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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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1966 FDA-FDLI Conference.—Some of the papers presented at the Tenth Annual Joint Conference of the Food and Drug Administration and the Food and Drug Law Institute are featured in this issue of the JOURNAL. Additional papers will appear in later issues. The Conference was held in Washington, D. C. on November 28, 1966. The theme was "Assuring Integrity of Food and Drugs."

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Food·Drug·Cosmetic Law
Journal

Advertising of Health Literature to the General Public

By IRVING LADIMER, S. J. D.

The Following Article Was Delivered at the Third National Congress on Medical Quackery on October 7, 1966 at Chicago, Illinois. Dr. Ladimer Is Vice President of the Food, Drug and Cosmetic Division of National Better Business Bureau, Inc.

IN THE WELTER OF ADVERTISING which crosses my desk daily at the National Better Business Bureau (NBBB), a growing and perplexing proportion seeks to sell fact and fancy sandwiched between the hard or soft covers of health and science books written for the general public. Literacy, hunger for new ways to win and keep health and the promises of today's technology evidently exert as much pull on the purse strings as the more obvious products—pills, potions, lotions, devices and regimens of diet and exercise. The simple consequence is that millions of Americans are beset by books and the publisher's presentations of their value and excellence. Add the newspaper and magazine columns, and you can understand why consumers are left bewildered as to what to believe and do.

Our Food, Drug and Cosmetic Division is regularly requested to comment on such advertisements proclaiming the success to be found through self-hypnosis; the secrets of health embedded in "carbo-cal" and diets presumably derived from the military; vitamin and drugless cures for arthritis, cancer and heart disease; the miracles inherent in metaphysics; and countless methods of avoiding the distress of headache, alcoholism, excessive smoking and eating. Baldness cures, bust development and slimming programs also

abound. Of course, these days, emphasis is placed on living longer, happier, wholesomer lives, so the spate of medical books carefully cultivates these fields. I have often thought that if I could simply curl up with these good books, listen to the soothing 33-⅓ rpm records, practice passes on a hypnometer and step out occasionally to attend the uplifting films and lectures on the strength of positive thinking and negative ions, I would have none of the worries that bedevil ordinary mortals. I could just read and dream myself to beauty and the best of everything.

Power of Books

We know that many books and articles for the layman can be truly helpful. Our public is far better informed today, largely due to honest and skilled scientific writers, educators and the professional and voluntary medical and health associations as well as government agencies. These prepare many excellent, constructive guidance pamphlets and, modestly, I include some of our own NBBB reports and booklets. For the most part, these publications warn against poor health habits, encourage good health and nutrition practices, suggest proper exercise and other regimens and carefully mark the boundaries between home medication and competent professional service.

There are, however, many publications which are clearly questionable and often downright detrimental. Dr. Erwin Di Cyan, consulting chemist and author, stated that claims on behalf of drugs which are too bold or ludicrous for labels and advertising may exist in books. Because of respect for the printed word, they are often uncritically accepted. Dr. Fredrick Stare, Director of Nutrition at the Harvard School of Public Health, in testimony before the Senate Committee on Health Frauds Affecting the Elderly, named a series of organizations and writers whose publications, in his view, are filled with misstatements, falsehoods and wrong implications.

Dr. Stare's Department issues a list of recommended and not-recommended books in the nutrition field. A similar guide for lay readers is published by Cornell University's College of Home Economics. Local services of this type are available from reputable nutrition and diet organizations. Recently, recommendations for librarians have been developed by the Library Association and the American Association for the Advancement of Science. The American Medical Association (AMA), The American Cancer Society and its chapters, the Arthritis Foundation and the American Heart As-

sociation, among others, provide such assistance. All these are premised on the power of books, for good and for evil, in the trust that recommendations from responsible sources will be followed.

