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Food Drug Cosmetic Law JOURNAL

Additional Papers Presented at the 1964 Joint National Conference of The Food and Drug Administration and The Food Law Institute, Inc.

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THE EDITORIAL POLICY of this JOURNAL is to record the progress of the law in the field of food, drugs and cosmetics, and to provide a constructive discussion of it, according to the highest professional standards. The FOOD DRUG COSMETIC LAW JOURNAL is the only forum for current discussion of such law and it renders an important public service, for it is an invaluable means (1) to create a better knowledge and understanding of food, drug and cosmetic law, (2) to promote its due operation and development and thus (3) to effectuate its great remedial purposes. In short: While this law receives normal legal, administrative and judicial consideration, there remains a basic need for its appropriate study as a fundamental law of the land; the JOURNAL is designed to satisfy that need. The editorial policy also is to allow frank discussion of food-drug-cosmetic issues. The views stated are those of the contributors and not necessarily those of the publishers. On this basis, contributions and comments are invited.

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FOOD DRUG COSMETIC LAW JOURNAL

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TO THE READER

1964 FDA - FLI Conference. — The afternoon session of the conference was devoted to a series of five simultaneous panel workshops on the general topic of "What Industry Needs from FDA for Better Compliance." Three of the papers from the workshop, "Sanitation and Quality Controls," were in the December issue. Three remaining papers from this workshop are in this issue beginning on page 52. The authors are *Jonas L. Bassen,* Chief, Industry Information Branch, Division of Industry Advice, Bureau of Education and Voluntary Compliance, FDA; *Franklin D. Clark,* Deputy Director, Bureau of Regulatory Compliance, FDA; *John M. Newton,* Director, Technical Sales and Services, Clinton Corn Processing Co.

"Pesticides and Food Additives" was the subject of a second workshop. Coverage of this discussion begins on page 64. *Kenneth E. Mulford,* assistant to the Executive Vice-President, Atlas Chemical Industries, Inc., emphasized "better" compliance in his opening remarks. Comments followed by panelists, *Joseph A. Noone,* Technical Director, National Agricultural Chemicals Association; *Kenneth Morgareidge,* Vice-President, Food and Drug Research Laboratories, Inc.; *L. M. Beacham, Jr.,* Director, Division of Food Standards and Additives, Bureau of Scientific Standards and Evaluation, FDA; and *F. J. McFarland,* Chief, Petitions Control Branch, Bureau of Scientific Standards and Evaluation, FDA. *L. L. Ramsey,* Deputy Director, Division of Food Standards and Additives, Bureau of Scientific Standards and Evaluation, FDA, summarized the discussion.

Papers delivered at a third panel workshop on "New and Investigational Drugs" are found in this issue beginning on page 75. Panelists urging improvements in this area were *Dr. Karl H. Beyer, Jr.* from Merck Sharp & Dohme Research Laboratories; *Dr. George L. Wolcott,* Medical Director, Consumer Products Division, American Cyanamid Co.; *Dr. Ralph G. Smith,* Director, Division of New Drugs, Bureau of Medicine, FDA; and *Dr. Frances O. Kelsey,* Chief of the Investigational Drug Branch, Bureau of Medicine, FDA. *Dr. William J. Evans,* Director of Medical Review, Bureau of Medicine, FDA, made summary remarks.

"Drug Labeling and Promotion" was the topic of another workshop. Speakers were *Harold F. O'Keefe,* Chief, Advisory Opinions Branch, Division of Industry Advice, Bureau of Education and Voluntary Compliance, FDA; *Dr. Frederick J. Cullen,* Medical Consultant, Proprietary Association; *Dr. Augustus Gibson,* Director, Medical Research Division, Schering Corporation; *Morris L. Yakowitz,* Director, Division of Case Supervision, Bureau of Regulatory Compliance, FDA; *Dr. Howard I. Weinstein,* Director, Division of Medical Review, Bureau of Medicine, FDA; *Charles F. Hagan,* Asst. Secretary of Chas. Pfizer & Co., Inc. These remarks begin on page 92.

"What the Public Wants" was the subject of another panel discussion. Two of the papers delivered here are in this issue beginning on page 106. The authors are *James L. Trawick,* Director, Division of Consumer Education, Bureau of Education and Voluntary Compliance, FDA; and *Paul S. Willis,* President of Grocery Manufacturers of America, Inc. Remaining papers delivered at this workshop will appear in the March issue.

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Sanitation and Quality Controls

Comments by JONAS L. BASSEN, Panelist

"Sanitation and Quality Controls" Was the Subject of One of the Afternoon Panel Workshops on the General Topic of "What Industry Needs from FDA for Better Compliance." Mr. Bassen Is Chief, Industry Information Branch, Division of Industry Advice, Bureau of Education and Voluntary Compliance, FDA. Comments by the Following Were Contained in the January Issue: Robert S. Roe, Moderator; Charles H. Brokaw, Panelist; Karl F. Lang, Panelist.

THROUGHOUT THE ADMINISTRATION of the Federal food and drug laws, the Food and Drug Act of 1906 and its successor, the Food, Drug, and Cosmetic Act of 1938—food sanitation programs have been an important part of enforcement activities. The educational approach has usually been coordinated with the regulatory, the form and emphasis varying through the years. The story of these educational efforts has never been adequately documented.

There are no records like *Notices of Judgment* to document compliance. Yet for every violation listed, there are daily thousands of acts of compliance. This is the positive side of the picture and it is manifest in the progress the food industries have made in food sanitation and quality control over the past fifty-eight years. Committed to increasing emphasis on promoting voluntary compliance, FDA is reviewing available records to gain an insight into what makes the educational approach work best. Let us look at some highlights in these efforts to improve food industry sanitation, viewing them in the perspective of the law and the period.

Period I—1906-1939: The Foods and Drug Act of 1906

Government scientists who provided both adminstrative and scientific support in enforcing this law were keenly aware of the importance of industry information in its successful administration.

Dr. Carl Alsberg, shortly after his appointment in 1912 as Chief of the Bureau of Chemistry, USDA, realized that if he was to win the confidence of the leaders of the regulated industries, as well as the public, he would have to explain very clearly the reasons for legal regulations and decisions. He therefore persuaded the Secretary of Agriculture to appoint an information specialist. The duties of this specialist included the task of translating administrative policies, legal regulations, and decisions, and especially the findings of scientific specialists into brief, interesting, informative language readily understandable by lay readers. This appointment of one information specialist led not only to the founding of the USDA Office of Information but to a pattern for Bureau scientists to emulate in their writings. One of the most helpful books for the developing food industries, *Hygienic Fundamentals of Food Handling,* published in 1924, was written by two of the Bureau's eminent scientists, Thom and Hunter.

It stressed the sanitary practices necessary to avoid bacteriological contamination of foods, because problems of enteric disease outbreaks from contaminated milk, cream, shellfish, poultry, and dried eggs were as critical to the industries concerned as some of our current microbiological problems.

Burton J. Howard, Chief of the Microanalytical Laboratory, who gained worldwide recognition for developing the mold count method, never missed an opportunity during his field surveys and in his writings to offer practical suggestions to producers and packers. Such recommendations were not required by law. If a food manufacturer chose to ignore them and could keep his products free of evidence of filth, the products would meet the legal requirements of a sanitary food under the 1906 Act.

Another aspect of the work of Howard's laboratory—the development of methods for measuring extraneous matter in foods—stimulated the food industries to adopt microanalytical quality controls. I will leave it to my distinguished fellow panelist Charles Brokaw, who recently completed a survey of quality control in the food industry, to evaluate Howard's influence more precisely.

Period II—1939-1955: The Impact of Section 402(a)(4) of the Act of 1938

Section 402(a)(4) by defining a food as adulterated: "If it has been prepared, packed, or held under insanitary conditions whereby

it may become contaminated with filth, or whereby it may have been rendered injurious to health," imposed new requirements on food manufacturers and distributors. It also obligated FDA to explain its basic concepts of insanitation to the regulated industries. Though there was practically no budget for industry information, FDA fulfilled its obligations by such means as:

(1) Publication in 1944 of Food and Drug Circular No. 1, "Microanalysis of Food and Drug Products" which contained a comprehensive statement on sanitation;

(2) Speeches by FDA personnel at trade association meetings;

(3) Participation by FDA scientists in industry sponsored schools for training technicians in mold counting and insect filth determinations;

(4) Basic studies on insect and rodent contamination of wheat and corn, followed by publication of the results and then by an intensive educational program launched with the cooperation of trade associations, farm groups and USDA.

(5) Discussion of insanitary conditions by FDA inspectors at conclusion of inspections. This long established policy was later reinforced by the requirements of the factory inspection amendment of 1953.

How effective were our low-budget industry informational efforts? In the absence of statistics, we could only gauge our effectiveness by the industry response. The FDA 1950 Annual Report gauged the response thus:

> That the organized food industries are becoming increasingly conscious of sanitation is a gratifying sign of the times. National and local milling, canning, dairy, and confectionery associations have attacked the problem of plant sanitation directly and forcefully. . . . Systematic housekeeping programs for use by individual plants have been developed . . .

Period III—1955-1964: Major Amendments to the Act

These amendments of the Act required premarketing clearance for the first time of pesticide chemicals, food additives, and color additives. The new requirements naturally raised many questions for industry and there was an unprecedented demand for information. It is unnecessary to tell this audience the role that the FDA-FLI annual conferences played in a better understanding of these Amendments except to illustrate the value of such a continuing forum. They helped to clarify principles but obviously could not answer questions about specific products. Therefore, FDA established a separate unit

in 1961 in the old Bureau of Enforcement, the Division of Advisory Opinions. This Division handled the thousands of letters, hundreds of phone calls and numerous requests for conferences from individual businessmen.

When enforcement policy is extended to new fields, such as occurred under these major amendments, FDA seeks the cooperation of trade associations in first launching an educational campaign to give the regulated industries an opportunity to achieve voluntary compliance. Frequently, a special leaflet is prepared with the cooperation of these associations. FDA's output of leaflets and other industry publications increased from two prior to 1955 to thirteen by 1964. Over two and a half million copies were distributed largely with the assistance of trade associations. There are still many areas where such "How to Comply Leaflets" are needed. We have on exhibit today currently available industry informational materials including two new publications just off the press.

Period IV—1964 and Beyond: Better Compliance

From this overlook it is evident that FDA always acknowledged the necessity for major reliance upon voluntary compliance by the regulated industries in maintaining proper sanitation and quality controls. That reliance has not been misplaced as increasingly higher self-imposed industry standards attest.

Part of this progress, impartial observors suggest, can be attributed to FDA's twin catalysts—legal sanctions and industry education. The latter has not always been used in equal proportions because of inadequate resources rather than skepticism about its power for change. Even in the last period when the use of this catalyst had increased—its use was fragmented among a number of FDA units, none assigned over-all responsibility.

The 1963 FDA reorganization recognized this and established the Bureau of Education and Voluntary Compliance with a separate Division of Industry Advice to provide the leadership and coordination necessary to improve our voluntary compliance program. This Division inherited a rich store of experience and numerous materials. We are making full use of this heritage. Since the price of progress is change, we acknowledge the need to provide new approaches. We therefore appreciate the opportunity afforded by this panel discussion to learn of industry's needs and to act upon them to the fullest extent possible. **[The End]**

Comments by FRANKLIN D. CLARK, Panelist

Mr. Clark Is Deputy Director, Bureau of Regulatory Compliance, FDA.

MR. BASSEN'S STATEMENT concerned the specific ways in which the Food and Drug Administration has helped industry comply with the law. He mentioned the need for coordination of the educational and the regulatory phases of enforcement programs of FDA. In my opinion, the connection may be even closer than might be inferred from this statement. The inspection process itself, which is the basic investigative technique for legal actions and regulatory programs, can and should be an educational tool and we intend that it shall be. When it is not, it may be a failure on the part of management to grasp the opportunity, or it may be that our inspector's message is not getting through and his role as an enforcement official is masking his educational endeavors. For my brief statement here today, I have been considering some of the ways in which our inspector's attitude and inquiries may be misunderstood. The individual items have been selected from case histories of complaints which have been received following inspections. A study of them may be helpful in coming to some understanding of how FDA can help those industries who are striving for better compliance.

FDA Inspector in a Food Plant

First, why has the inspector shown up at a particular plant on a particular morning? His presence may stem from several basic reasons, but the chances are quite strong that it is what is known as "routine coverage" and there is no insidious reason behind it. Occasionally, the inspector will be there because he does have a specific complaint about the plant or its output and, if it is in the consumer interest, he will announce this reason and seek the full cooperation of management.

Preliminary Inquiries of Inspection

The inspector will introduce himself, display appropriate credentials, and present a "Notice of Inspection." He will then probably ask a series of questions, including some about the organizational structure of the firm, responsible individuals, the kinds, volumes, and value of food packed and whether either the finished product or the raw materials moves or has moved in interstate commerce.

Some firms have objected to furnishing detailed financial information indicating that it is probably none of our business. Our purpose in having the inspector accumulate this information is to get our file on the firm completely up to date and to place the firm in a proper category—is it a small operation or one whose business extends nationwide? The dollars and cents are not important per se and we never object if they are given in very approximate terms.

Detailed Inspection Procedure

Following these preliminary inquiries, the inspector will start his detailed inspection. We are sometimes told that inspectors seem to prefer to be given the run of a plant and resent being accompanied by a plant official. On the contrary, we encourage management participation where the motivation is to gain the benefit of our inspector's experience and to make the inspection a cooperative and fact-finding venture. We do not encourage channeling or unduly hurrying the inspection.

