Legislation is attached to these minutes as Exhibit B.

Mr. Kelly said that there will probably be no legislation this year, but possibly next year, and that PMA will oppose premarketing clearance.

He said further that there are two schools of thought within FDA: (1) the only way to approach the regulation is through premarketing clearance procedures, and (2) devices should be classified as to those which must undergo premarketing clearance, those for which only standards must be promulgated, and those which require neither standards nor premarketing clearance.

7. Indirect Food Additives

Dr. Miller's report covering Dr. Frawley's proposal regarding Indirect Food Additives is attached to these minutes as Exhibit C. The committee commended Dr. Frawley for his proposal.

Because of the potential benefit to the chemical industry, it was decided to request the secretary to obtain from MCA member companies data that will help establish or disprove the validity of the proposal. Dr. Miller agreed to supply the secretary with copies of Dr. Frawley's ACS paper which will help explain what data is required.

It was also decided to discuss at the next meeting what stand might be taken by MCA with respect to the proposal, when the solicited data should be available for review.

Mr. Zuckerman said that the proposal might run into difficulty with color additives.

Mr. Marusi offered to get in touch with Mr. Cruse of SPI to ascertain their position and contemplated action, so that this information would be available to the committee before the next meeting.

8. Carcinogenicity of Food Additives and Cosmetics

The chairman appointed Dr. Carpenter, Dr. Spencer, and Mr. Meyer as the task group to carry out the committee's project on carcinogenicity. Dr. Carpenter is to serve as chairman of this task group.

During a brief discussion of Massachusetts House Bill No. 642, which proposes a commission to study cancer-producing ingredients in packaged goods, it was decided to request the secretary to ascertain whether packaging materials or the products themselves are in question, what in general the objectives are, and what is being done with respect to the bill.

9. Plant Inspections

The chairman appointed Messrs. Bell and Knoop as the task group to carry out the committee's project on plant inspections. Mr. Bell is to serve as chairman of this task group.

10. Codex Alimentarius

Dr. Spencer reported briefly on the fourth session of the Codex Alimentarius Commission held in Rome, November 7-14, 1966.

He referred the committee to the official report of the U. S. delegation to the session, and specifically to the following two paragraphs having to do with the need to strengthen communications between industry and government:

"The working arrangements between U. S. government agencies and the food and chemical industries have proven to be effective and efficient. This fact is important in the development of the Codex Standards, but even more so in the deliberations of the commission. Because of the close consultation between industry and government, the U. S. delegation had available highly competent recommendations and suggestions in all of the fields under discussion. The U. S. delegation was able to participate effectively in the work of the commission in such a way that the United States position was understood and, in the main, received majority support.

"As the number of Codex Standards being developed increases and as these standards advance in the step procedure toward acceptance, the cooperation between industry and government agencies will be even more important. Therefore, every opportunity should be taken by U. S. delegates to strengthen communications between parties interested in the various Codex Standards. This will strengthen the program by keeping more people informed about the progress and ramifications of the proposed standards."

To acquaint the committee with established lines of communication, Dr. Spencer made specific mention of the "Flow Diagram for International Acceptance of Food Additives," and to "The Joint FAO/WHO Food Standards Program." A copy of the former is attached to these minutes as Exhibit D, and the latter as Exhibit E.

Dr. Spencer also referred the committee to two publications which will be particularly helpful to industry. One is a brochure telling what the Codex Alimentarius Commission is, why it is important to the U.S., the role of the U.S., and the names of the U.S. delegates to the various Codex Committees. It is published by the USDA, and is titled "Codex Alimentarius Commission." The other is the "1966 Yearbook of Agriculture" containing (in the chapter on international food standards) a highly useful section on the organization of the Codex Alimentarius Commission. The yearbook is available at $2.50 from the GPO, or through congressmen.

The secretary was requested to inform the MCA membership of the list of flavoring materials to be considered at the eleventh meeting of the Joint FAO/WHO Expert Committee on Food Additives, which is to be held in August 1967. This list is attached to these minutes as Exhibit F

It is important that toxicological and related data from manufacturers of these substances be in the hands of committee members well in advance of the meeting. The information, including published articles and unpublished reports, should be sent to Dr. Frank C. Lu, Chief, Food Additives, World Health Organization of the United Nations, Palais des Nations, Geneva, Switzerland.

11. Food Chemicals Codex

Dr. Spencer reported that Dr. Paul E. Johnson at the NAS-NRC will head up further work on the Food Chemicals Codex, and that a meeting has been called for February 3 to discuss the mechanism of supplementation and revision.