These programs have provoked a backlash, as might be expected. An article in the February 1966 issue of the Bulletin of the National Health Federation spells out the "victory" won in permitting the sale of a book "Back to Eden," described as a human interest story of health and restoration to be found in herbs, roots and barks and the home remedies found successful by the author, the late Jethro Kloss. Charles Orlando Pratt, National Health Federation Counsel who tells this tale, notes that "only the advertising of the book that included expressed or implied therapeutic claims for the book has now been banned" under terms of a Postal Order, not the book itself. This is detailed as a newly-won victory but the fact is, as I will discuss, that no Federal agency bans books, as such, but only certain representations. A trailer to Pratt's article reports that "Books on natural health often end up on the FDA 'black list.' The public is warned not to read them, yet those who do read them and apply the knowledge report an improvement in health." The article concludes with the question: Are the Food and Drug Administration (FDA) and the AMA afraid of the influence of these books on the American people?

Books and Advertising

It should be made crystal clear at this point that neither book censorship nor book banning and certainly not pre-publication control is within our scope or interest. The NBBB is not and cannot assume the role of censor and, in any event, holds the conviction that there must be no denial of free speech or press. To my knowledge, every government agency, medical and professional society and health group, even though deeply concerned with the content and the message given to the public, declares against any denial of free speech, no matter how apparently objectionable or unorthodox the views expressed. Indeed, books are the established, protected and privileged means for expressing new, different and unorthodox views and this particular liberty, in my view, should not be curtailed or limited.

This conviction, however, is matched by the equally critical conviction that the advertising or any other representation for the commercial sale of writing to the general public may have the capacity to mislead and the legal cover of our Constitution's First Amendment does not apply. Nor on an ethical basis do we necessarily have to

submit to barring a book because we consider whether a promoter properly or improperly seeks its sale.

On this point, it is instructive to recall the decision of the majority in the Supreme Court's affirmation of the conviction of Ralph Ginzburg, publisher of *Eros* and other publications. Although these publications dealt in alleged obscenity, a concept which the Court had liberalized over the years, that element was found by virtue of the manner in which the material was presented in advertising, promotion or display. Standing alone, the material might not have been judged obscene, but the circumstances of production, sale and publicity—the setting in which the publications were presented—proved to be determining factors. Thus, the advertising and the promotion, in the Court's words, "support the determination that the material is obscene even though in other contexts the material would escape such condemnation."

Fortunately, our Bureaus do not have to judge and do not become involved in matters of pornography or obscenity, but restrict themselves in evaluating advertising essentially to matters of truth. The impact of the Ginzburg case, however, is to remind us of the significance of advertising in portraying any item for sale, whether a book, record, lecture or any other product claiming to have a therapeutic or preventive health benefit.

Federal Agency Positions

Three federal agencies which are concerned with health matters as presented to the general public have established some type of jurisdiction under their statutes over the advertising of books or the use of books as advertising.

Federal Trade Commission

The Federal Trade Commission (FTC) has often asserted its authority to proceed against the false and misleading advertising of literature, including so-called health books. From the cases it has accepted, it is clear that the Commission claims jurisdiction not only where the contents of the books are misrepresented in advertising but also where the advertising holds out to the prospective buyer by false and misleading representations certain therapeutic benefits attainable by following the recommendations. The Commission therefore not only can issue an order to cease and desist where, for instance, a book is advertised as original or in special edition or part of a sale when it is not, but, more important, when it recites facts

reflecting the book's message or substance which cannot be supported by scientific belief.

For the most part, the Commission has prevailed in its views through ordering cessation of the offending advertising, but it has also enjoyed some support when respondents have appealed to the federal courts. In a typical case which ended with the Commission's Order, not appealed to the courts, a Complaint was entered against both publisher and advertising agency alleging that advertisements in newspapers and magazines for "Mirror, Mirror on the Wall," a health book by Gayelord Hauser, provided relief and short cuts for weight reduction, protection from heart trouble, beauty formulas and increase in sexual potency. Although the First Amendment protection was claimed, the Commission stated succinctly in its Conclusion, citing numerous other cases: "No question is properly raised . . . since there is no attempt to enjoin the publication of the book itself, but merely to prevent the use of unfair and misleading methods of advertising to induce its sale."

It is often argued that many people do not regard a book seriously or that those who are sophisticated or experienced will not be misled by the representations for a particular book. As to these points, the Commission concluded that while it is improbable that a well-informed person would believe the advertising for the Hauser book, such representations are capable of, and would have a tendency to, mislead many persons who are exposed to the newspaper supplements and other media in which the advertising appeared. It has been made abundantly clear that the test with respect to false advertising is unlike that abiding faith which the law has in the "reasonable man." It has very little faith indeed in the intellectual acuity of the "ordinary purchaser" who is the object of the advertising campaign.