If the inspection is primarily for sanitation, it will involve these basic determinations—(1) Is the product being prepared, packed, or held under insanitary conditions whereby it may become contaminated with filth, or rendered injurious to health? (2) Does the firm's output consist in whole or in part of any filthy, putrid, or decomposed substance? Therefore, the sanitary inspection is concerned primarily with the condition and storage of the raw materials used and the sorting and other preparation to which they are subjected before process; the conditions to which the products are exposed during their journey through the establishment, and the conditions under which finished products are stored. His inquiries, therefore, will include a detailed examination of the raw material area and the raw materials themselves; an inspection of the processing equipment, and the gathering of information about formulas, processes, and procedures. In this area, there is sometimes a question about furnishing this information on the basis of an opinion that it is not legally required and the divulgence of it may in some way work to the advantage of a competitor. We cannot positively guarantee that such information may not at some time have to be divulged in a court of law or to some other body with investigative rights. We can guarantee, however, that our inspectors are trained and cautioned to treat any information obtained in a factory inspection, whether or not it is labeled as particularly confidential, as if it were. A specific instruction in the Inspectors Manual on establishment inspections reads:

Don't reveal information about other firms or their practices. Exploratory questions from management about competitors may be dismissed by tactful reference to the privileged nature of information obtained in his plant as well as in others.

Bear in mind that casual and seemingly innocuous statements or questions during establishment inspection may reveal privileged information. Be constantly alert to avoid divulging any information, which through misinterpretation, might in anyway compromise your integrity and the confidence enjoyed by the Administration.

The statutory protection is, of course, in Section 301(j) of the Act, which reads:

> The following acts and the causing thereof are hereby prohibited:
>
> > The using by any person to his own advantage, or revealing, other than to the Secretary or officers or employees of the Department, or to the courts when relevant in any judicial proceeding under this Act, any information acquired under authority of section 404, 409, 505, 506, 507, 704, or 706 concerning any method or process which as a trade secret is entitled to protection.

Our inspectors are equipped with cameras and they will sometimes supplement their word descriptions with photographs. The inspector reaching for his camera infrequently triggers a defense mechanism and lengthy arguments. At times, these situations involve the firm's legal department. There should be no fear of "rigged" pictures or unfair ones—the only desire is to retain the image of what anyone could have seen at that time if they looked at the objective of his camera. Our position is that the taking of photographs is within our inspectional authority. If this activity is denied, this is a fact of inspection and will be recorded. If the inspection is ever introduced in litigation, the fact that photographs were denied might become pertinent.

Our inspector will inquire into the quality control program of the firm and will be especially interested in the fate of any lots of raw material or finished product that has been rejected. Although he is not a mathematical statistician, he is not unfamiliar with acceptance levels and sequential programs. He may be able to offer helpful suggestions.

Usually, the last part of a plant to be inspected will be the shipping room and at this point the inspector will ask for a list of interstate consignees or a list of recent interstate shipments. This does not necessarily mean that the inspector has decided to order sampling of the firm's entire output. It does mean that he is finishing his job of demonstrating that the firm does ship in interstate

commerce and he is accumulating information that will provide his supervisors with the information necessary so that samples can be obtained if the facts of his inspection dictate. Sometimes this information is denied on the basis that we are not entitled to it. FDA, of course, has other resources to obtain interstate consignees and shipments which, although more time consuming, are quite effective. Most firms are quite cooperative in this regard.

Finally, our inspector will conduct an exit interview with a responsible representative of management. He is required by law to leave with management a written report of any observations he has made which indicate insanitary conditions or product contamination. He will gladly discuss each item on any such report and in addition will discuss other observations he might have made over and above the requirement for the written report.

Inspector's Recommendations

Our inspectors are sometimes criticized for not being specific in their recommendation for remedial measures when they have observed insect or rodent habitation. Although our inspectors are all trained in some aspect of science, and through our food and drug training have learned considerably about the life histories and habitat of insects and rodents, they are not entomologists or exterminators. Their function is to point out the evidence and leave to management the task of employing properly trained people to make the functional correction. Our inspector will also leave with management a receipt for any samples he collected during the inspection and, in case these are examined in our laboratory for filth elements, a copy of the results of such analysis will be furnished management.

We sincerely hope that our meeting today and others like it will result in a better understanding of our inspector's mission when he visits your plant. Although he is primarily there for law enforcement purposes, it is the policy of FDA to make him also an arm of our educational organization and he is instructed to that end.

Let me close with another quotation from the Inspectors Manual:

An establishment inspection also affords the inspector an opportunity, which he alone enjoys, to do a service to the public by correcting potential violations of the law at their source. **[The End]**

Summary Remarks by JOHN M. NEWTON

Dr. Newton Is Director, Technical Sales and Services, Clinton Corn Processing Company.

THE MODERATOR of our "Sanitation and Quality Control" panel set the theme of the discussions by stating, "Let us hope that in remembering the errors and mistakes of the past we can avoid repeating them as we apply our past learning to our current problems."

The FDA always has and will continue to coordinate the educational approach with enforcement. There are no records to document compliance, but *Notices of Judgment* always document noncompliance. Yet every FDA and industry representative knows there are thousands of acts of compliance for each single act of non-compliance. Committed to increasing emphasis on promoting voluntary compliance, the FDA is currently reviewing available records to gain an insight into what makes the educational approach work best.

Past FDA Efforts in Educational Approach

Let's look at FDA efforts in the past—

1. As early as 1912, Dr. Carl Alsberg, Chief of the Bureau of Chemistry, USDA, realized that if he was to win the confidence of the regulated industries, as well as the public, he would have to explain very clearly the reasons for legal regulations and decisions. Inspectors were encouraged to offer practical suggestions to producers and packers. Bureau scientists went to work to develop and publish methods to assist industry in carrying on adequate quality control.

2. The enactment of Section 402(a)(4) in 1938, imposed new requirements on food manufacturers. It also obligated FDA to explain its basic concepts to the regulated industries. FDA fulfilled its obligation by

(a) developing additional procedures,

(b) presenting informative speeches,

(c) participating in industry sponsored schools for training technicians,

(d) basic studies of insect contamination of wheat and corn, and

(e) discussion of insanitary conditions by FDA inspectors at conclusion of inspection.

3. Major amendments to the Act from 1955-64 introduced premarketing clearance for food and color additives, and pesticides. The flood of inquiries resulted in FDA establishing, in 1961, the Division

of Advisory Opinions in the old Bureau of Enforcement. The Division of Public Information also was established. Details about these services can be obtained from FDA by requesting the new leaflet "Industry Information Materials".

Today, when enforcement policy is extended to new fields, FDA seeks cooperation of trade associations in first launching an educational program to give the regulated industries an opportunity to achieve voluntary compliance.

4. What about tomorrow?

Industry education has not been adequately used because of limited resources, and because its use was fragmented among several FDA units. The 1963 FDA reorganization established the Bureau of Education and Voluntary Compliance with a separate Division of Industry Advice. FDA intends to use this division to provide the leadership and coordination necessary to improve the voluntary compliance program.

Inspection Procedure Reviewed

It was stated that "The inspection process itself . . . can and should be an educational tool and FDA intends that it shall be". The FDA inspection procedure was then reviewed. Of special informational value are the following:

1. If an inspection is the result of a complaint and "it is in the consumer interest" the inspector will announce this reason at the beginning of the inspection and seek management's cooperation.

2. Requested financial information [may be furnished] "in very approximate terms."

3. Inspectors do not want "the run of a plant" but encourage management participation.

4. FDA guarantees that "inspectors are trained and cautioned to treat any information obtained during a factory inspection, whether or not it is labeled as particularly confidential, as if it were." In fact, statutory protection is written into Section 301(j).

5. FDA considers the taking of photographs as within their inspectional authority. This was questioned. A question was asked regarding concealed tape recorders. Inspectors are now instructed not to use concealed tape recorders during establishment inspections.

6. Inspectors always conduct an exit interview and are required by law to leave a written report of any observations he has made

which indicate insanitary conditions or product contamination. Reports are always made on samples collected during establishment inspection and analyzed for filth elements.

7. Inspectors only point out the evidence and leave to management the task of correction.

Educative Role of FDA

Although the inspector is primarily an arm of enforcement, it is the policy of FDA to make him also an arm of its educational organization and he is instructed to that end.

One of the most frustrating problems of any large organization is the difficulty in maintaining speed of communications. Speedy replies from FDA have not always been the rule. This unfortunate reputation is not necessarily deserved at the present time, but it will require continued pressure by FDA management to correct the past impressions.

There is still a woeful lack of knowledge about Food and Drug matters among food technologists. To correct this void, one approach would be to cooperatively sponsor workshop sessions in various geographical areas. These workshops should be aimed at middle and supervisory technical management and slanted toward working level problems, the real "bread and butter" aspects of food compliance, and not theoretical or philosophical propositions. New techniques such as closed circuit TV should be considered.

A strong feeling exists in industry that many FDA inspectors are not adequately trained. Perhaps industry can help by offering special technical workshops for each of the most important food processing groupings. Such an approach has many pitfalls, from the view of FDA as well as industry. Nevertheless, it could work towards better training of inspectors and improvement of their real understanding of industry problems. An FDA-baking industry workshop was suggested.

An aspect of control which continues to trouble many food manufacturers is that of fill, or net contents, of containers. Manufacturers suffer from excessive overfill, but so do consumers, who ultimately pay the extra cost. Since exact fill is simply not practical, the concept of variability has been recognized by FDA. It was recommended that FDA clarify through all appropriate media the basic rules of container fill, allowing reasonable variation in individual packages and utilizing sound statistical concepts.

During questioning the policy of weights of "average if reasonable" was stated. Generally, results obtained by a reputable manufacturer using good manufacturing practice are used as the guide.

Most food manufacturers welcome FDA inspectors. Further, many companies invite the public to inspect their operations and conduct public tours of the plant. These consumer groups are encouraged to ask questions about processes and controls, storage of ingredients and finished products and their distribution. Information is only limited when it is necessary to protect "know-how." Open inspection of this type makes it mandatory to maintain good sanitation practices and the very best manufacturing procedures at all times. Not inspection, but "a quality control program, coordinated with a sound sanitation program supported by management is the answer to compliance". A continuous, cooperative program of education is necessary to make every employee and supervisor "conscious of the desire to produce clean food, in a clean factory, with clean people."

What does industry need from FDA to improve this program?

1. Continuance of FDA's education program, such as workshops, publications, distribution of answers to queries without identification of parties concerned, etc. were suggested. Replies are made only to the inquirer. FDA personnel does try to answer common inquiries in their speeches.

2. Better inter-government agency agreement on certain interpretations.

3. Clearly defined tolerances for mold and insect fragments.

4. Inspectors should always express "helpfulness, assistance, cooperation, etc.," not "what can we pin on this guy." The inspector is FDA's salesman and public relations officer. He often is the only representative of FDA known by the food processor.

Let's assist, help and educate in a cooperative program so that every inspector can be greeted with open arms and a feeling of "glad you stopped in."

The question of biological standards was discussed. It was suggested that "biological limits" would be more appropriate. Surveys are in progress and results are being published. For example, on frozen precooked foods, etc.

Throughout the panel presentations and discussions, there existed a strong expression of willing cooperation by all present. Now that the cooperative atmosphere is created, let's follow through with cooperative action. **[The End]**

Pesticides and Food Additives

Comments by KENNETH E. MULFORD, Moderator

"Pesticides and Food Additives" Was the Subject of One of the Afternoon Panel Workshops on the General Topic of "What Industry Needs from FDA for Better Compliance." Mr. Mulford Is Assistant to the Executive Vice-President, Atlas Chemical Industries, Inc.

AS YOU KNOW the theme of the panel workshops being held this afternoon is "What Industry Needs from FDA to Do a Better Job of Compliance." This workshop has before it the specific subtitle "Pesticides and Food Additives." In other words, our workshop subject narrows down to "What Industry Needs from FDA to Do a Better Job of Compliance in the Field of Pesticides and Food Additives."

Mr. Grey referred to a definition of compliance in his paper. I should like to say that an alternative definition in most dictionaries seems to be a disposition to yield to others or subservience. In contrast to this definition, I believe that what we are discussing today is better compliance with the law and legal regulations thereunder. Neither do I believe that our discussion will involve the wilful and intentional violator of the law. We gladly leave such people to the enforcement branch.

What we do know is that the difference between compliance and non-compliance is not always a sharp line and that a proper understanding of the complexities of the law and regulations is not easy. As Mr. Depew indicated earlier, a manufacturer who follows a conservative advisory opinion may find himself in a difficult competitive position if his competitors do not, and FDA takes no action.

A "Better" Job of Compliance

I should also like to emphasize the word "Better" in the title of today's subject—"a *better* job of compliance." It seems to me that when you consider the word "better" in the title you are immediately confronted with the question "better than what?"

This reminds me of the manager of a factory or plant where the total man hours worked per year are, let us say, 10,000 man hours. This plant manager is competing in a safety record contest with other plants and he winds up the year with 10,000 man hours worked and no lost time hours due to an accident. In other words—a perfect record. Yet he can't win the contest because another plant in the competition has 20,000 man hours worked without a lost time accident.

Both are perfect records yet one is better than the other. Also you can bet that neither plant manager is going to sit back and rest on his laurels. On the contrary, both will be looking for areas in which they can improve conditions to decrease even further the likelihood of an accident to a worker.

In my opinion industry is doing an excellent job of compliance with the pesticide and food additive provisions of the law and regulations. I should like to feel, therefore, that a very important and possibly the most important part of this conference is the development of areas in which there are needs or opportunities for improvement. It is only after such areas are determined that we can really direct our attention to industry's needs from FDA, or anyone else, for that matter, to do a better job of compliance.