12. Economic Poison Disclaimers

It was the feeling of the meeting that MCA has a stake in the current "war" on economic poison disclaimers being waged by USDA, and that a united industry front should be established.

To assist in this, it was decided that close contact should be maintained with other industry groups, and that a report from each should be sent to the FDCC Committee. Dr. Fiero agreed to do this for CSMA, Dr. Peterson for AHI, and Dr. Carpenter for NACA.

13. Next Meeting Subjects

In addition to items in these minutes which will carry over to the next meeting, it was suggested that the secretary invite Mr. Settle of the MCA Staff to discuss public relations activities of interest to the FDCC Committee, and to schedule a discussion on micro-organisms in foods and drugs with particular emphasis on salmonella. With regard to the latter, Mr. Zuckerman agreed to get in touch with Mr. Lee Harrow of General Foods to see if he will be willing to make a presentation, and to notify the secretary at which time an official invitation would be sent.

14. Next Meeting Date and Place

It was decided to hold the next meeting on Tuesday, June 13, 1967 in the MCA Conference Room in Washington, starting at 10:00 a.m.

M. M. Hoover, Secretary
Food, Drug, and Cosmetic
Chemicals Committee

MMH:sel
February 20, 1967

EXHIBIT A
(Page 1 of 5)

ANIMAL CARE LEGISLATION

By: Dr. G. J. Stopps

Until 1966 the battle between the self-styled "humane movement" and the research community had been conducted as a series of sporadic skirmishes with the research workers regarding the dog lobby as a nuisance rather than a threat. This situation altered in 1966 when nationwide exposés of pet stealing and of brutality among animal dealers caused a shift of emphasis by the humane movement. The focus of action now became animal procurement rather than the attempt to reduce and restrict animal experimentation which had always been a subject too sensitive for congressional action. Public interest rose to almost unprecedented heights. The House Agriculture Committee alone received over 20,000 letters following two days of hearings on "pet-napping" bills, and individual congressmen reported mail from constituents running far higher than the combined mail on Vietnam, inflation, poverty, and civil rights. This shift of emphasis away from the sensitive area of the regulation of experimentation to the more readily supported attempt to improve animal care and handling resulted in Public Law 89-544 which was signed in August 1966. Whether this is the end of further legislation in the realm of animal care for the immediate future is difficult to forecast, not because the "humane movement" will give up its struggle for what it considers a just cause but because too many intangibles go into the building of the political climate to make the prediction of legislative events beyond one session of Congress worthwhile.

The laboratory animal care law as passed in August 1966 is appended to these remarks, together with the comments of the Joint House-Senate Conference Committee. Most industrial laboratories would not find the intent of the law to be very different from their own guide lines for the conduct of testing and research procedures using animals. It is obviously in our own interest to have healthy, well-housed animals, and worthwhile research requires good record keeping - all of which are the stated aims of the law. Some discussion arises at the point when the methods by which these aims are to be achieved are published.

On December 15, 1966, the proposed laboratory animal welfare rules were printed in the Federal Register. The usual 30-day period for the submission of views was allowed; but in this case, this period covered both the Christmas and New Year holiday which produced some inconvenience for those wishing to submit a statement.

Part I of the proposed rules deals with definitions of terms. Part II covers procedures for implementing the law such as dealer licensing and fees, registration of research facilities, identification of dogs and cats, and record keeping requirements, etc.

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A research facility unlike an animal dealer is merely required to register with the Department of Agriculture, whereas the dealer obtains a license for which a fee is payable.

The research facility applies for registration on forms provided for the purpose by the veterinarian in charge of the program. Along with the forms will be sent a copy of the standards to be followed, and acknowledgment of the receipt of the standards is included with the registration forms when the application is filed.

Dogs and cats (but not other animals) obtained by research facilities must be identified by an aluminum tag embossed with the letters USDA and numbers and letters identifying the state, dealer, and animal. These tags are affixed to the animal's neck by the dealer; and if removed by the research facility, the tag must be retained until called for by a Department of Agriculture representative.

In connection with all dogs and cats purchased or otherwise acquired, a research facility must keep the following information on forms to be supplied.

1. The name and address of the person from whom the animal was obtained, and the number of his license if he is a dealer.

2. Date obtained.

3. Description and identification of the animal.

If animals are transported or disposed of to another person, suitable records must be maintained of these events and all records must be kept for at least two years.