The Commission also found that the advertisement was meant to be taken seriously and inferred that the public interest "requires protection of the credulous and hopeful beauty seekers even though no such protection would be needed for their scholarly sisters."

Incidentally, in this case, despite objection that the Commission considered statements on the dust jacket claimed to be part of the book, it was held, from inspection of the jackets and their eye-arresting effects, that they were designed as advertising to attract customers. This observation, which we have all doubtless enjoyed, now has some legal significance as well.

The Commission, however, has not prevailed where the book or pamphlet paraphrased an author's view or opinion and the advertisement clearly set this forth. Thus, its Order against Scientific Manu-

facturing Company to halt representations in connection with sales of certain pamphlets was set aside by the Federal Court on the theory that the pamphlets which falsely disparaged aluminum cooking ware as poisonous and dangerous dealt only in opinions. The firm did not itself sell any type of cooking utensils. However, the Court noted that the same opinions if scientifically unsupported might become material if the Commission might establish they were used in the trade to mislead the public or harm a competitor.

Another case, undertaken some 25 years ago, and requiring ten years between Complaint and Order, involved the right of the Commission to order cessation of representations for books and pamphlets propounding the virtues of "Glyoxylide," "B-Q" and other preparations of the Koch Laboratories and the Koch individuals. These purported to cure a veritable army of diseases, particularly cancer infection, on some theory of oxidation mechanism, which when activated, promotes natural immunity and resistance to disease. On petition to review the Commission's Order, the Circuit Court of Appeals held that despite the fact that about 30 medical witnesses testified for each side, and that the Commission's witnesses did not have clinical experience with the product, the record as a whole supported the Commission's findings. These were to the effect that the representations were false in material respects, that the products had no therapeutic value and that advertisements were sent not only to medical professionals, as claimed, but to others.

On this last point, it is of interest that the FTC Act states in part that:

"No advertisement of a drug shall be deemed to be false if it is disseminated only to members of the medical profession, contains no false representation of a material fact, and includes, or is accompanied in each instance by a truthful disclosure of, the formula showing quantitatively each ingredient of such drug."

Although this section is largely superseded by the 1962 Amendments to the Food and Drug Law which also gives the FDA jurisdiction of advertising to physicians, the advertising is not outside the Commission's scope simply because it goes solely to doctors; it must also be free of material misrepresentation and include the full formula. The Glyoxylide advertisements did not. The Court, however, did rule that Dr. Koch's book on immunity and a report of one of his lectures were not advertisements since they were primarily opinions.

The case against the Koch methods stands for one further example of the reach of the Commission, namely, its right to prohibit future practices in the public interest. Even though the Koch Lab-

oratories had been dissolved before conclusion of the case, possible resumption was proscribed.

The Commission's standing in these cases is yet to be fully tested. Now on appeal to the full Commission is the initial decision of a Hearing Examiner recommending a Cease and Desist Order against further representing in advertising of recommendations found in several books by the Rodale Press. Involved are several self-help and self-health books, principally "The Health Finder" which is a compendium of methods to avoid or prevent such illness as the common cold, ulcers, constipation, fatigue, cancer, heart disease and other ailments. The other matter goes to the heart, suggesting "How to Eat for a Healthy Heart" and telling how "This Pace is *Not* Killing Us." It is conceded by the Examiner that not all the material in the books or the advertisements is false, misleading or deceptive but the attack here, he states, is against the advertising of the publication through false therapeutic claims.

"Respondents are free to advance any theory they wish in their publication . . . However, if they wish to advance the sale of their publication, as a commercial product, and to induce the public to purchase it, then they have no right to falsely advertise the therapeutic benefits which purchasers of their product will receive, merely because that product is a book." The Examiner noted that it is not the opinion about the book which is under attack by the Commission's Complaint, but affirmative representations in commercial advertising.