I have been advised by Mr. Depew and Mr. Grey, the co-chairmen of the entire panel program, that in all of the planning it has been unanimously agreed that the panels will not be used as a forum for airing individual gripes, discussing industry problems, decisions, etc., on a case-by-case or experience-by-experience basis. They observe that we have a tight schedule and it is imperative that the panel operate effectively and efficiently to discuss the theme and bring out the pertinent and important facts.

On the other hand, it has been the experience of your moderator that there is a large gray area between general principles on the one hand and specific cases on the other. Also, it is frequently advisable to consider specific cases in the application or the development of a general principle to make sure that the latter is properly framed and understood by all.

Consequently, while I am sure we all desire to comply with the spirit of the comments by Mr. Grey and Mr. Depew, particularly with respect to individual gripes and problems, it will not be the policy of your moderator to rule that specific illustrations or experiences are out of order if they contribute to the over-all discussion. In fact, I can visualize that specific illustrations will be very useful if they are representative of a problem area.

I should like to emphasize that, while we have designated panelists on the program, it is my hope that all of you will consider yourselves to be panelists so that we can have a real workshop discussion of a constructive and beneficial nature. We constantly read and hear about problems in communications. Well, this is our opportunity to communicate, and let us make the most of it. **[The End]**

Comments by JOSEPH A. NOONE, Panelist

Mr. Noone Is Technical Director, National Agricultural Chemicals Association, Washington, D. C.

WE IN THE AGRICULTURAL PESTICIDES FIELD feel that our industry has a good record of compliance with the applicable laws. However, this panel and our industry are concerned with what might be done in order to achieve better compliance on our part.

We believe that the most important and immediate need is a more realistic and practical policy on the part of the Food and Drug Administration as regards zero tolerances and no-residue registrations. This is a matter which our Association has discussed with the Food and Drug Administration on numerous occasions over the last several years. In December 1961, we submitted to the Food and Drug Administration a proposal which we believed would have resolved problems in this area if it were adopted. However, for some reason or other it was not adopted.

Zero Tolerance and No-Residue

Most, if not all, of you are familiar with the fact that the Food and Drug Administration jointly with the U. S. Department of Agriculture in the spring of this year submitted a request to the National Academy of Sciences-National Research Council requesting that a special committee be appointed to study the technical aspects of zero tolerance and no-residue. In other words, from a technical standpoint, what is zero with respect to pesticide residues? Is there any such thing as *absolute* no-residue? Can we say with certainty that there is not one molecule of a pesticide or a degradation product therefrom present on a raw agricultural commodity?

We applaud FDA and USDA for taking this step, in accordance with the recommendation of the President's Science Advisory Committee on the "Use of Pesticides," commonly known as the "Wiesner Committee." A very excellent committee has been appointed by NAS-NRC and has had several sessions to date. We believe that the report of the Committee should serve to clarify this very complex situation. However, the report will have to be implemented by proper action on the part of the FDA. We hope that the FDA will recognize the full ramifications of any new regulatory approach to this problem and allow the industry and agriculture sufficient time to make any adjustments which might be necessary on their parts.

We think that FDA should have a greater appreciation of, and consideration for, the effects of their decisions and actions on pesticide producers, farmers, dairymen, grocers, and consumers. We believe that FDA should carefully consider the potential impact of their actions on these groups before deciding, talking, or acting. For example, we believe that raw agricultural commodities should not be condemned because they bear some minute detectable residues which are not hazards to the public health solely on the basis that there is no tolerance or a zero tolerance in effect on those commodities. We have in mind the fact that with our newer, more highly sensitive methods of analysis, we can detect extremely minute residues which a few years ago were undetectable. We believe that agriculture and the pesticide industry should be given an opportunity to adjust to the new residue situation and take such steps as are necessary for this purpose, whether it be obtaining a tolerance or changing spray schedules. We want to make it clear that we are not requesting or suggesting that this period of adjustment should be afforded agriculture and industry whenever there would appear to be any imminent danger to the public health involved. There, prompt action by the Food and Drug Administration is properly indicated.

Notice of FDA Policy Changes

We believe that FDA should not change the ground rules as regards the regulation of pesticides and residues thereof without advance notice to all interested parties, unless imminent danger to the public health is involved and precludes such advance notice. For example, we think that if the data requirements to obtain a tolerance are to be increased, the industry should be given prior notice. We also think that if new, more sensitive methods of analysis are to be used for enforcement work, prior notice should be given to the industry, USDA, land-grant colleges, and grower organizations.

Our industry has good relations and fairly good communications with FDA. We know that we are always welcome to sit down and discuss our problems with the Administration. However, we believe that there would be better compliance with the Federal Food, Drug, and Cosmetic Act and the various amendments thereto on the part of our industry and agriculture if we had better communications, particularly in advance of pending policy, data requirements, and enforcement decisions. **[The End]**

Comments by KENNETH MORGAREIDGE, Panelist

Dr. Morgareidge Is Vice-President, Food and Drug Research Laboratories, Inc.

SIX YEARS OF EXPERIENCE since the enactment of the Food Additives Amendment have given both FDA and industry a much clearer understanding of their respective responsibilities under the law. The record of compliance on the part of industry has been in the main exemplary, and intentional violations may be assumed to be relatively rare if any, insofar as responsible manufacturers are concerned.

At the present time it is fair to say that industry has many fewer causes for complaint than formerly, due to a considerable growth in mutual understanding. Nevertheless, ignorance and a lack of appreciation of the regulatory requirements is still a major stumbling block to a substantial segment of the food processing industry and its suppliers. Despite its oft stated "open door" policy, FDA remains an uncharted wilderness to the uninitiated who still outnumber, numerically, those who may have acquired some familiarity with both the published regulations and the corridors of "Tempo-S."

Suggested Aids for Better Compliance

Several thousand substances have now been covered by regulations under Title 21, Part 121, for a variety of food additive applications, both direct and indirect. One of the most exasperating problems facing a manufacturer considering a new product or the reformulation of an old one is to determine whether any of the proposed ingredients are, in fact, food additives subject to existing regulations. Reference to the regulations themselves is often confusing and fraught with the danger of overlooking a crucial citation. Private initiative has seen the need for comprehensive and systematized listings of all substances covered by regulations and several of these are available at rather high cost. Useful as these are, they are not widely available and they lack the authoritative guarantee of accuracy and freedom from errors of omission which could be expected from an official list. In the opinion of this panelist, one of the most helpful services which FDA could provide in the interest of better voluntary compliance would be the publication of a systematized compilation of all substances covered by regulations. The rate of new additions to this list has now fallen to the point where annual or at most, semi-annual publication of new editions would probably suffice for most users.

Furthermore, in the course of compiling such a list, FDA chemists should re-examine the nomenclature by which substances are identified, especially in the case of the omnibus regulations which appear in Subpart F. Many of these still reflect original industry lists gathered from different sources and some are nondescriptive to the point of ambiguity.

Another source of much confusion which hampers voluntary compliance is the question of equivalency of commercial grades of chemicals which may be regarded as suitable for use in foods or in contact with them. In compiling such a list as has been proposed, the opportunity would exist of clarifying such terms as "good manufacturing practice" and "suitable for the proposed use." In the field of substances suitable for use as direct additives, FDA is urged to give at least quasi-official recognition to such specifications as those of *Food Chemicals Codex,* the first edition of which is scheduled for publication in 1966.

Finally, in the handling of petitions for new substances or for new uses of old ones (usually by amendments to earlier regulations), FDA could further stimulate voluntary compliance by streamlining and expediting its own review and evaluation procedures. In all fairness and with due acknowledgement of the improvements resulting from its recent reorganization, the logistical problems which still appear to exist within the Bureau of Scientific Standards and Evaluation are known to be formidable. This is judged by the fact that the Bureau still finds it very difficult due to lack of adequate staff to operate within the statutory time limits imposed by Congress in the processing of petitions. Business management being what it is, this delay engenders a lack of empathy between industry and government which key personnel on both sides find frustrating. Under the stimulus of strong, or even unfair, competitive situations, technical violations of the law may be encouraged which would not occur if the petition process were less time-consuming. However, unwisely, managements may at times be persuaded to "jump the gun" in the use of an additive while the "red tape" slowly unwinds itself. **[The End]**

Abstract of Comments by L. M. BEACHAM, JR., Panelist

Mr. Beacham Is Director, Division of Food Standards and Additives, Bureau of Scientific Standards and Evaluation, FDA.

INDUSTRY NEEDS a thorough understanding of the requirements of the law, as FDA conceives them. These are set forth in various categories of regulations, which are added to or amended as circum-

stances require. FDA can assist by publishing these in lucid language and convenient form.

In the enforcement of the requirements of the law, administrative policy comes in to play. FDA must make this policy known, together with any changes in policy that take place. The reasoning that supports the policy should be made public to achieve a better understanding and acceptance of it. FDA seeks to give this information by formal publications, by frequent public speeches made by FDA personnel at industry and scientific meetings, and by direct correspondence.

Often industry needs analytical methods. We have a program of developing and improving these. We publish these in scientific journals as they are developed and are also always ready to communicate them to those interested either by letter or by personal conference.

[The End]

Abstract of Comments by F. J. McFARLAND, Panelist

Mr. McFarland Is Chief, Petitions Control Branch, Bureau of Scientific Standards and Evaluation, FDA.

UNDER THE PROCEDURES specified in the Food, Drug, and Cosmetic Act and the implementing regulations, those who wish to use or promote the use of pesticides or food additives present to the Food and Drug Administration petitions containing scientific data in support of the safety of the proposed use. The data may be classified under identity, use, methodology, residues, and toxicity of the chemical. General guidelines for the types of data required in petitions to support clearances for such substances are set forth in the law and the regulations. The scope and depth of the information needed have been described and discussed in speeches, articles in scientific journals, and reports of advisory committees.

The FDA is aware of the need to give industry as much advance notice as possible of changes in petition requirements and regulatory action criteria. We try to time such changes to avoid to the extent possible disruption of industry practices in mid-season. However, action cannot be delayed if we find that doing so would involve a substantial hazard to the public health.

Interpretative, procedural, and tolerance regulations are published in the *Federal Register*. Reprints of regulations as well as copies of the summary of pesticide tolerances and exemptions are sent to 2,100

names on the pesticide mailing lists and 4,300 names on the food additive mailing list.

Informational material such as news releases, copies of speeches, pamphlets, and movies are available through the Division of Industry Advice, Bureau of Education and Voluntary Compliance.

Our doors are always open to those who seek information and guidance on petition procedures for pesticides and food additives.

Among the important committees established to consider special problems in this field are the following:

(1) Committee reviewing tolerances for aldrin and dieldrin;
(2) Chlordane Advisory Committee;
(3) Zero tolerance committee of NAS-NRC;
(4) Interdepartmental Agreement Committee; and
(5) Federal Committee on Pest Control.

[The End]

Summary Remarks by L. L. RAMSEY, Reporter

Mr. Ramsey Is Deputy Director, Division of Food Standards and Additives, Bureau of Scientific Standards and Evaluation, FDA.

THE MODERATOR OPENED the discussion with a statement that although the industry had an excellent record of voluntary compliance it was the purpose of this workshop to develop areas where there is a need for improvement and explore the ways in which this improvement can be accomplished. The discussion was to be directed toward the responsible segment of the industry; irresponsible, unscrupulous members of the industry, who are indeed an insignificant minority, must be legally forced to comply.

FDA Promotion of Voluntary Compliance

The FDA members of the panel described the present efforts of FDA to promote voluntary compliance through its educational and informational programs. These can be listed as follows:

1. Distribution of regulations promptly upon promulgation with respect to all areas under the law including food additives and pesticides. Any interested party may have his name placed on the mailing list upon request.

2. Distribution of speeches and papers by FDA's administrative and scientific personnel. Available upon request.

3. Distribution of reprints of research papers including those on analytical methods by FDA's scientists, which are published in the scientific journals. Available upon request.

4. Distribution of miscellaneous information material such as press releases, pamphlets, and movie films.

5. Providing informal advisory opinions in response to letters from the industry.

6. The "Open-Door Policy" conferences.

Suggestions for Improvement

The industry members of the panel made several specific suggestions as to what FDA should do for improving voluntary compliance:

1. Provide an official index to the voluminous food additive regulations, which would include all substances listed in the regulations.

2. Re-examine the nomenclature of the substances covered by the food additive regulations with a view toward eliminating any ambiguous names.

3. Define food grade chemicals by giving some form of official recognition to the specifications of the *Food Chemicals Codex*.

4. Meet the deadlines, statutory time limits, for promulgating food additive regulations as a stimulus to voluntary compliance.

5. Adopt a more realistic and practical policy as regards zero tolerances and no-residue registrations for pesticides.

6. Provide advance notice and time for accommodation to any change in ground rules, policy, etc., with respect to pesticides unless an imminent hazard to the public health is involved (examples: Data requirements for a tolerance, and the use of tolerance enforcement methods having an increased degree of sensitivity).

In commenting on the industry suggestions FDA members agreed that they all had considerable merit and either were currently under consideration for a policy decision by the Administration or it was believed a solution had been achieved. (Numbered paragraphs correspond to the industry comments above.)

1. FDA has an index to the food additive regulations, which is now restricted to use by its own personnel. Whether this index should

be made available to the public is now under consideration by the Administration, but a decision is complicated by the fact that private companies have taken the initiative and provided this service.

2. Although there may well be a few isolated instances in the food additive regulations where a substance is not clearly identified, it is the policy of the FDA to use a common or usual name, if there is one, and if not, to use a name consistent with the nomenclature system of Chemical Abstracts. Furthermore, interested parties have a reasonable time in which to make suggestions for changes or clarification in the nomenclature after the filing notice has been published. In fact, erroneous names of substances in a regulation may be called to the attention of the Administration at any time.