One of the more controversial portions of the proposed rules is that headed "Miscellaneous."

"2.125 Information as to business; furnishing of by dealers and research facilities.

Each dealer and research facility shall furnish to authorized representatives of the Secretary any information concerning the business of the dealer or research facility which may be requested by them in connection with the enforcement of the provisions of the Act, the regulations and the Standards in this subchapter, within such reasonable time as may be specified in the request for such information.

"2.126 Inspection of records and property of dealers and research facilities.

Each dealer and research facility shall, upon request, during ordinary business hours, permit authorized representatives of the Secretary to enter his place of business, to examine records requested pertaining to the business of the dealer or research facility and to make copies thereof, and to inspect such property and animals as such representatives consider necessary to enforce the provisions of the Act, the regulations and the Standards in this subchapter. The use of any room, table, or other facilities necessary for the proper examination of such records and inspection of such property or animals shall be extended to such authorized representatives of the Secretary by the dealer or research facility, his agents and employees."

These two sections are too general in their wording and a form of words which would restrict the information demanded to that which is strictly relevant to the care and housing of the animals should be substituted.

Section 2.128 deals with "Inspection for Lost Animals", and this is of importance since it was the alleged traffic in lost and stolen pets which was one of the principal reasons for enacting the legislation. Dealers and research facilities are required under this section to permit authorized representatives of legally constituted law enforcement agencies to enter the place of business to inspect animals and records for the purpose of seeking lost or stolen animals. Such inspection shall not extend to animals undergoing research. It will be noticed that inspection under this section is limited to searches by officers of the law (not owners themselves). The Joint House-Senate Conference Committee in a comment on this section says "legally constituted law enforcement agencies are to be agencies with general law enforcement authority and not those agencies whose law enforcement duties are limited to enforcing local animal regulations."

In the last section of Part II provision is made under certain circumstances for the confiscation and destruction of animals by Department of Agriculture representatives if an animal is found to be suffering as a result of the failure of the dealer or research facility to comply with the act or its provisions. This right of confiscation does not apply to animals on test or in a research program. The administration of the laboratory animal welfare regulations will be in the hands of the U. S. Department of Agriculture through the Animal Health Division, Agricultural Research Service.

Part III of the proposed rules deals with the standards for dogs and cats and requires that the facilities used to house the animals shall be well built and maintained, have water and electric power, storage and isolation provisions, wash rooms and sinks, and adequate waste disposal facilities. The indoor facilities are further required to provide adequate heating, ventilation and lighting. These standards are unlikely to be onerous for most industrial laboratories and seem reasonable. The standard for lighting if strictly applied could however be a source of trouble since it specifies an intensity of 30 foot-candles to be uniformly distributed when measured from a distance of 36 inches off the floor. The requirement to have uniform illumination is obviously difficult, and a better phrase would be well distributed rather than uniformly distributed.

The standards for outside facilities are generally reasonable, although some existing laboratories may need to review their provision for shelter from sun, rain, and snow where outside runs are used.

Section 3.4 sets out the dimensions of the enclosures to be used. In the case of dogs housed in rooms, pens, or runs 8 square feet is to be provided for each dog measuring 2 feet or less in length and a minimum of 12 square feet for each dog longer than 2 feet. No more than ten dogs can be held in one enclosure.

Where cages are used, they must be 6 inches taller than the dog in height, and the length and width of the cage must be 6 inches greater than the length of the dog. After a dog has been held for thirty days in such a cage, larger quarters are required. If a cage is still to be used, it must now measure 1 1/2 times the height of the dog and the other dimensions must be twice the length of the animal.

Cats are to be housed in such a way as to give each cat 3 square feet of floor space; and if in a cage, the height of the cage is to be at least two feet. There are to be no more than ten cats in a pen or run and no more than two in a cage.

These space requirements are somewhat more generous than those laid down in the "Guide for Laboratory Animal Facilities and Care", published by the U. S. Department of Health, Education and Welfare. This guide, while not having the force of law, was used by many laboratories in designing their facilities; and if the new regulations are strictly applied, these facilities would now constitute a violation of the law. It is customary in such a situation to introduce a "grandfather clause" exempting previously built premises that complied with an earlier recognized standard. There is no such clause in the present act. The present act also makes no allowance for a reduction in cage size if an exercise area is also provided.

The requirements regarding animal health and husbandry are in general those established as good practice.

The regulations regarding the cage sizes for guinea pigs, hamsters, and rabbits are slightly more generous than previous standards and open water containers are not allowed for guinea pigs or hamsters.