At issue, however, is the whole basis of the Commission's review of book advertising when it relies on content. According to one of the Commissioners, Philip Elman, who dissented when the majority rejected an interlocutory appeal request, all that is challenged here are the book and its ideas. These ideas may be silly or senseless, he says, but Rodale has a constitutional right to disseminate them. He asks whether FTC could enjoin advertising for a book proposing abolition of our Senate. "Congress did not create this Commission to act as a censor of unorthodox ideas and theories in books, whether they deal with politics or health. We should not forget that, in both fields, today's heresy may become tomorrow's dogma." He believes the Complaint is an unwarranted intrusion into an area from which it is excluded by the Constitution and statute. So significant is this case that the Civil Liberties Union, in a rare appearance before this body, entered an *amicus curiae* brief for Rodale espousing the Elman point of view. And among the supporters of Rodale is a respected scientist-

physician whose testimony for FTC in other health cases has been decisive.

Food and Drug Administration

Although the Food and Drug Law does not include books as a drug, cosmetic or device, books have on occasion been construed both by the FDA and by the Courts as labeling. Without doubt, the best known case is that relating to the book by Dr. Taller "Calories Don't Count" which referred to particular safflower capsules for weight reduction. When sold in company with the products, it was subject to seizures as false labeling. Based on earlier decisions, it was held that the book need not be in direct physical juxtaposition so long as there is a clear indication of relationship between the literature and product by the method of selling. The FDA regularly includes pamphlets, bulletins and placards, for example, as part of product seizures under this theory. Also, FDA has held oral representations in such context as labeling, thereby halting house-to-house spielers, lecturers and other pitchmen.

But the FDA suffered a setback in New York where the Federal Circuit Court upheld an appeal against the agency's seizure of "Arthritis and Folk Medicine" and "Folk Medicine" by Dr. D. C. Jarvis. The books recommended Sterling vinegar and honey as a health food and, holding that it was part of the labeling, FDA seized a supply in the warehouse of Balanced Foods, since both the books and the other articles were on display in the same shop. Although the Court recalled that in a case involving Lelord Kordel's pamphlets which were mailed in separate packages, the labeling concept applied, that was considered part of an "integrated transaction" serving the same function as the customary label on the package. Here the relationship was not established. "There was no evidence of any joint promotion of either book with Vinegar and Honey." It might be considered that sale of the books would tend to promote sale of the folk compound, but the Court concluded "there can be no inference that it sold the books for that purpose." The store ordered and sold the books two years before and later stocked the products which sold in far less quantity. There was no basis for finding that Balanced Foods did more than carry two related products, along with other books and products, without any joint display. No appeal has been announced by the government.

Post Office Department

Since 1872, when the mail fraud statutes were enacted, the Post Office has been able to proceed against certain improper use of the

mails. False advertisements for books, pamphlets and writings are included. The two primary laws both prohibit use of the mails in any scheme to obtain money or property by means of false or fraudulent representations, pretenses or promises. The first provides felony penalties of jail and fine; the second, which is administrative, permits the Department to refuse to deliver mail to the promoter, thus shutting off mail order operations. Most often in medical cases, the second course is used, involving presentation of evidence at a Departmental hearing, rather than arrest, indictment and possible Federal trial proceedings. Commonly, the promotion is halted through voluntary signing of Affidavits of Discontinuance.

One of the more colorful was the advertising for "Slumberslim" which was promoted as capable of effecting weight loss while sleeping, with the catchy phrase, surrounding a dreaming damsel, stating "Floats Fat Right Out of Your Body." The text was so worded that many consumers wondered precisely what their three dollars would buy. Return mail brought a soft-cover pamphlet, presumably summarizing a book by a doctor, stressing the wondrous effects of will power and certain diet recommendations. Another Post Office case resulted in damming the sales of "Diaitis," a theory that poor nutrition caused cancer, as propounded by an author who had plenty of time to develop his ideas since he performed his research in the library of the prison in which he had been confined.

Another compelling case involved the advertising for the writings of one Morris Katzen who called himself St. George. In his books he claimed that too much elimination by the body gave rise to various distresses and argued that war prisoners who had no opportunity to relieve themselves nevertheless remained healthy. Like others who combine health and spiritualism, he also cited the Bible as support for his contention. The Post Office has in many cases had to demonstrate not only that freedom of the press has not been denied but that freedom of religion has been respected, but it has declined to permit occasional or vague reference to the Deity to discount deception. Interestingly, when the Koch Laboratories saw FDA inspectors closing in on "Glyoxylide," which I noted in the FTC case, the firm dissolved and reorganized as a religious society, "The Christian Medical Research League."