3. The Administration has the question of the *Food Chemicals Codex* under consideration at this time, but since publication of the bound volume is not scheduled until 1966, a final decision may possibility be delayed, pending this publication.

4. FDA recognizes the need for meeting the statutory time limits for food additive regulations and the records show that with few exceptions in recent months, the time limits are being met. These few exceptions, more often than not, involve policy decisions which do require time. Petitioners generally have been willing to wait when faced with the alternative of a negative order within the time limit. However, in the early days of administration of the Food Additives Amendment, it was not physically possible to handle the tremendous workload within the time limits.

5. An FDA decision in the area of zero tolerances and no residue registrations awaits the recommendations of a special advisory committee.

6. The essence of the suggestion here is actually the policy of the FDA. However, it should be added that occasionally there are differences of opinion among pharmacologists of FDA and those of the industry and when there is a difference, FDA will resolve any doubts as to safety in the interest of the consumer.

The question and answer period following presentations by the panel members resulted in a very interesting and lively exchange of views with audience participation, ranging over a wide range of topics.

Of marked significance was the view of several industry members in the audience and the panel Moderator that the advisory opinions of FDA do not, but should, reflect enforcement guidelines, that there is a wide disparity between what FDA says in a letter is illegal and

what it actually will take regulatory action on. This situation often leaves an alert responsible company, which sought FDA's advice, at a competitive disadvantage with a company which did not write FDA but used its own judgment to arrive at a more lenient interpretation of the law or regulations. The industry called for closing this gap. However, an FDA spokesman pointed out that simply because an offending company is not subjected to regulatory action does not make its behavior legal, and that the question is indeed an old and troublesome one, with no completely satisfactory answer at hand.

Consumers in the audience expressed some concern over the use of such feed additives as stilbestrol and did not appear to be satisfied with the answer that the data show no residues in the meat.

In conclusion the plea of the industry is for better communications, particularly in advance of decisions with respect to petition requirements, enforcement guidelines, and overall general policy. It is fully recognized that the ultimate safety of the usage of chemicals in the production or processing of food, be they pesticides or food additives, rests upon responsible and informed usage—upon the desire and determination of the industry to be familiar with the law and regulations, to understand them fully, and to comply with them *voluntarily.* **[The End]**

"TEA PARTY" SETS TEA STANDARDS

The Nation's annual official "tea party" was held at the New York FDA laboratories on February 8, 1965. The seven-member U. S. Board of Tea Experts met around a large revolving table to sip, but not swallow, hundreds of samples of tea to determine the minimum standard for each variety of tea permitted to be imported into the country for 1965.

The Tea Importation Act of 1897 was originally requested by the trade itself to prevent the importation of low quality tea. Today tea enters the country under bond until it is tested by FDA examiners. Half-pound tins of each tea variety are made available to interested persons at cost. These are used by the trade and the FDA to assure that future shipments meet the quality standards established by the Board.

New and Investigational Drugs

Comments by KARL H. BEYER, JR., M. D., Ph.D., Panelist

"New and Investigational Drugs" Was the Subject of One of the Afternoon Panel Workshops on the General Topic of "What Industry Needs from FDA for Better Compliance." Dr. Beyer Is with Merck Sharp & Dohme Research Laboratories.

TWO YEARS AGO most of us in industry were telling each other that things would have to get worse at the FDA before they got better. We were right; there has been a period of adjustment to the agency's broader responsibilities under the new law and the new regulations.

Today, we are looking optimistically for things to improve despite circumstances that are still less than optimal.

I accepted the invitation to appear on this panel to be helpful and to point out several areas in which improvement should be sought in connection with the FDA evaluation of new drugs.

Rejection of New Drug Applications

In recent years, there has been created both a pattern for and a climate for the seeming automatic rejection of a New Drug Application on the first response. I doubt whether an NDA could be written today that would not be rejected on perhaps the 179th day and the 11th hour, regardless of the soundness of the presentation or the merits of the therapeutic agent.

One factor working against acceptance during the allotted time, of course, is the fact that almost any New Drug Application today is a tremendously complex document. It is prepared by numerous individuals who are intimately and expertly familiar with specific aspects of the total application. Understandably, when one of its sections is read by a physician or scientist in the Food and Drug Administration questions may arise in his mind having to do with clarity of language, adherence to prescribed format, adequacy of data, interpretation of data, and so on, especially since he has not lived with the development of the preclinical and clinical documentation and cannot be expected to have the same insight into the full sweep

of the study. There are three principal stumbling blocks in the initial interactions between FDA and the sponsor of the rejected NDA. (1) There are many other opportunities for inadequate communication simply because of the increased complexity of the NDA. (2) There are proportionately fewer individuals reading the NDA's who have the background and experience to assess their adequacy in substantial over-all terms. And (3) there seems to be a practice to seek a defensible basis for at least an initial rejection of the NDA by reference to changing administrative procedures or by accenting honest differences in evaluation and by assertion of the personal attitudes of the FDA's medical and preclinical staff.

Need for Improved Review Procedures

With regard to administrative practices, are there any more ways we can help cut a few days, weeks, or months off the administrative time it takes to handle a New Drug Application? I would hope so. Just several weeks ago the industry learned for the first time that the sometimes elegant job of compiling and binding a New Drug Application is both wasteful and a deterrent to review. The NDA's are torn apart when they are received in Washington, and the copies are rebound in two-inch color-coded binders which may take weeks to be completed and circulated. Any sort of logic suggests that the industry would be agreeable to sending the applications down to Washington in the form the FDA wants for subsequent distribution.

On the FDA's side . . . is it possible for each NDA to be given a preliminary check by a clerk armed with the latest list of detailed requirements, so that the individual specialist at FDA will find what he is likely to want as he reviews the material three, four or five months later? If, either by oversight or by lack of familiarity with ever-changing requirements, some important details have been omitted which necessarily make the application incomplete, the sponsor of the NDA would surely like to know this as soon as possible so that he might correct the deficiency prior to formal review.

It is upsetting to find, for example, after half a year of waiting that the sequence of indications, contraindications, and warnings in the package circular are requested to be presented in a different way from the last time. Even when these changes are complied with promptly, months can go by before the busy examiner can find time to review the revised labeling again. It seems to me that there are enough of these changes in format, procedure, or requirement that

the industry would gladly subscribe to their publication prior to their being put into effect. Perhaps the new "Investigational Drug Circular," issued by the Bureau of Medicine of the FDA, could serve this function.

In any case, I think it only fair that if the FDA is going to take a full six months before the first rejection of an NDA, they should make an effort to provide a full disclosure *within that time* of what they consider to be the sum of the inadequacies of that application. Certainly this must have been the intent of those who approved the new drug regulations. But I do not feel the FDA has acted consistently within this intent. Perhaps it is physically impossible to do so. However, the present practice of declaring an NDA incomplete on the basis of a partial analysis of even a single section—and this at the end of perhaps five months or so of waiting—makes a mockery of the regulatory change that extended the time limit for decision from two to six months. By this device of rejection on partial review, final approval of an NDA can be postponed indefinitely unless it is withdrawn or the sponsor elects legal rather than scientific redress—and this is saddening.

While full disclosure of the basis for rejection by the end of six months (180 days) would be a real improvement, it would be better still if the FDA could make known to the sponsor the basis for rejection of any individual section of the NDA as soon as that review is finished, so that the sponsor could be helpful in interpreting the difficulty or be able to start accumulating the additional information that seemed needed. If the FDA reviewer does not understand some aspects of an NDA or wishes additional specifications, for example, a telephone call to the sponsor may easily clarify an obscure point. This is a sensible approach that has not only advanced the common cause of making new developments promptly available to the physician and the patient, but it has also created a great deal of good will in the instances when it has been followed.

At the first level of interaction between the sponsor and the medical officer or scientist responsible for judging the NDA incomplete, there are three matters that frequently need to be resolved.

First, there is the supplying of information which has been omitted by oversight, which is newly required, or which deals with clarification of the language of labeling. These things can usually be handled promptly if communications are adequate, but even the

most trivial change in the NDA may postpone further action on it up to six months, and usually does. There appears to be no direct provision for adding new data that may be helpful in evaluating an NDA without the certain risk of extending the time for decision another six months. This is a most frustrating practice that should be resolved fairly.

Secondly, there may be requests for one or more additional studies seeking information that may in fact be anticipated in perhaps another manner in the NDA, or may be so well established in the background of experience in the field that the sponsor has felt further documentation should not be required. When a request for such an additional study is on the record, there is a disinclination on the part of the immediate supervisor at FDA to set aside the imponderable that has been created it it can be rationalized, and so the sponsor's resources are cluttered up with work which does not contribute usefully to the advancement of therapy except in a supportive way. In my opinion, a request for additional work on the part of a sponsor should be reviewed by the next line of authority at the FDA to be sure it is adequately justified, for such diversions have become a serious drain on the resources of laboratory and clinical investigators alike.

Third, and most important, within the past year or so the industry has had to cope with an alarming incidence of issues that are matters of principle—issues that do not relate to the safety or efficacy of the proposed therapeutic agent that go beyond the proper purview of the FDA, and which sometimes cannot be reconciled without the sponsor's seeking recourse from higher authority within the agency. It seems to me that there is need for an orderly way of handling such issues without undermining the position or challenging the competence of those who create them. Certainly no sponsor would wish to embarrass an employee or his supervisor, and certainly no one relishes the need to seek legal redress. I feel confident that time, organization, and the more complete assimilation of the large and newly recruited group of physicians and scientists into the FDA framework will minimize this friction. It needs prompt attention.

I have spoken as if the New Drug Application takes many months or years of negotiation before its acceptance. It does. Regrettably, the duration of review and negotiation does not bear any relationship to the importance of the new drug to the patient. Nonetheless, with patience, perseverance, time, and sometimes extraordinary effort,

the NDA may be approved. However, there is one last, and to me ridiculous, administrative gesture: the sponsor finally receives a letter from the FDA which announces that the NDA (which may have been submitted many months or even years previously) was filed on such and such a date, and that it was approved on a date perhaps a few weeks or a month later. This practice permits the FDA records to show prompt action in filing and approving the NDA. Perhaps it serves a more useful purpose than merely to evoke the indignation of the sponsor, who knows how long ago the application which he considered adequate to document safety and efficacy, was really submitted.

Summary

In summary:

1. There is a need to improve general administrative practices in processing the NDA and a need for the changes to be made known promptly and systematically to industry.

2. There should be a thorough study of the actual NDA, from concept to format, in order to minimize the inevitable barriers to communication of highly complex information between those who are familiar with it, having prepared it, and those who are less familiar with it but must judge it.

3. The FDA and the industry must search for a less ponderous way for the agency to arrive at a *total* view of the safety and effectiveness of a new drug presented through a New Drug Application.

4. A better protocol is needed for the prompt and informal resolution of differences in concept that inevitably arise from time to time, lest—without anyone's wanting to—there be a trend toward the more frequent use of the more legalistic recourses available.

Finally, our hopes for a clearer policy consistent with the spirit of the regulations for strengthening of procedures, and our admiration for sustained performance under adverse circumstances, are directed to the FDA's physicians and scientists who must maintain their own perspectives as they bring stature and give direction to this essential federal institution. I know I can pledge to the FDA the understanding and cooperation of the physicians and scientists in industry as long as the objective is to recognize and resolve our problems and to discuss and equalize our differences. This must be our common objective, with action taken based on mutual respect and mutual trust, if there is to be progress in the efficiency and the fairness with which the multitude of almost daily interactions

between us are handled. The burden of those interactions has become, temporarily at least, so overwhelming that the progress of important new drugs is faltering alarmingly today as they advance from theory to therapy. We have the capacity to correct the situation if we have the wisdom and the incentive to do so. **[The End]**

Comments by GEORGE L. WOLCOTT, M. D., Panelist

Dr. Wolcott Is Medical Director, Consumer Products Division, American Cyanamid Company.

ON THE BASIS of recent discussions with representatives of industry, it almost would be possible for me to report to you that the pharmaceutical industry has no FDA problems in the field of investigational drugs. More correctly, I must report to you that there is a great reticence among industry representatives to discuss the intimate details of problems in this area.

Problems indeed do exist, and in order to provoke panel discussion, let's review some conclusions drawn in mid-1964 by the Subcommittee on State and Federal Legislation and Regulations as contained in the final report of the Commission on Drug Safety:

> All aspects of the 1962 drug amendments place awesome responsibilities on the FDA, corresponding to its broad new powers. Its implementing regulations will decide the future of this country's prescription drug industry. Wisely conceived and properly drafted, they might have encouraged an expanding research effort. Instead, the FDA has issued certain regulations which, in the few short months they have been in effect, have already had serious deterring consequences for research scientists, clinical investigators, and research-oriented organizations. Paper work and other controls, including virtual step-by-step government approval of projects, have brought about a reduction of research effort in some quarters, frustrated many research scientists and investigators to the point that they have forsaken these fields for others, and driven several drug companies to abandon research and development activities. . . .

Deterring Consequences for Research

Just a month ago, some of these serious deterring consequences for one research scientist were dramatically portrayed to The American College of Clinical Pharmacology and Chemotherapy by Dr. Carl C. Pfeiffer of Princeton, New Jersey.

Pointing out that the new regulations had made profound changes in the activity of the basic clinical pharmacologist, especially in the areas of interesting new drugs with little or no possibility of broad commercial sale, Dr. Pfeiffer expressed even greater concern about

burdensome restrictions on the study of new uses of already licensed drugs. Let me quote a few statements from his paper:

> We have . . . retreated from the advancing edge of therapeutic science and taken refuge in the more intensive study of control drugs, such as phenobarbital.