An objection has been heard from those persons working with subhuman primates that the cage sizes specified are for adult animals and some reduction of size should be allowable where young animals are handled.

In summary, the portions of the law causing greatest concern to the most people will probably be:

1. The lack of a "grandfather clause."

2. The loose phrasing of the section on the inspection of records and facilities.

3. The size of the cages. If these regulations are strictly enforced, most laboratories using animals would be forced into expensive reconstruction programs.

4. The phrasing of the lighting standard.

5. The abolition of open water containers for guinea pigs and hamsters.

6. It may be anticipated that any extra expenses incurred by the dealers in complying with the regulations will be passed on to the research facility thus resulting in more expensive animals.

GJS/dyb
Attachments (2)

EXHIBIT B
(Page 1 of 2)

MORE PROPOSED FEDERAL REGULATION FOR MEDICAL DEVICES

For the past few years, the Administration has sponsored legislation to bring medical devices under regulations now applicable to drugs. This proposal has caused our industries to share another mutual problem. Before this matter is finally resolved, many more industries will have discovered in it their own grave concerns.

The invitation to appear before you today to discuss this proposal is both flattering and pleasant. Flattering because it suggests that we can inform you about some of its aspects with which you may not be familiar, and pleasant because it brings me among friends. I have organized my discussion in three parts. First, to report briefly what the Administration's devices proposal is designed to do, assuming of course that it follows the same format it has since 1961. Second, to tell you how PMA views such provisions; and third, to report some of the drug industry's experiences under the 1962 Drug Amendments, which should give us some idea of what will happen if this proposal were enacted into law.

I.

The principal new requirements of previous Administration proposals are these:

1. As is now the case with drugs, a device would also be deemed adulterated if manufacturing and control procedures do not conform with good manufacturing practice.

Presented by John T. Kelly, Legislative Counsel, Pharmaceutical Manufacturers Association, January 25, 1967, before MCA's Food, Drug, and Cosmetic Chemicals Committee, Washington, D. C.

2. All new devices would be subject to the same premarketing requirements as new drugs, and Section 505 of the FDC Act would be amended to insert the words "or devices" after the word "drug" wherever it appears. Therefore, both safety and effectiveness would have to be shown, and all the types of information needed now to support a new drug application would have to be furnished before a new device could be marketed. Clearance procedures would be identical, and denial of device applications and withdrawal of approvals would be based on the same grounds as for new drugs. Investigations of new devices could be conducted only by experts qualified to investigate the safety and effectiveness of devices, and the Secretary would be able to condition investigational exemptions on the same basis now allowed by the Act with regard to new drugs.

3. A new subsection to Section 501 (a) would be added to provide that a new drug or new device would be considered adulterated if there were no approved application in effect with respect to it for the uses recommended in its labeling or it fails to conform to the approved application. Exemptions are provided for investigational drugs and devices, those exempted by regulation, and devices licensed by the A.E.C. The prohibition under 301 (d) against introducing into interstate commerce an article in violation of Section 505 would also apply to devices because of the incorporation of devices in 505, and Section 301 (l) would be amended to prohibit representations that an application covering a new device or cosmetic has been approved.

II.

What in essence are the main objections to this proposal? In general, there is good reason to feel that this proposal is unrealistic, unworkable, and unneeded. Moreover, it will seriously interfere, without compensating benefit to the public, with the development and use in medicine of a wide variety of medical devices.

Premarketing clearance of drugs under the present law is an expensive and lengthy process involving extensive tests, voluminous record keeping and frequent reports to FDA. Whatever its justification in the case of newly developed drugs, we know of no comparable evidence requiring such unusual controls for devices.

The new drug procedure was introduced into law by the 1938 Amendments, and while Congress felt that it was necessary to regulate devices as well as drugs, it did not subject devices to premarketing clearance as it did drugs. It therefore concluded that the misbranding and adulteration provisions of the 1938 law governing devices were adequate for them, but that because of the inherent differences in devices and drugs, new drugs should be further regulated by premarketing clearance. Thus, in 1938, Congress made a decision that devices are not analogous to drugs and do not lend themselves to the same techniques of regulation as do drugs. This proposal, by trying to force device regulation into the same pattern as drug regulation, is seeking to overturn this prior decision of Congress.

So far as we are aware, there are no particular problems in the field of devices which cannot be adequately handled under the provisions of existing laws which include seizure, injunctions, and criminal penalties for devices which are adulterated or misbranded, and action against manufacturers who falsely advertise devices. The laws are administered by the FDA and FTC which have never been bashful about vigorously enforcing all laws assigned to them.