The Post Office won out in a case involving representations for pamphlets issued by a so-called Cardiac Society which advocated a vitamin E product for heart disease and, as late as 1966, won another action against promotion for a book by a Dr. Krimm. The "Doctor"

stood for Ps. D. His book, "Health, Success and Happiness for You," published by the Health Press of California was promoted by advertisements captioned "Why Be Sick," promising that the reader would be able to overcome constipation, colds, backache, arthritis and other ills. A similar question mark "Why Grow Old Before Your Time?" promising a Hy-Dro-Aid medical course of water and honey to rid the body of waste, went down the drain via the Affidavit.

Both criminal and administrative actions by the Post Office require the presence of an intent to defraud on the part of the promoter. It is not enough that the claims be false; it must be shown that he knew or should reasonably have known the falsity involved and nevertheless continued. According to the postal authorities, this burden understandably weakens their ability to halt medical frauds through mail stoppage, particularly where there is a dispute among experts and no established universality of scientific belief. A bill to relieve the Department of this burden in civil cases (H. R. 16706) passed the House in the last session of Congress.

On this important point of intent, I should like to report briefly that the Circuit Court of Appeals in New York unanimously upheld the trial judgment in the notorious Regimen case which was based mainly on alleged violations of the mail and wire fraud statutes. The Court grounded its opinion strongly on two features demonstrating the scientific falsity of the claims used in magazine, press and television advertising that the Regimen Tablets could effect weight loss easily and without dieting: The views and studies of medical experts; and the notice provided by Bulletins and statements of the NBBB and its President raising questions about the effectiveness of the product. Continuation of the advertising representations in the face of such advice plus the imputed knowledge of factual falsity based on the advertising agency's instructions to the so-called live endorsers was sufficient to uphold the criminal conviction of the manufacturer and his firm.

Views of Other Agencies

The American Cancer Society which has long had an active and aggressive program to combat misrepresentation, carried on through its Committee on Unproved Remedies, has given forthright attention to the difficulties raised by unfettered publication. As reported recently in its journal *Ca* (March-April 1966),

> An important factor in the promotion of unproven remedies is our free press, which makes it possible for books, newspapers and mass media to present

seemingly favorable information on unproven cancer remedies. Books on medical science, especially if they are on so-called controversial medical problems, are quite appealing to the reading public.

In the five-year period ending 1965, at least eight books describing favorable results obtained with specific unproved methods were published and three general books on cancer appeared, suggesting unestablished ways to prevent or cure. According to Dr. Ronald Grant and Irene Bartlett, of the Cancer Society, who have studied these trends, this type of book is often so skillfully written that the average reader concludes he can make a valid judgment as to treatment. Pro and con facts are distributed throughout the book to create impartiality but the weight of argument favors the touted method. A principal factor in the promotion of Krebiozen, they believe, was the wide distribution of three favorable books.

Books are but a small part of the verbal barrage. Magazines and periodicals, either specializing in health or awarding space to such articles are among the proponents of nonmedical approaches to health. Many people get their first ideas about treatment and mistreatment from such sources. This complaint against the eager press and the air media has been echoed by other organizations which have had the sad duty of informing arthritis patients, for instance, that remedies imported from Canada or drugs developed from woodpulp and sawdust are worthless. A speaker representing the FDA, James L. Trawick, told the recent AMA Conference on Health Education that a national magazine article predictably led to a black market in dimethylsulfoxide (DMSO), since patients could not get this new wonder remedy legally from their doctors. Many got the chemical for self-treatment and were injured, before the FDA put a stop to unauthorized research on the product. Until the nature of reactions in test animals can be determined, DMSO will not be available for standard human use.

Senator Harrison Williams of New Jersey, Chairman of the subcommittee on Frauds Affecting the Elderly, has expressed concern about the uncritical press announcements of research breakthroughs and wonder drugs which seduce thousands of sufferers into unwarranted reliance on untested and even abandoned drugs and methods.