Even in this seemingly isolated area of research, Dr. Pfeiffer found obstacles created by the new regulations. This led him to say—

> A further and even more grievous difficulty with the current situation is that the present restriction of drugs to their licensed uses alone is a travesty on the physician's free choice in the practice of medicine.

A few sentences later, Dr. Pfeiffer stated:

> The evidence for the commercial claim for this new use is the only factor which should concern the FDA.

Although it is obvious that Dr. Pfeiffer has overstated the problem with respect to impairment of the individual physician's free choice in the management of any single patient, this is not the case when a *new dose* or a *new use* of an already marketed drug is tested by a physician in a group of his patients, particularly when this effort is characterized as a clinical research study.

In the field of OTC drugs, these "new use" and "new dose" of old drugs attitudes seriously can impede the development of more extensive understanding of these useful preparations. Consider that best known of all OTC preparations—aspirin. As I understand the situation, any dosage greater than 10 grains per 4-hour period or 60 grains per 24-hour period converts the preparation into a "new drug." That this is not a precise standard is manifest from the fact that a number of products have been extensively marketed with recommended dosages exceeding the 4-hour limit but not the 24-hour limit.

I believe a convincing case can be made today for the safeness of 15 or 20 grain single doses, particularly when 24-hour dosage does not exceed 60 grains. Consider, however, the extent of non-contributory paper work which today must precede the formal testing of such doses in an attempt to secure data adequate to support claims that would be used in marketing.

In my opinion, it is possible for FDA to simplify their regulations relating to clinical investigation of "new uses" or "new dosages" of already marketed drugs. Do not relax the requirements for premarketing proof, but do make it simpler to acquire such proof in the investigation of these extensions of already marketed drugs.

Elsewhere in the problem area, several industry representatives commented on current difficulties in securing FDA comment on the

suitability of efficacy designs in investigational drug studies. Properly or improperly, it is now generalized that the investigational drug branch is concerned only with safety and does not attempt to comment on efficacy phases. This may be suitable to FDA as an internal administrative procedure, but FDA must furnish a modification that will provide adverse criticisms of efficacy designs *before* rather than *after* the studies are completed.

The only other frequent comment on problems had to do with seemingly needless, minute-detail reviews at NDA level of reports or data originally submitted and presumably fine-tooth combed at investigational new drug (IND) level. In connection with the loss of understanding and comprehension attributable to change of reviewing officers from IND to NDA level, this lack of continuity is obviously responsible in part for the delays in approving NDA's.

Summary

In summary and as a focus for discussion by this panel, consideration should be given to providing simpler regulations to enable clinical study of (1) interesting new drugs of no foreseeable commercial value and (2) "new uses" and/or "new doses" of already marketed drugs. Additional consideration should be given to prompt review of efficacy designs in IND studies with immediate notice to sponsors of any FDA adverse views. Finally, better continuity is needed in the review at NDA level of data originally submitted in the IND phase. **[The End]**

Comments by RALPH G. SMITH, M. D., Panelist

Dr. Smith Is Director, Division of New Drugs, Bureau of Medicine, FDA.

PROBLEMS WITH INDUSTRY on new drugs have been a subject of discussion, either directly or indirectly, at meetings of various types for more than twenty-five years. In spite of this, the subject apparently has not been exhausted. Audiences and speakers change. Probably more important has been a change in various aspects of the subject itself. Even under the 1938 law there was a gradual increase and tightening of requirements, occasionally by regulation, but irrespective of regulations, as a result of the development of improved methods of investigation and manufacturing practices. With such improvements it was inevitable that requirements would

increase and it was found that applicants were able to meet the requirements.

The Kefauver-Harris amendments have given the subject a new lease on life. Although over two years have passed since their enactment, both industry and FDA are still in an experimental stage with the effectiveness provisions, the impact of the "current good manufacturing practice" section of the Act, and the changed procedures in the technical handling of applications.

Everyone recognizes this transitional state as a painful one, not only as a result of the increased requirements but by uncertainties in interpretation of the law and regulations. The broad aspects of the new requirements are well understood but there is still need for progress in agreement on their application to practical day-to-day problems. In this short presentation it is possible to touch on only a few of the difficulties. Undoubtedly the discussion to follow will be more fruitful.

Difficulties in Applying New Regulations

It has been and still is common practice for industry to consult FDA on the new drug status of products which it proposes to market. With rare exceptions our opinions have been accepted, although not always without argument. Prior to 1962 our decisions were reached on the basis of whether or not we believed there was a general recognition of safety. It is true that we did include efficacy with safety in our consideration of drugs recommended for conditions where these two factors were closely interwoven. Such cases were the exception rather than the rule.

With the inclusion of lack of general recognition of effectiveness in the definition of a new drug the latter must be considered in all instances. Does this make our task more difficult or easier? It is easier if every old drug or combination of old drugs introduced on the market is regarded as a new drug on the basis of a lack of general recognition of effectiveness if not of safety. We do not believe that such is the case. Certainly, some will be protected by the grandfather clause by virtue of the same composition and labeling as one marketed on October 9, 1962. Further, however, each product is considered individually against the background of knowledge of the action of the ingredients and general acceptance of the claims made for them. It is true that the majority of proposed products have been regarded as new drugs but there have been exceptions.

Incidentally, I believe it is common knowledge that since the passage of the Kefauver-Harris amendments all timed disintegration dosage forms are considered as new drugs, irrespective of whether the ingredients are regarded as safe and effective in ordinary dosage form. The reason for this is obvious and it is doubtful that any product of this type can lose new drug status to the extent that a new drug application will not be required for the product of each new manufacturer.

Undoubtedly the most important change in the new drug application requirements is that of substantial evidence of effectiveness. There has been much discussion on this subject and many questions raised for which there is not a simple "yes" or "no" answer. Firstly, the law does not require absolute proof of effectiveness. This might be more difficult to define, in addition to attain, than substantial evidence which is legally defined. I believe however [that] the definition makes it plain that although there may be a degree of judgment involved the evidence must be truly substantial, when it says "* * * on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have * * *". With your knowledge of experts and their differences of opinion, how far away is this from proof?

Such questions as "To what degree must the product be effective in individual cases?" and "In what percentage of cases must it be effective?" cannot be given a simple answer. It will vary with the conditions for which the drug is recommended and with other circumstances. Probably it boils down to the general question "In consideration of the hazards of the drug and the conditions for which it is recommended, should the drug be available for use?" If the answer is in the affirmative it should be stated clearly in the labeling, on the basis of the results of investigation, to what extent the drug is effective. Marketing may be justified if it has an incidence of effectiveness in 10 per cent of cases or even less for certain conditions or if under certain circumstances it only partially alleviates an otherwise uncontrollable symptom. Honest full disclosure in the labeling will solve many problems with respect to the effectiveness requirements.

It is hoped that in this area the Medical Advisory Board or ad hoc expert committees, as planned by the Medical Director, will be most helpful.

For several years, new drug applications have been gradually increasing in size, definitely more so since evidence for effectiveness has been required. Most of the material consists of case reports. The bulk

per se of the application undoubtedly presents a problem for pharmaceutical firms. It certainly does so for us. An application of 30 two-inch volumes takes a long time to review, and considerable filing space. Recently there have been conversations and meetings with industry to explore methods of ameliorating this problem. Proposals for the submission of comprehensive and responsible summaries, of data on punch cards or magnetic tape, and of applications in the form of microfilm have been discussed. To what extent these measures are acceptable or can be helpful in solving our difficulties has [have] not yet been resolved.

Investigators are now required to prepare detailed records of their investigations and to submit them to the sponsor of the drug. In turn, the applicant is required by regulation to submit all reports which he receives. Much of the material in many applications is of little help in evaluating the safety or effectiveness of the drug. It is suggested that the volume of the reports might be controlled to some extent at their source by the more careful planning of an investigation and choice of investigators to acquire what is needed and to eliminate reports of little value. It is realized that this is not a simple matter and that excellent planning sometimes goes awry. It is also known that several firms are attempting to do this but the effort could be expanded.

As previously indicated the requirements for acceptable manufacturing facilities and controls were gradually tightened before the Kefauver-Harris amendments. In this connection we might cite the requirement for stability data, factory inspections in certain instances before the approval of an application and the checking in our laboratories of methods of assay and of specifications. The amendment on current good manufacturing practices and the regulations pertaining to it which apply to all drugs set standards of procedure which at least must be met for new drugs along with those presented in the new drug application form. The rash of recent drug recalls (involving new as well as old drugs) resulting from inadequacies in controls, particularly for the packaging and labeling of drugs raises the question of whether FDA requirements and supervision are yet sufficiently stringent. In the handling of applications we have not insisted that applicants, in all cases, conduct laboratory tests after the final labeling process. It now appears that such a requirement may be necessary.

Finally, a word should be said about the new procedures for handling applications. It is no secret that many applicants are dissatisfied

with the prolongation of the processing period under the new amendments. The initial period of 180 days rather than 60 was a welcome change from our standpoint as was the elimination of the automatic clearance of applications in the absence of formal objection. It was our hope that the period of 180 days would allow time not only for initial evaluation of the application but also for requests for additional information and data, when indicated, and its review—in other words, for a complete processing of the application. We have found that this has not been possible to date since increases in staff have not kept pace with additional responsibilities and work load. It is still hoped that we can accomplish this objective with further increments of staff and improved facilities.

These comments do not adequately cover the field but they may serve as a preface for the discussion period. **[The End]**

Comments by FRANCES O. KELSEY, M. D., Ph.D., Panelist

Dr. Kelsey Is Chief of the Investigational Drug Branch, Bureau of Medicine, Food and Drug Administration

TO DATE, THE INVESTIGATIONAL DRUG BRANCH has received approximately 2,200 Notices of Claimed Investigational Exemptions for a New Drug. Approximately 75 per cent of these have been sponsored by industry. Some 250 investigations have been discontinued by the sponsors.

In many instances discontinuation was undoubtedly prompted by notification to the sponsor by the Food and Drug Administration that preclinical data presented in support of his clinical studies were inadequate to permit evaluation of the safety of these proposed studies in human subjects. A number of these investigations have been resumed following modification of the investigational plan or the submission of additional animal or control data.

Of the dozen or so investigational new drugs (IND) that have been terminated by the Food and Drug Administration, about 25 per cent were submitted by the drug industry. At least one of these was reinstated following submission of additional preclinical data.

"IND" Review Procedure

For review of notices there are at present 14 M. D.'s attached to the Investigational Drug Branch. There is a broad representation of the specialties within the Branch and several of the Medical Officers are fluent in one or more foreign languages. Additionally, two medical officers in the Antibiotic Branch deal with investigational drug filings pertaining to antibiotic preparations which constitute approximately 10 per cent of the IND's.

IND's are also reviewed by the Division of Toxicological Evaluation and the Controls Evaluation Branch. The Division of Toxicological Evaluation has 14 pharmacologists who review applications and in addition can call on the assistance of 10 pharmacologists in other divisions. The Controls Evaluation Branch presently allocates 10 chemists to full time review of the investigational drug notices.

Comments to the sponsor regarding the deficiencies of an IND are not sent out until reports have been received from the reviewing medical officer, pharmacologist and chemist. It is recognized that this procedure may entail a delay but it is felt that a complete critique would be more acceptable to the sponsor than separate ones arriving at different times. However, if any of the reviewing officers feel a matter of considerable urgency exists then the others may be alerted for a more rapid review or the sponsor may be contacted on that particular area.

It is realized that some delay has occurred between the submission of the IND's or the amendments thereto, and the acknowledgment of the receipt of these to the sponsor. We are hoping that with more efficient procedures we can cut down this serious time lag. The submission of IND's bound with the kind of fasteners and jackets we use would help us in this respect. Our materials and instructions are available to sponsors who are willing to use them.

The chief over-all deficiency noted in the IND's submitted, concerns the preliminary animal studies. For a limited human use in the hands of experts, we naturally do not expect the same extensive animal work-up as would be required for an NDA. Nevertheless, we do feel certain minimal studies are essential. For example, we believe that LD 50's by the proposed route or routes of administration are mandatory. We believe some repeated administration studies are necessary with adequate observation and also pharmacodynamic studies appropriate to the type of compound. We believe that the

data supporting the safety claims should be submitted in sufficient detail to permit an independent judgment of their adequacy. Generally speaking we do not believe a summarized report is adequate and consequently have requested more detailed information. Any material submitted with the IND can, of course, be incorporated in a future NDA by reference.

After an NDA has been submitted for a drug, investigational work will ordinarily be continued while the NDA is under consideration. In some instances, the sponsor may wish to undertake investigational work in new areas not considered in the NDA. In other instances, he may send in material in response to a request for data for an NDA from the Medical Evaluation Branch or for an IND from the Investigational Drug Branch. However, information relative to safety and effectiveness of a preparation must be considered by both branches. Therefore, when a sponsor or an applicant directs additional material to a single document he should identify, preferably by a separate letter, other submissions to which it is pertinent.

The qualifications of both the preclinical and clinical investigators are of considerable concern to us. We realize the relative scarcity of well-trained investigators in the fields of animal and human pharmacology compared with the rather large number of drugs under test at any given time. We believe, however, particularly in Phase I and Phase II, studies should be undertaken only by persons thoroughly conversant with the action of drugs. Additionally, in Phase II studies, the initial use of the drug for diagnosis, treatment or prophylaxis of disease, the investigator should be familiar with the condition(s) for which the drug is used, the other drugs used and the methods of drug evaluation. It is our impression that on occasion drugs of rather diverse nature are being investigated by individuals whose training and facilities appear to be inadequate for the magnitude of the tasks that they have undertaken.