An attempt has been made to justify this proposal on the basis of the so-called "quack machines." There is adequate authority to meet this situation under present law as witness the FDA seizures in the field. There seems to be ample evidence indicating that the public is adequately protected against the practice of quackery. Full exploration of the use of all enforcement techniques should be made, in any case, before extraordinary legislative remedies are proposed. We do not believe this has been done.

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Furthermore, the proposal extends far beyond remedying any alleged enforcement problem that may exist with respect to unsafe or ineffective therapeutic devices. It would subject many thousands and various kinds or classes of devices to the same extensive premarketing clearance procedures which now apply to new drugs.

These proposals would undoubtedly deter the improvement of many existing devices. For example, in the case of equipment for the administration of fluids or blood to humans, many improvements are made, such as changes in size or shape of the equipment or in its composition, which do not necessarily increase sales by the suppliers. The expense of premarketing clearance procedures would not be justified, and no need has been demonstrated for such a procedure for these devices. Among other things, there are a limited number of suppliers of this kind of equipment, which is sold and used exclusively through professional channels.

These proposals would also deter the development of new devices, many of which are developed by professional people for use in medical practice and made available to other experts. Such devices are not always sponsored by industrial concerns and the procedures which have been adopted by FDA are wholly inapplicable to the development and use of such devices. To apply these procedures to industrial concerns performing a service to the medical profession is to destroy the capacity of private industry to perform this valuable function.

The term "device" presently has an extremely broad definition in Section 201(h) of the Act which defines it to mean:

> "instruments, apparatus, and contrivances, including their components, parts, and accessories, intended (1) for use in

> the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; or (2) to affect the structure of any function of the body of man or other animals."

As is clear, this definition covers a tremendously wide variety of articles.

Some idea of its broad scope is gained from the fact that the FDA has ruled in the past that "devices" include such diverse articles as ankle supports, athletic supporters, combs labeled "for dandruff and scale infections," dental plates, dental supplies, sleep-inducing phonograph records, surgical instruments (such as knives, forceps, saws, mallets, chisels, needles, drills, nails, and screwdrivers), suspensory bandages, syringes, clinical thermometers, rubber gloves sold for use by surgeons, tongue depressors and applicators, and elastic and leather wrist bands.

Many different industries are involved in the manufacture of devices under the proposal. Actually, the pharmaceutical industry probably manufactures only a small portion of the total devices embraced by the proposed definition. Some of the other industries which will be affected by the proposal are your industry, the surgical instrument industry, the dental supply industry, the optical supply industry, the electronic industry, the electrical industry, the hospital equipment industry, and even the shoe industry.

The fact that so many different industries are involved in the production of devices emphasizes the differences which exist in devices themselves and the differences which exist between devices and drugs. There are different methods of production and distribution and of research and development. There are wide differences in methods of use. Some devices are developed by experts for their own use and made available to other experts. A few are "quack" remedies promoted to the gullible public. All are now subject in one way or another to the FDC

Because of material differences within the device grouping and between devices and drugs, we are convinced that the proposed requirement that all devices generally be integrated under the drug control law and be pretested and cleared for safety and effectiveness would impair the development and use of many important devices and for others would require work which, insofar as we are aware, is not necessary for the public interest, with resulting waste of time, money and effort on the part of both the Government and the industries involved.

At a time when the FDA is still struggling to digest the Drug Amendments of 1962 and is still attempting to expand its staff sufficiently to meet the added work load imposed by those Amendments, one can only guess as to the enormous additional demands which would be imposed upon the FDA were the premarketing clearance of all devices to be required. In light of what has gone before, the capacity of FDA to administer the proposed devices legislation should be carefully evaluated.

III.

If the experience gained under the 1962 Drug Amendments can provide realistic guide lines as to what we may expect if the devices proposal is enacted--and we believe it does--here are some things like to happen. Since the passage of the 1962 Amendments, there has been a steady decline in the introduction of new drugs, and their development and production costs have greatly increased.

In 1959, the introduction of new single chemical entities in the United States prescription drug market reached a high of 63. This compares with 23 in 1965, 17 in 1964, 18 in 1963, 28 in 1962, and 41 in 1961. And this year there

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were only 11.

Data concerning the submission of new drug applications is much the same. In fiscal year 1959, 369 were submitted and 230 approved; in fiscal year 1963, 179 and 67; in fiscal year 1964, 160 and 84; and in fiscal year 1965, 203 and 53. The approval picture is a little brighter in 1966 with 108. I do not presently have the figures on the number of applications submitted.

During this same period, industry spending on research has soared. In 1959 it was $197 million; in 1960, $212 million; in 1961, $238 million; in 1962, $251 million; in 1963, $282 million; in 1964, $298 million; in 1965, $339 million; and in 1966, about $400 million. More time for processing individual applications has also been very evident, thus adding to the delay and increasing the manufacturer's over-all premarketing expenditures. The average is now two or three times what it was in 1960. Consider what is involved when a new drug product is invented. From the time a new chemical is isolated until its clinical trial has been completed, a minimum of 4, and possibly as much as 6 or 7, years have elapsed. During this time, a minimum of $1 million, and as much as $5 or $6 million, have been invested, and if the information collected reflects that the product justifies marketing, an application must be made to the FDA for approval to do so. From this point another time lapse of from 6 months to 2 years or more takes place.

We recognize that some of our sad experiences under the 1962 Drug Amendments are due to lack of facilities and a shortage of qualified personnel. We are the first to acknowledge that FDA has its dedicated people--there are not enough of them to meet the burdens this law has thrust upon it, or the additional

ones it seeks. Certainly, the myriad of new responsibilities, accompanied by the need to recruit more qualified people in admittedly short supply argue most dramatically against hasty, unneeded and potentially harmful legislation.

Before legislation proposing additional controls on devices is enacted, it would seem to us that a thorough study is badly needed. This has not been done. Such a study should focus on (1) whether there is a need for additional controls, (2) what kind of devices should be further controlled, and (3) what kind of controls should be used and whether different types of devices require different controls.

Only when all of this information is available and carefully analyzed, and any problems revealed thereby have been delineated and understood, will it be possible to legislate intelligently concerning the wide, complex and heterogeneous field of devices.

As we have all heard, the FDA has been meeting with various groups, individuals, and organizations on a new study it is making of the regulatory controls it feels are required in the field of devices. No doubt numerous suggestions and approaches will be offered. Whether FDA remains wedded to the premarketing clearance approach, in light of the overwhelming evidence we believe militates against it, remains to be seen.

EXHIBIT C
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STATUS REPORT - INDIRECT FOOD ADDITIVES

Meeting of MCA Food, Drug, and Cosmetic Chemicals Committee
January 25, 1967

Many of you heard or have been informed about Jack Frawley's paper at the September 1966 ACS Symposium on Migratory Food Additives. With all existent problems in obtaining FDA clearance for packaging materials, Jack came up with a new and different proposal to help the current chaotic situation under the existing law. His conclusion was:

> "Any component of an article contacting food which is present in the article or its coating at a level not exceeding 0.2% by weight is generally recognized as safe, provided it is not a heavy metal or pesticide."

This paper and its conclusion, backed by scientific evidence, have created much comment and discussion, as well as interest, in the regulated industry - and the Food and Drug Administration. If adopted, it would eliminate many of the citations and regulations in Subpart F of the Food Additive Regulations and relieve industry of the need, red tape, and expense to obtain clearance of a multitude of packaging components that cannot be unsafe in their use anyway. It would get away from the long lists of packaging chemicals and complex regulations we now have, with no increased public health hazard. It would free many people to work on more important things and make available talent and money to investigate real environmental health problems. Only the truly significant migratory compounds would require investigation.

I will not go into the details, with the scientific evidence, of Frawley's proposal at this time. I am here only to give your committee a status report. The reaction to the paper was immediate; most of industry supported it, or at least the principle that something like this could and should be done to improve the indirect food additive situation. They wanted to read and study it - over 400 copies have been distributed in the United States and many foreign countries. Several of the latter have food packaging regulations under consideration - we hope they will profit from our mistakes.

The first reaction to the GRAS conception for packaging materials was to look for exceptions and flaws. It seems that everyone tried to find an example that didn't fit. There may be exceptions or other types of chemicals that should be exempted from the conclusion, but as yet we have to find one. The fact that people were looking for exceptions at least demonstrated that they were thinking about it - a step forward to try and find a reasonable solution to the problem. We must keep pressing toward the next step - action.

I doubt if there is one FDAer involved with indirect food additives that hasn't read the paper. In fact, copies were circulating throughout FDA a few days after presentation of the paper. Mr. J. Kenneth Kirk, Associate Commissioner for Compliance, has read it and told us it has much merit. He even has referred Frawley's conclusion to the FDA Bureau of Science for study and recommendations. They are considering it seriously but have reached no conclusion as yet.