In regard to drugs that have been discontinued by the sponsor we ask for information concerning the reason for discontinuance, a brief summary of results that reflect effectiveness and safe use of the drug, and information concerning steps taken with respect to unused supplies. Further, we wish assurance that the investigators have been told that the investigation has been discontinued. In these amendments, as with others, we may request additional information if it is not adequate for us to evaluate safety of the procedures adopted.

Throughout the year we have had considerable assistance from our Advisory Committee on Investigational Drugs. We have frequently consulted them on the reasonableness of our requests for preclinical data on investigational drugs and have enlisted their assistance in solving some of the more pressing problems in the Branch. Additionally, they have served as a bridge between sponsor-investigators and the Food and Drug Administration, helping to interpret the regulations to such investigators and bringing our attention to some of their problems in interpreting or complying with the regulations.

In summary, we believe that the investigational drug regulations provide additional safety during the testing procedure with the drug. Furthermore, we are hopeful that the suggestions or requests issued from our Branch may serve to assist the sponsors in ultimately securing an approved new drug application. We welcome comments or inquiries on our procedures. **[The End]**

Summary Remarks by WILLIAM J. EVANS, Reporter

Dr. Evans Is Director of Medical Review, Bureau of Medicine, FDA.

MUTUAL RESPECT AND UNDERSTANDING are primary requisites in order that the Food and Drug Administration and Industry may walk hand in hand to further the advance of the assault on illness and disease.

The Amendments of 1962 to the Federal Food, Drug, and Cosmetic Act, have caused problems for the Food and Drug Administration as well as for industry. The strangeness of a new law, radically changing the processes of the past, is always met with some consternation. In retrospect, the "safety" factor in the old law concerning New Drug Applications, led to the use of poorly documented studies in many applications. Safety and efficacy are or should be synonymous, because relative balance between them, based on the conditions of use, are of the essence in drug research.

The just administration of the law is the essential ingredient in regulatory work. A freely flowing stream of knowledge is important, but the health and safety of the populace is our first order of business.

Delays in Reviewing Procedure

A number of the problems encountered by Industry in submitting Investigational New Drugs and New Drug Applications were discussed at length by the Panel in response to inquiries from the audience and Industry's representatives on the Panel. The primary concern of Industry, which was made emphatically clear, is the time required for the processing of New Drug Applications. Profound criticism was aimed at the Food and Drug Administration, which has some basis in fact, and this was duly acknowledged by the Food and Drug Administration's representatives. However, it must be clearly borne in mind, that there is no defense mechanism as has been intimated for automatically turning down New Drug Applications. There is no doubt, that from the viewpoint of Industry, there has been undue delay, and much of the resulting criticism is warranted.

Delays are due to such problems as deficient "Mail Room Distribution" but this problem is being investigated by a Food and Drug Administration "task force" to establish a smoother and faster "mail flow" within the Bureau of Medicine and the Administration. This goal will be accomplished.

Delays also occur at the level of the reviewing Medical Officer. This is due to the overload of work borne by the experienced physicians, and this is accentuated by the "newness" of those recently appointed to the staff. Training of these Medical Officers takes time and effort by experienced men, further complicating the picture, but despite "growing pains," progress is being made. Rejection of New Drug Applications does occur, and the frustrating part of this to Industry is that it occurs so long after submission. To counter this unfortunate delay, Industry has, through the medium of this panel discussion, called on the Food and Drug Administration to present a "full disclosure" of its own, in order that Industry may be readily and promptly informed concerning "inadequacies" in their submitted New Drug Applications.

Most problems have two sides, and therefore, we must examine both ends of the spectrum. As true friends self-examination and the subsequent prevention of problems should be a joint goal. In the first place, the Food and Drug Administration must re-examine its procedures in order to facilitate faster review of New Drug Applications, New Drug Supplements and Investigational New Drugs. Experience and increased manpower, together with the consolidation of

the Medical Bureau in its new quarters, thus overcoming inefficiency due to crowding will be a major step in this accomplishment. More open channels of communication and a more trusting relationship between the Food and Drug Administration and industry will accelerate the process. A full Medical Bureau staff, when it has been meticulously recruited and trained, will accomplish the Food and Drug Administration's goals in the prompt processing of New Drug Applications.

Industry must do its part for the problems in the delay of New Drug Applications is not all one-sided. Better preparation of material for submission would be helpful, e.g. using the Food and Drug Administration's format and jackets would save much time. More meticulous detail in the preparation of submissions, particularly omitting none of the essential data necessary for evaluation. More definitive animal and clinical studies with more adequate scientific design in some cases would hasten the review of Investigational New Drugs and New Drug Applications, thus freeing medical officers, chemists, and pharmacologists to handle other submissions.

Other Problems

Although the time lag in the approval of New Drug Applications appeared to be the major problem confronting Industry in this field, several other problems were discussed. One of these was the problem of submitting Investigational New Drug Applications for drugs that are used primarily in research with little or no commercial value. In these cases the user, who is an expert, may act as the sponsor. There is no need for a long application. In most of these cases, the requirements are similar to those requested by University and Hospital Research Committees.

In summary, the problem of the "New Drug Application slowdown" is of great importance. An all-out effort to achieve smoothness, and efficiency in processing the New Drug Applications is under surveillance and will be accomplished. Industry, through more definitive submissions together with comprehensive and responsible summaries, will more than aid in obtaining this goal. As a result, an earlier determination of deficiencies in applications could be found and be brought to the attention of the firm involved. Thus in a spirit of mutual respect, the goal of voluntary compliance may be attained for the greater health of all the people. **[The End]**

Drug Labeling and Promotion

Introductory Remarks by HAROLD F. O'KEEFE, Moderator

"Drug Labeling and Promotion" Was the Subject of One of the Afternoon Panel Workshops on the General Topic of "What Industry Needs from FDA for Better Compliance." Mr. O'Keefe Is Chief, Advisory Opinions Branch, Division of Industry Advice, Bureau of Education and Voluntary Compliance, FDA.

I HAVE BEEN CHOSEN as your moderator. I assume that those preparing the program felt that anyone could moderate a panel of such able and distinguished men as I have associated here with me. These would be a self-sufficient group in any setting. They are:

(1) Frederick J. Cullen, M. D., Medical Consultant, The Proprietary Association;

(2) Augustus Gibson, M. D., Director, Research and Development, The Schering Corporation;

(3) Howard I. Weinstein, M. D., Director, Division of Medical Review, Bureau of Medicine, Food and Drug Administration; and

(4) Morris L. Yakowitz, Director, Division of Case Supervision, Bureau of Regulatory Compilance, Food and Drug Administration.

And last, but by no means least, our distinguished reporter, Mr. Charles F. Hagan, Assistant Secretary, Chas. Pfizer and Company. Mr. Hagan has the very difficult job of summarizing and reporting this session to the full attendance later this afternoon.

May I reiterate that the theme of this meeting is "What Industry Needs from FDA to Do a Better Job of Compliance." We do not wish to use this panel for airing individual gripes that would not be of interest to the total audience, discussing individual problems, decisions, etc. on a case by case or experience by experience basis. Rather we wish to receive from you your ideas, suggestions, and recommendations as to how the Food and Drug Administration may serve you within its statutory limitations.

To set the stage for the discussions, we have asked each of our panelists to present a brief statement and then we will follow with questions and discussions from the floor and from communications that have been sent to us in advance of the meeting. **[The End]**

Comments by FREDERICK J. CULLEN, M. D., Panelist

Dr. Cullen Is Medical Consultant, The Proprietary Association.

AT THE OUTSET, I WANT TO SAY that my statements today represent only my own views which are based on 30 years' experience in this field. I am NOT speaking in any capacity for the Proprietary Association or for any of my clients; I have NOT discussed with them any aspects of this panel meeting. Any statements that I make today are based solely on my own personal opinions.

I believe that EDUCATION is one of the most important functions of the Food and Drug Administration—not only in the consumers' field but in that of industry as well. This is borne out by statements included in committee reports that were issued during the time that the 1938 Federal Food, Drug, and Cosmetic Act was pending in Congress and this also applies to its subsequent amendments.

Purpose of Proposed Committee

I realize that it has been reported in drug trade papers that an ad hoc committee of 18 persons has just been appointed to meet twice a year to discuss special problems. But, do you realize the proprietary drug industry is not represented on that committee. Therefore, in my opinion, one of the greatest services that could be rendered by the Administration-industry to assist the drug manufacturers in complying with the provisions of the FFDC Act and its regulations would be by the cooperative formation of an Administration-Industry Committee to meet at specified times. The purpose would be to exchange ideas to clarify questions that may arise on both sides and to discuss various problems in such a way as to assist in preventing what may appear to some to be a "surprise attack" on either a single ingredient or a finished product.

Activities of Administration-Industry Committee

While the Food and Drug Administration cannot and would not condone what it considers a violation of the law or of a regulation, but this does not mean there cannot be discussions of various problems in order to allow a manufacturer to become familiar with the Administration-industry's viewpoint and vice versa. It is always helpful to know and to understand thoroughly the reasons for a decision and on what it is based—is it a section of the law? a regulation? or is it past history of enforcement that is involved?

Certainly in the case of phenacetin, in my opinion, there is no doubt that a discussion prior to all of the lay publicity that was released would have been of great benefit not only to the manufacturers who have included phenacetin in their products for many years but also questions would not have been raised in the mind of the average consumer causing doubts and fears as to the dangers involved by taking a product that contains phenacetin, this in turn undermines the confidence of the consumer in all medicines whether over-the-counter or Rx.

A question has arisen numerous times with reference to new-drug applications. For instance, a manufacturer submits to the Administration-industry a combination of old ingredients with a proposed label—and inquiries as to whether or not he must file a new-drug application. After waiting a certain period of time he receives a letter in which the most important words to him are—quote and unquote—IN OUR OPINION . . . followed by further instructions as to what he may or may not do. Just what is the legal status of such an opinion? Could a discussion at a round table give the manufacturer a clearer and more distinct idea as to his legal rights?

Would it not be possible, if a problem arises, to discuss certain types of old products that are presently on the market?

In case the Administration-Industry considers it advisable to modify a formula, a labeling, or to remove one of these products from sale, would it be possible to give the manufacturer some information as to the length of time he would have in which to complete such a change? Remember this example covers old products and not new drugs.

Also, does the Administration-industry have available for its own use a list of dosages for various drugs that are considered satisfactory for use in over-the-counter products? A discussion of a list such as this would be of great value.

Also, there are certain words and phrases that are considered misleading by the Administration-industry. Cannot these be discussed? In other words, let's try to understand one another.

If such an Administration-Industry Committee is formed, the Durham-Humphrey amendment must be taken into consideration. As you all know, this amendment provides, in substance, that certain drugs must be dispensed only on prescription; and that all other drugs must be adequately labeled. Hence, many phamaceutical companies are marketing adequately labeled products that are not ad-

vertised to the general public but which can be purchased without a prescription. Therefore, such a proposed committee should include official representatives of the pharmaceutical manufacturing industry as well as those of the proprietary industry.

The dates of the meetings and the size of the committee would have to be determined, and if formed, the official industry representative must be granted the authority to bring an attorney or a technical man or both. The FDA would, of course, select its members from its staff.

Periodic meetings of such a committee, I am sure, would be of great value to the drug industry as a whole—as well as to the members of the Federal Food and Drug Administration.

It is my opinion that a temporary Food and Drug Administration Industry Advisory Committee be appointed as soon as possible to make studies and recommendations in order to get the "ball rolling."

[The End]

Comments by AUGUSTUS GIBSON, M. D., Panelist

Dr. Gibson Is Director, Medical Research Division, The Schering Corporation.

SINCE I AM NOT DIRECTLY CONCERNED with labeling and advertising, I asked my associates in these fields what their problems were. The comment was, "We can live with the new regulations." Of course, man has also found it possible to live in Antarctica but no doubt there are pleasanter climates. However, judging by the speeches this morning, we are apparently living in a much warmer atmosphere than in the recent past.

I should like to say a word about the function of advertising and promotion before we get into specific problems.

There seems to be a general assumption that all promotion and advertising is bad and that every effort should be made to confine and minimize it. Perhaps it is not realized that advertising and promotion are strong forces for improvement in drugs as in other commodities.

The first demands for proof of efficacy did not come from the FDA. They came from the potential prescribers of our products and they were channeled to us by our advertising copy writers and detailmen. They kept asking of us in research, "How is your new drug different? How is it better than the competition? What evidence can we present to prove superior efficacy and safety?"

It is a misconception to think that the advertising writer welcomes the challenge of trying to promote a "me, too" product. Quite the contrary. He is constantly suggesting ways in which we should try to improve our products, and serving as a stimulus to new research efforts directed towards greater safety, efficacy and convenience to the user.

Problem of Claims for Efficacy

To return, however, to our assigned topic, it is on the problem of claims for efficacy that we most need help with the new regulations. It is not particularly difficult to live up to the requirements covering inclusion of precautions and side effects. In fact, the new regulations have largely abolished the distinction between labeling and advertising since both must carry full disclosure. Now, we merely include the precaution and side effect section of our package insert, or an abbreviated version of it, in our advertising.

When we come to efficacy, however, although the allowable claims are clearly to be based on those in the approved New Drug Application, the FDA issued special recommendations concerning adequate balance between reports indicating efficacy and those indicating lack of efficacy.

Further, they have drawn a distinction between reports from good and qualified investigators and those who are less well qualified. These problems of fair balance, qualifications of investigators, and quality of clinical studies, involve very delicate value judgments on which there doubtless will be perfectly justifiable differences of opinion.

I do not expect the Food and Drug Administration to furnish us with hard and fast guidelines since these cannot possibly exist and since the agency cannot properly divide clinicians into various classes of competence.