As I mentioned, a few questions, objections, and mental reservations have been advanced about this proposal, but there have been none which has altered the conclusion. In fact, since the paper was presented, we are even more convinced that it is sound and conservative. In September, Dr. Frawley had located two-year

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chronic toxicity studies on 143 compounds on which to base his conclusion regarding toxicity. He now has accumulated 220, probably over 90% of those ever conducted. They all support the original conclusion.

In December, the Food Packaging Materials Committee of the Society of the Plastics Industry held a question and answer panel discussion with FDA staff members. Some of you probably were there. The committee submitted a list of questions to FDA in advance so that answers could be prepared. All questions concerned indirect additives and included many of the "sticky" and bothersome questions often encountered. During the discussion additional pertinent questions were asked from the floor and the answers discussed. Aside from the answers to specific questions, it was obvious that FDA recognizes the complexity of our packaging regulations and the need for revision; however, they informed us they did not have the time or manpower to execute such action and asked for the assistance of industry. I believe they really would like to have our recommendations to overcome this dilemma, and we hope to offer some concrete suggestions. They already are talking about some type of notification system as an alternate or compromise to the Frawley proposal, so perhaps progress is underway.

I have attempted to furnish you a brief status report on this latest new proposal to simplify our food packaging regulations. The next phase seems to be up to industry to follow up or propose some other type of action to accomplish our purpose. I thought I would use the remainder of the time to answer any questions.

Thank you.

Robert M. Miller
Medical Department
Hercules Incorporated

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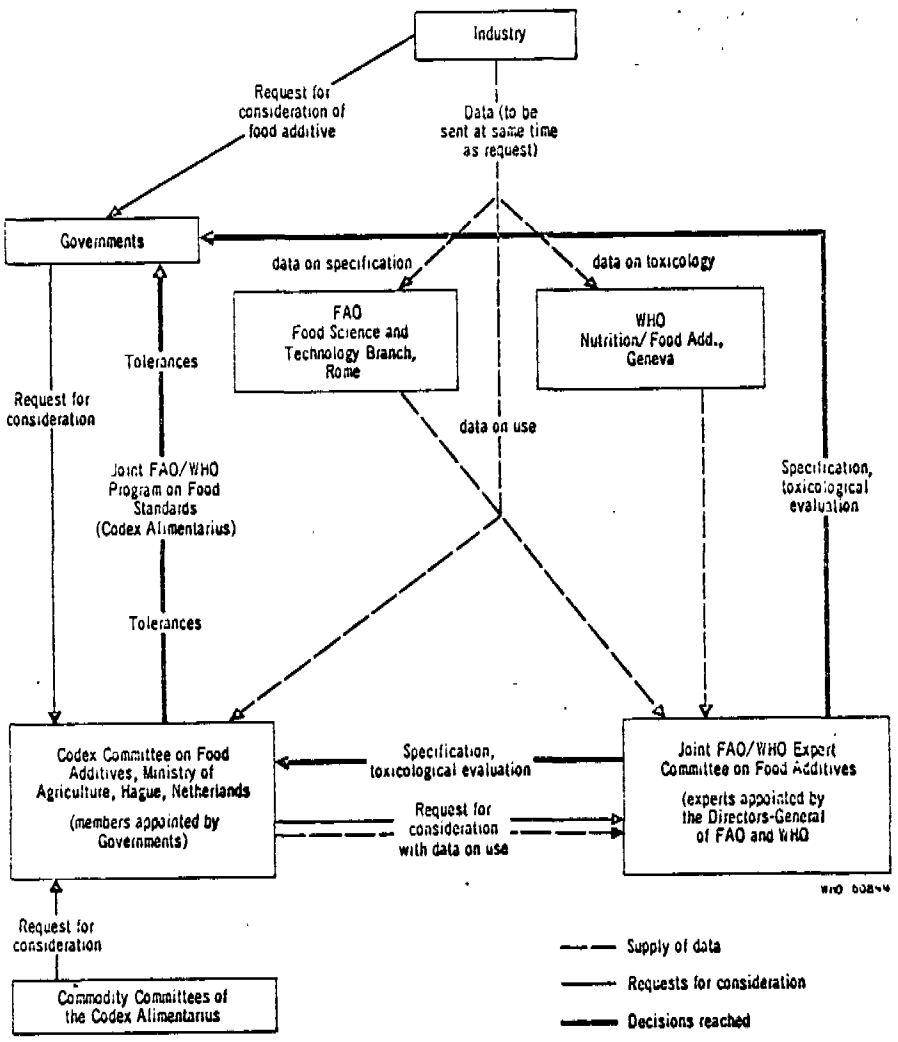
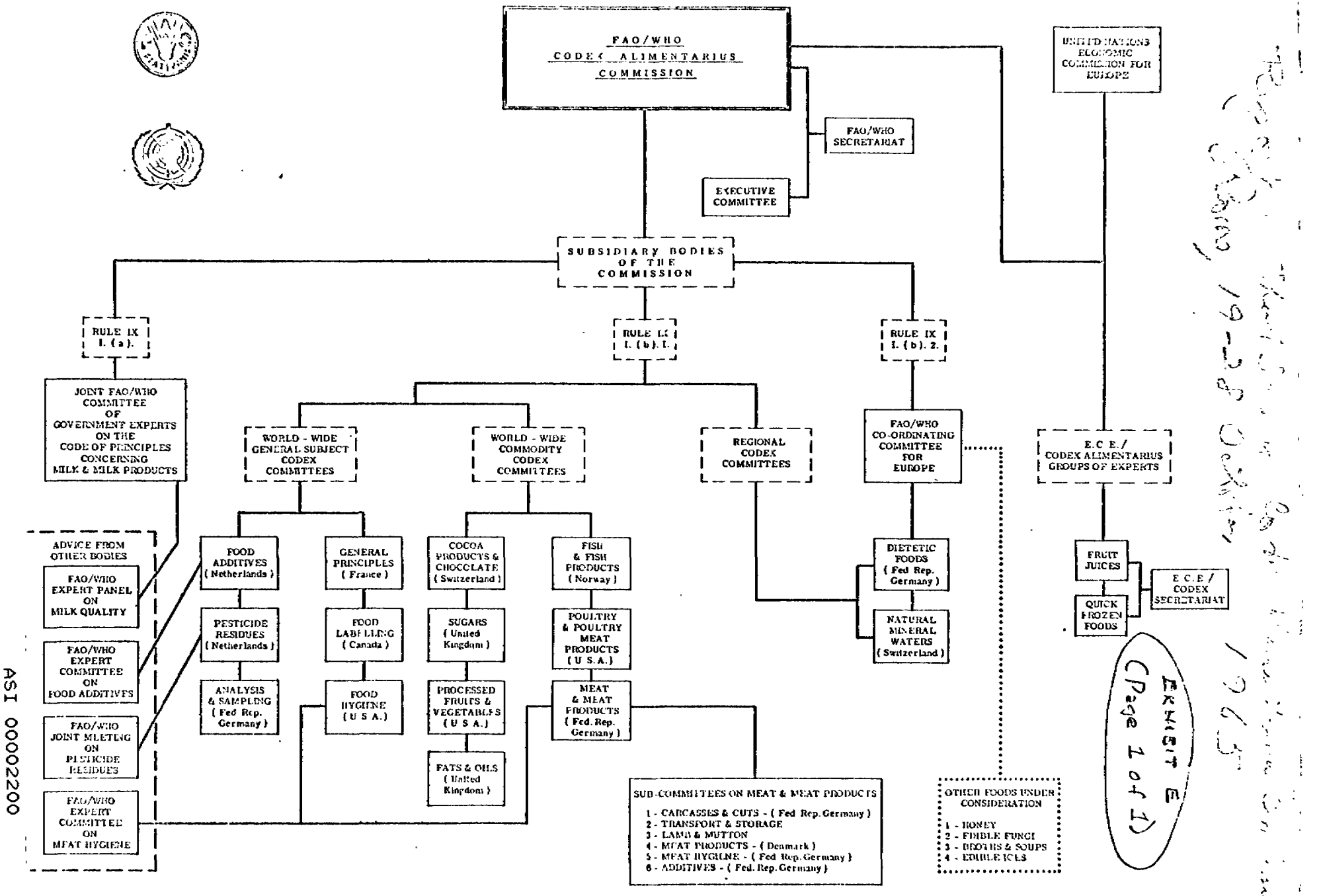
Annex 5

FLOW DIAGRAM FOR INTERNATIONAL ACCEPTANCE OF FOOD ADDITIVES



JOINT FAO/WHO FOOD STANDARDS PROGRAM — (NOVEMBER 1965)



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