In these questions, where opinion as well as medical fact must enter in, I think we can be greatly helped by frequent and friendly discussion between physicians in industry and those in the regulatory agency. Furthermore, we can obtain assistance from consultation with experts. There is a danger here, however, which I want to warn against. The opinion of an expert is still only an opinion and is not worth as much as a fact presented by a lesser authority. We must not allow ourselves to fall into the error of blind acceptance of authoritarian opinion, nor base our judgments on rank in a scientific hierarchy.

With full discussion, however, and examination of available facts, one may expect that areas of agreement will be mapped out and that we can prepare advertising and labeling which reflects qualified medical opinion based on adequate evidence. **[The End]**

Comments by MORRIS L. YAKOWITZ, Panelist

Mr. Yakowitz Is Director, Division of Case Supervision, Bureau of Regulatory Compliance, Food and Drug Administration, U.S. Department of Health, Education, and Welfare.

BECAUSE MEDICAL JOURNAL ADVERTISING has a major impact on the prescribing of drugs by physicians, Congress dealt with such advertising in the Kefauver-Harris Drug Amendments of 1962. This law established the legal requirement that a prescription drug advertisement must include the established name of the drug and the same quantitative ingredient information as that appearing on the bottle label, plus "such other information in brief summary relating to side effects, contraindications, and effectiveness as shall be required in regulations which shall be issued by the Secretary (of Health, Education, and Welfare)."

Regulations Provide Advertisers with Guiding Principles

The regulations that have been adopted under the prescription drug advertising section of the law provide a set of guiding principles which enable the advertiser to comply with the law but which allow him a reasonable degree of latitude for promoting his product. These guiding principles may be stated in the following simple terms—any information presented in the advertisement concerning the therapeutic value of the drug must be truthful and must be so combined with information regarding the drug's side effects and contraindications as to provide a fair and balanced picture of the good and the bad of the drug.

To illustrate the latitude granted the advertiser, we point out that the regulations do not prohibit use of graphic presentations, headlines, or similar advertising techniques. Somewhat different size type may be used for presenting information with respect to side effects and contraindications than that used in the "headlines" that deal with the usefulness of the drug. However, there must be no concealment, subordination, or de-emphasis of the essential side effect and contraindication information that would minimize its disclosure as a part of the total message the advertisement conveys.

If the prescription drug is subject to an approved new-drug application or is subject to the certification provisions, the advertisement must not recommend or suggest any use that is not in the labeling accepted under the approved new-drug application or the certification provisions. In the case of a drug not subject to the new drug provisions or the certification provisions, the advertisement may recommend its use only for those purposes for which there exists substantial clinical experience, on the basis of which it can fairly and responsibly be concluded by qualified experts that the drug is safe and effective for such uses.

Regulations Encourage Voluntary Compliance

We believe that the regulations adopted under the prescription drug advertising law are an excellent example of an aid to voluntary compliance by the industry. The advertiser who abides by the spirit of these regulations need have no fear of regulatory action.

As a final point, FDA's Advisory Opinions Branch stands ready to provide comment on proposed prescription drug advertising submitted by industry. **[The End]**

Comments by HOWARD I. WEINSTEIN, M. D., Panelist

Dr. Weinstein Is Director, Division of Medical Review, Bureau of Medicine, Food and Drug Administration, U. S. Department of Health, Education, and Welfare.

THE FEDERAL FOOD, DRUG, AND COSMETIC ACT divides drugs into two broad classes, (1) drugs which are safe for unsupervised use by the public and which may therefore be sold "over-the-counter," and (2) drugs which require the supervision of a licensed practitioner and which are therefore restricted to dispensing on prescription. The rules covering the package labeling of an over-the-counter drug have not changed since the enactment of the Federal Food, Drug, and Cosmetic Act in 1938, and may be stated as follows—the labeling must provide the name of each active ingredient (plus the name and amount of certain ingredients specified in the law), proper indications for use, appropriate dosage instructions and any other directions needed for effective use of the product, plus any warning information needed by the layman for safe and effective use of the product. Obviously, all of this information must be in terms that will be understood by the public.

"Full Disclosure" Regulations Affect Labeling of Prescription Drugs

For prescription drugs, it was not required at an earlier time that the package include full information regarding use of the drug—our older regulations were satisfied if the drug manufacturer made the brochure available upon the physician's request. However, the large number of new medications that have appeared on the market in recent years has made it increasingly difficult for physicians to keep adequately informed about these newer remedies. We therefore promulgated the present "full disclosure" regulations several years ago requiring that the package labeling of a prescription drug must state the amount of each active ingredient and must bear full information regarding use of the drug by physicians, including indications, side effects, dosages, routes of administration, frequency and duration of administration, and any relevant warning information needed for safe and effective use of the drug by physicians. Our "full disclosure" regulations are written in general terms and permit the manufacturer a satisfactory degree of latitude in choosing his own phraseology and arrangement of format for his labeling pieces. However, we recognize that there are some drugs for which adequate use information is commonly known to physicians, and such drugs are not required to include "full disclosure" information in the package labeling. Further, the regulations permit the so-called "reminder piece" labeling which gives the name of the drug, but which does not state any indications for use or dosage information. However, if a mailing piece or other piece of promotional labeling contains indications for use or dosage information, the regulations require that such mailing piece, etc., must include essentially the same "full disclosure" information as that appearing in the package labeling.

Summary

In summation, the changes that have come about in the prescription drug labeling regulations are intended to provide the guidance needed by drug manufacturers for preparing informative labeling, but without unduly restricting the drug manufacturer as to choice of phraseology and format in his promotional pieces. **[The End]**

Summary Remarks by CHARLES F. HAGAN, Reporter

Mr. Hagan Is Assistant Secretary of Chas. Pfizer & Co., Inc.

THE FIRST SPEAKER from the Food and Drug Administration, Mr. Morris Yakowitz, began by summarizing the requirements imposed on prescription drug advertising by the Drug Amendments of 1962: namely, each advertisement must include the established name of the drug, the formula information required for labels by Section 502(e) of the Act, and "such other information in brief summary relating to side effects, contraindications, and effectiveness as shall be required in regulations which shall be issued by the Secretary."

Regulations Governing Prescription Drug Advertising

He commented that the regulations that have been adopted under the prescription drug advertising section of the law provide a set of guiding principles which enable the advertiser to comply with the law but which allow him a reasonable degree of latitude for promoting his product. These guiding principles may be stated in the following simple terms—any information presented in the advertisement concerning the therapeutic value of the drug must be truthful and must be so combined with information regarding the drug's side effects and contraindications as to provide a fair and balanced picture of the good and the bad of the drug.

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stantial clinical experience, on the basis of which it can fairly and responsibly be concluded by qualified experts that the drug is safe and effective for such uses.

Regulations Encourage Voluntary Compliance

The FDA believes that the regulations adopted under the prescription drug advertising law are an excellent example of an aid to voluntary compliance by the industry. The advertiser who abides by the spirit of these regulations need have no fear of regulatory action.

As a final point, Mr. Yakowitz reminded the audience that FDA's Advisory Opinions Branch stands ready to provide comment on proposed prescription drug advertising submitted by industry.

Advertising Force for Drug Improvement

The first industry spokesman, Dr. Augustus Gibson, opened by remarking that there seems to be a general assumption that all promotion and advertising is bad and that every effort should be made to confine and minimize it. Perhaps it is not realized that advertising and promotion are strong forces for improvement in drugs as in other commodities.

The first demands for proof of efficacy did not come from the FDA. They came from the potential prescribers of our products and they were channeled to us by our advertising copy writers and detailmen. They kept asking of us in research, "How is your new drug different? How is it better than the competition? What evidence can we present to prove superior efficacy and safety?"

It is a misconception to think that the advertising writer welcomes the challenge of trying to promote a "me, too" product. Quite the contrary. He is constantly suggesting ways in which we should try to improve our products, and serving as a stimulus to new research efforts directed towards greater safety, efficacy and convenience to the user.

Regulation Requirements Fulfilled in Advertisements

On the subject of the advertising regulations, Dr. Gibson remarked that it is not particularly difficult to live up to the requirements covering inclusion of precautions and side effects. We merely include the precaution and side effect section of our package insert, or an abbreviated version of it, in our advertising.

Problems in Reporting Drug Efficacy

As to statements regarding effectiveness, however, Dr. Gibson foresees problems in view of the press release issued by FDA on November 23, 1964, which listed some types of statements concerning effectiveness which may lead to enforcement actions. He cited specifically the portion of this release which suggests that there should be an adequate balance between reports indicating efficacy and those indicating lack of efficacy; and he also cited the distinction referred to in the release between reports from good, qualified investigators, and those who are less well-qualified.

He remarked that these problems of fair balance, qualifications of investigators, and quality of clinical studies involve very delicate value judgments on which there doubtless will be perfectly justifiable differences of opinion.

In such matters, where opinion as well as medical fact must enter in, Dr. Gibson suggested that all can be greatly helped by frequent and friendly discussion between physicians in industry and those in the regulatory agency. Furthermore, we can obtain assistance from consultation with experts. There is a danger here, however, which Dr. Gibson warned against. The opinion of an expert is still only an opinion and is not worth as much as a fact presented by a lesser authority. We must not allow ourselves to fall into the error of blind acceptance of authoritarian opinion, nor base our judgments on rank in a scientific hierarchy.

Dr. Gibson concluded by stating that with full discussion, and examination of available facts, one may expect that areas of agreement will be mapped out and that industry can prepare advertising and labeling which reflects qualified medical opinion based on adequate evidence.

"Full Disclosure" Regulations on Prescription Drugs

The next FDA spokesman, Dr. Howard Weinstein, discussed the "full disclosure" regulations which apply to labeling, as opposed to advertising. He pointed out that until 1961 there was no general requirement that each package of a prescription drug contain adequate directions for use on or within it, except as such a requirement was imposed as a condition to new drug clearance or antibiotic certification. In that year, the "full disclosure" regulations were issued imposing the requirement that there be full disclosure of uses, side ef-

fects, contraindications, etc. on or within each package of a prescription drug. The only exceptions from this requirement are those drugs for which the uses, side effects, contraindications, etc. are commonly known by the medical profession.

To the criticism that this "package insert" requirement is wasteful since the vast bulk of inserts wind up in pharmacists' waste baskets, Dr. Weinstein commented that package inserts are as close to physicians as the nearest drug store and many physicians do obtain package inserts from pharmacies.

FDA-Industry Committee Proposed

The final spokesman from industry, Dr. Frederick Cullen, expressed the belief that one of FDA's most important functions is education of industry as well as of consumers. He proposed the formation of an FDA-industry committee to meet at intervals for the purpose of discussing problems involving over-the-counter drugs.

Dr. Cullen mentioned that meetings of such a committee might assist in preventing what may appear to some to be a "surprise attack" on a drug ingredient or finished drug. He cited the recent publicity about phenacetin and expressed the opinion that a full discussion between industry and FDA, prior to any releases to the press, would have been of benefit not only to the manufacturers of products containing phenacetin, but also to consumers who now may have doubts about the safety of such products.

As another example of the benefits that could be derived from meetings by such a committee, he indicated that if FDA has a list of drugs, and dosages thereof, that are considered acceptable for over-the-counter sale, a discussion of that list would be of great value. Similarly, a discussion of certain words and phrases which FDA considers misleading could lead to better FDA-industry understanding.

Dr. Cullen concluded with the hope that a temporary FDA-industry advisory committee could be appointed soon to get the "ball rolling."

Question and Answer Period

Among the matters having the greatest general interest, which arose during the question and answer period, were the following:

Time Allowance for Labeling Revisions

The FDA panelists were asked what they would consider to be a reasonable time at which to begin including in labeling changes which FDA correspondence indicated were to be made at the "next printing." The FDA panelists indicated that this is a difficult question to deal with in general terms. However, they suggested that a reasonable time within which to commence use of such revised labeling would vary between three and twelve months.

Grandfather Benefits as Affected by New Drug Provisions

The FDA panelists were also asked for their view as to whether the pre-1938 grandfather exemption from the new drug provisions is lost if a manufacturer deletes one of several pre-1938 indications for use. The FDA panelists replied that, generally, it would be FDA's view that such a deletion would not result in loss of grandfather protection, but in certain factual situations FDA's view might be otherwise.

In this same connection, there was considerable discussion as to whether the labeling changes for dipyrone and aminopyrine, which FDA has recently indicated it will require, cause loss of grandfather protection from the new drug provisions, and entitle FDA to require submission of New Drug Applications for these pre-1938 drugs. The view was expressed that FDA's position that such labeling changes would result in loss of grandfather protection, could operate in other situations where FDA felt that labeling changes should be made in a pre-1938 drug, to discourage manufacturers from making such changes voluntarily.

Changes in New Drug Application Form

Two changes in the new drug application form engendered some discussion.

Prior to issuance of the revised application form in the June 20, 1963 regulations, the form provided that the NDA would become effective on submission of final printed labeling identical in content to the labeling copy submitted with the NDA. Under the revised application form, however, the application does not become approved on submission of such identical printed labeling, but only on subsequent receipt of a final approval letter from FDA. There was some discussion of the delays that have been encountered in obtaining the final approval letters, and several instances were cited where FDA insisted on changes, not previously mentioned, after printed labeling was submitted.

The other change in the NDA application form which was discussed involved paragraph No. 9 of that form. Until recently, that paragraph read that the representations made in the NDA continued until a supplemental application proposing changes was approved, or until FDA said a supplement was not required for a particular change, "or the article is no longer a new drug." The *Federal Register* for September 30, 1964 contained notice that this last quoted language was deleted from the form. While the intended significance of this deletion is not clear, if the deletion is intended to mean that a manufacturer is bound by the provisions of an NDA after the drug ceases to be a new drug, the validity of such a position was strenuously questioned. **[The End]**

NEW REGULATIONS FOR NEW DRUG LABELING AND MANUFACTURING ISSUED

New regulations have been issued to expedite improvement in new drug labeling and manufacturing procedures in the public interest and to permit a more orderly review of the claims of effectiveness for drugs. The revised regulations, published in the *Federal Register,* January 30, 1965, 30 F. R. 993, authorize immediate elimination of false or unsupported claims, the addition of any needed warning information in labeling, and improvements in manufacturing procedures and controls, without waiting for specific FDA approval.

Formerly New Drugs were marketed under conditions specified in New Drug Applications, and when a change in conditions was needed —in labeling, manufacturing procedures or controls—it was necessary for the application holder to file a supplement to this approved application and to await FDA approval of the change.

Under the revision, any changes proposed in supplemental New Drug Applications which call for deletion of false, misleading or unsupported claims, for the addition of warnings, side effects or contraindications or for manufacturing and control improvements, can be put into effect immediately—without prior FDA approval. However, the FDA must be notified in detail immediately and this information—actually a supplemental New Drug Application—will be reviewed by the agency and subjected to approval or disapproval at a later date. The firm's notification to the FDA constitutes an agreement by the applicant to an extension of time for formal action by FDA. The amended regulations also stipulate all promotional labeling and advertising should be revised promptly consistent with labeling changes submitted to FDA. FOOD DRUG COSMETIC LAW REPORTS ¶ 71,304, 71,309.

What the Public Wants

Introductory Remarks by JAMES L. TRAWICK, Moderator

"What the Public Wants," Dealing with Consumer Education, Was Discussed at One of the Afternoon Panel Workshops on the General Topic of "What Industry Needs from FDA for Better Compliance." Mr. Trawick Is Director, Division of Consumer Education, Bureau of Education and Voluntary Compliance, FDA.

I AM SURE SOME OF YOU have joined us only this afternoon, and perhaps have not attended previous joint meetings of the Food and Drug Administration and The Food Law Institute. I therefore yield myself a few minutes to orient you to the purpose and nature of these meetings and of our objectives this afternoon.

Objectives of Joint FDA-FLI Meetings

These joint meetings have been dedicated to a mutual understanding between FDA and industry so that we can best work together to achieve safe, wholesome foods; safe and effective drugs; safe cosmetics; and honest packaging and labeling of these products.

In other years, these joint meetings have included, in addition to their general objectives, such specific subjects as:

— discussion of the 1958 food additives amendment;
— the 1960 color additives amendment;
— the 1960 Hazardous Substances Labeling Act;
— laboratory developments in food and drug regulations; and
— the Kefauver-Harris Drug Amendments of 1962.

Last year, the meeting was an occasion to observe the 25th anniversary of the enactment of the Federal Food, Drug and Cosmetic Act, and to review regulatory and scientific problems confronting the joint sponsors.

In continuation of this series, the over-all theme of today's session is "Education, Information, and Voluntary Compliance."

Three Dimensions of Joint Objectives

Now, even-handed law enforcement and the encouragement of voluntary compliance might be considered as two dimensions of the

joint objectives of FDA and FLI. These dimensions and the respective roles of FDA and of industry are well understood. We have worked together for many years in these areas.

But our session here this afternoon is concerned with a *third* dimension—namely, consumer education. In this area, we are on much less familiar ground. We are here to explore what the public wants in consumer education, or put another way: How can the FDA and the industries and firms represented by The Food Law Institute help the consumer to get maximum benefits from the laws enforced by FDA? What more does the consumer need—and how can it be made available to him—so that he can make the wisest possible choice in the market place? It is axiomatic that *freedom of choice* and the *ability to choose wisely* go hand in hand and that both are essential to our system of free enterprise in this country.

FDA Consumer Education Program

FDA has had a modest consumer education program since 1952. In that year we first established part-time consumer consultants in our field districts. Our activities along this line were stepped up in 1962 by the establishment of a Consumer Education Branch in our Division of Public Information. Then, last year the entire program was again strengthened by consolidating these various activities in a new Division of Consumer Education.

The Division program now includes preparation of various types of materials for consumers—pamphlets, exhibits, slides, movies, radio-TV public service spots, materials for the older American, the low-income and foreign-language groups, and materials for students and teachers. Copies of some of these are on the tables near the doors and you are welcome to take them if you wish. To aid in distributing these materials, in making consumer contacts at the grass roots level, and in reporting consumer views back to us, the consumer consultant program beginning this year includes a *full-time* specialist at each of our 18 field district offices. Mrs. Carla Williams is the Chief of the Consumer Consultant Branch of our Division.

Branch Researches Consumer Views and Practices

In the Division we also have a new unit—the Consumer Survey Branch—to help determine consumer understandings, attitudes and habits that could be helpful to FDA in better administration of the law.

We know that the food, drug, and cosmetic industries have carried out various consumer education activities—some as a public service—for much longer than has FDA. Perhaps Dr. Scheele and Mr. Willis will tell us about some of them.

But we still find that the public at large is still vastly unknowing—and sometimes unwise—in its choice and use of many products.

For example, it has been established that the public spends upwards of a billion dollars a year on worthless or falsely promoted medicines and medical devices, and food supplements and so-called health foods that they do not need.

In another area, we know that many consumers are confused—and sometimes unnecessarily concerned—about the presence of additives in foods-additives that are to their great advantage and which scientists are convinced are safe. There is as yet not good understanding of existing safety controls. This is a matter for consumer education, because an individual is not able to exercise his freedom to choose in the market place if his mind is slave to false information or needless fear.

In another area, we find that most consumers have little appreciation of their role and responsibility—and opportunity, if you please—in such governmental processes as the making of food standards. Here, consumer views are *needed* in order to carry out the will of Congress that food standards shall promote honesty and fair dealing in the interest of consumers. We have found it difficult to establish a two-way flow of information that assures useful and effective consumer participation in such matters. This is a matter for consideration by the consumer organizations. Mrs. Housewife as an individual is not likely to be interested as a rule.

In still another area, we know that hundreds of thousands of persons—most of them small children—are injured every year as a result of careless handling of household products that are exceedingly useful and quite safe if properly stored and used. About fifty children die each year because parents leave an aspirin bottle in the wrong place. Yet, aspirin bottles are labeled "Keep out of the reach of children." The special law already mentioned requires warning labels and consumer protection information on other hazardous household substances—the cleaners, solvents, fuels, polishes and so on. Attention to label information might well prevent tens of thousands of accidental poisonings in the home.

Consumer Education—A More Effective Force

So, what can we do about these things through consumer education? How can we make consumer information a more effective force for consumer protection? These are our topics for today. What can we come up with that will help the Food and Drug Administration and The Food Law Institute help the consumer to help himself? In the case of the consumer organizations represented here today, who in turn represent many millions of their consumer members, what can we do to help you to better serve your members?

Now, with that as background, we will hear a brief statement from each panel member, after which we will open the meeting for questions or comments from the floor. Then, if there is time, we will invite each panel member to elaborate his remarks, or to react to what the others have said. **[The End]**

Comments by PAUL S. WILLIS, Panelist

Mr. Willis Is President of Grocery Manufacturers of America, Inc.

IT IS A PLEASURE to participate in this meeting because as food manufacturers, we have a great interest in the food and drug laws of this country. Our manufacturers produce most of the products that are available in the supermarkets throughout the United States, and we accept the responsibility that these foods are safe, nutritious and wholesome. Because of this interest, we have worked in the fullest cooperation with Congress and with the government agencies in the enactment and the administration of the numerous laws which provide protection to the American people.

We, of course, have a great interest in the Food Law Institute because it was in 1949, that GMA established it.

I also want to note with great pleasure that it was in 1941, that GMA established the Nutrition Foundation with which you are very familiar.

Consumer Education Assurance of Benefit and Protection

Consumer education has long been recognized by our industry as an essential activity for the fullest assurance of consumer benefit and protection. That benefit and protection results from economic, scientific and legal developments, and applies to the entire life-line

of food, from farm to table—including the farmer, the manufacturer, the distributor, and the consumer.

These economic benefits are shown in government figures which reveal that the share of income which the American consumer spends for food has been steadily declining. Today she can buy her food for 19 cents of her after tax dollar compared with 26 cents fifteen years ago. This is the smallest share of income spent for food anywhere in the world at any time in history. By comparison, consumers must spend 29 per cent of their income for food in England, 31 per cent in France, 45 per cent in Italy, and 53 per cent in Russia. This further observation is significant: The American factory worker earns the cost of his monthly market basket in 37 hours, as compared with 60 hours fifteen years ago. Therefore, we can truly say that for the American consumer, "Food Is a Bargain" and her greatest value.

To this economic achievement, farmers have contributed greatly by producing crops of better quality, in greater variety and abundance. Manufacturers have contributed by their mass production and mass marketing techniques; by creating new products and improving existing ones; by developing new and more protective packaging; and by effecting cost savings and distribution economies. Distributors have also contributed many cost saving economies and improved services. They have done this by modernizing and streamlining their operations, and by establishing attractive, conveniently located supermarkets throughout the United States.

GMA Consumer Education Program

GMA and its members have taken many steps to enable consumers to make full and intelligent use of these developments in their free choice of foods. GMA, for example, recently distributed more than one million copies of a consumer booklet entitled, "The Label Tells The Story," and more than 600,000 copies of the booklet, "Your Grocery Dollar." Both booklets have timely, helpful information for consumers.

Earlier I referred to The Food Law Institute and the Nutrition Foundation. While these organizations were created by GMA and are largely financed by food manufacturers, who are also members of GMA, both organizations function totally independently. As you know The Food Law Institute is headed by the able Mr. Franklin Depew. The Nutrition Foundation is headed by Dr. Paul Pearson.

It should be said again that the food industry supported the 1906 Food and Drug Act, and also the Federal Food, Drug, and Cosmetic Act of 1938—probably the strongest food law of any in the world today. GMA has consistently supported the enactment and enforcement of specific legislation designed to prohibit adulteration and misbranding of food products.

What I have said emphasizes the importance that industry places on consumer education, and such consumer education is directly served by the participation of industry in this fine series of annual conferences which have been held for the past eight years.

What the public wants is assurance that their foods and drugs are safe and properly labeled, and it wants the government and industry to work together to determine what the consumer needs so she can buy and use products intelligently. An example of such working together is the recent cooperation between the National Conference on Weights and Measures and the food industry concerning the regulation of quantity declaration, prominence and placement, minimum type size, etc. Our industry, along with others, created an Industry Committee on Quantity Declaration which filed a report with the National Conference Committee on Laws and Regulations. The National Conference on Weights and Measures then adopted a model regulation on package labeling which industry now supports. This regulation basically protects the public by requiring a prominent quantity declaration, yet it does not discourage research, innovation and improvements, nor does it limit the consumer's freedom of choice.

Survey Results Favorable to Food Industry

In order to find out more about consumer attitudes, GMA has just completed a nation-wide survey conducted by Opinion Research Corporation to learn what consumers think about the food manufacturing industry. The results show that: (1) consumers have a favorable view of the food industry and what it does for them; (2) there is a pattern of satisfaction and enthusiasm for the quality of food and other grocery products offered to consumers today; and (3) in general, consumers are well pleased with the packaging of food and other groceries. Moreover, after the pollster explained proposals for changes in packaging practices, and about industry viewpoints in respect to them, most consumers expressed satisfaction with present industry practices. The study further revealed that the few con-

sumers who favored changes, considered it the manufacturer's responsibility, rather than a matter for government action.

The most advanced sampling methods were used by the O. P. R. to ensure the greatest possible validity and reliability of the findings, and to ensure their projectability to the total American population of household heads, both male and female.

We are, of course, greatly interested in consumer attitudes and hence, are in accord with a recent report of the Federal State Regulations Committee of the Association of Food and Drug Officials of the United States, which said in part:

> Expression of consumer views and complaints is being invited and is gaining audience at federal, state and local levels. This consumer interest should be encouraged to channel into constructive rather than destructive criticism, and should be channeled through regulatory agencies rather than being a political tool. The food and drug faddists and the petty complainants should be discouraged from monopolizing facilities intended for consumer protection activities.

[The End]

CHANGES IN REGULATIONS CONTROL INADVERTENT PENICILLIN CONTAMINATION

Changes in drug manufacturing regulations to control inadvertent contamination of other drugs by penicillin were announced on January 28, 1965, by Commissioner George P. Larrick, FDA. Under the amendments, injectable drugs contaminated with 0.05 unit or more of penicillin for each maximum single dose, and oral drugs contaminated with 0.5 unit or more of penicillin for each maximum single dose may not be marketed. Products on the market or being held in reserve should be recalled if contaminated with penicillin in excess of the amounts stated above.

The changes followed recommendations by an Advisory Committee on Penicillin Contamination which was called by FDA's Medical Director, Joseph F. Sadusk, Jr., M. D.

In most cases contamination appears to occur because air currents in the pharmaceutical plants carry penicillin dust to areas where other drugs are made. The Advisory Committee stated that inadvertent exposure is a hazard to a significant segment of the population which is hypersensitive to penicillin. In addition to setting tolerance levels, the Advisory Committee also recommended that the FDA, with the cooperation of manufacturers, should try to develop methods to eliminate penicillin contamination of other drugs. This would reduce the hazard of serious inadvertent penicillin reactions in hypersensitive persons.

The order was published in the *Federal Register* on January 29, 1965, 30 F. R. 932. Food Drug Cosmetic Law Reports ¶ 72,103, 72,106, 72,108, 72,111.

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