Many others have made similar observations. While reputable articles are valuable, the irresponsible journalist, on the other hand, seeking a byline, becomes the doctor rather than the licensed professional. Indeed, it might well be said that he is practicing license without a medicine.

Doctors Share the Responsibility

Despite these outcries, efforts and legal actions, these problems continue. We know that both unscrupulous promoters, writers and publishers among them, and well-meaning but misguided advocates, writers and publishers particularly, contribute to building this Tower of Babel. But, the medical and health professions cannot sit by and accuse. They could not, in good conscience, cast a stone at the sinners, for they share the blame.

Blame is of several kinds. First, most obviously, a fringe minority of licensed physicians are among the authors who, strangely enough, partake in persuading people away from standard medicine by their untested diet proposals, use of so-called natural foods, self-help for conditions requiring careful treatment and promises of long life, vigor, sexual strength and beauty through methods without meaning in any approved scientific circle. Although it must be said that only a few doctors create these problems, the publicity they generate casts question on the entire profession. The States which license them and the professional groups which include them generally take no action against them. Disciplinary proceedings are possible. And the public or professional press, to announce such housecleaning, is also available. At the Connecticut Congress on Quackery, several years ago, Dr. Jean Mayer of Harvard University, pointed his finger at this condition and voiced the hope that proper action would be taken. It is preferable and proper that internal regulation rather than external accusation prove to be the guiding force.

Second, the professional organizations have been lax in condemning publicly, in the same media which carry the literature they lament, the patent falsity and the actual dangers which such books and lectures may produce. There is need and room for critical comment and ample opportunity for those who read and writhe to lead and write.

Third, many authors are misrepresented by the publishers, advertising agencies and promoters who try to sell their writings in completely unprofessional ways. Two instances of correction achieved by the National Bureau's Food, Drug and Cosmetic Division may be instructive. In one case, a reputable consulting nutritionist, who did not follow up on use of his publications by a vitamin company, withdrew permission to quote him when advised by us of evident misquotation of his views. Another doctor, whose book was presumably summarized and issued as a reducing program through sleep and

relaxation forbade further flamboyant and captious use of his writings. Our files also show that a psychologist who wrote a popular but serious work on management practices was able, with our forthright support, to make the publisher tone down his mail-order advertising so that it fairly represented his position. Authors should be made aware that they have a moral obligation as well as the duty to reserve a legal right to insist on approving the manner in which their publications are presented to avoid actual or subtle deception.

What We Can Do

From the brief review of the difficulties facing government agencies and our general dislike of laying the law to literature, it must be clear that we cannot and should not rely on government to solve these problems. There are both positive and punitive approaches within our power.

1. We can and should share information, since many of these books and papers cover many fields and the journalist authors who write under their own or other names reach across all medical areas and disciplines. Such sharing would alert simply and swiftly the voluntary agencies in cancer, heart, arthritis, diabetes and other specialties of the writing which may influence the special groups within their concern. Appropriate reviews and publicity can then be disseminated to all who may be affected.

2. We can speak out; indeed, we must speak out. This takes time, interest, courage and the willingness to be the subject of controversy, if necessary. Dr. Fred Stare, for example, became the defendant in a libel suit, in a sense for all of us, when he criticized the unsupported views of the Boston Nutrition Society. But the Court vindicated him and established his right to comment. The significant outcome rests in the statement by the Court which, paraphrased, holds that truth is the defense of libel as long as it is not said with intent to harm but to inform. The professional person in his field has a privilege to differ with others and to speak out strongly as long as his comments are made without malice. In some jurisdictions, libel and privilege statutes are strict, so bravery must be accompanied by knowledge of the law and community standards. I would advocate some instruction here, so that good and proper intent is not misspent.

3. As respected professionals, we should make ourselves freely and courteously available to publishers, advertisers and media. At

previous Quackery Congresses, responsible editors and copy executives have stated that they would welcome the advance advice of medical and technical experts. From a purely business view, they are interested in printing properly substantiated reports, books and commentary. Medical science and practice, as we know, are least susceptible to simple yes-and-no answers and indeed encourage novel and experimental theory, but there is a well-established scientific underpinning and a professional community that can be tapped.

As far back as 1933 and several times thereafter, the AMA's House of Delegates condemned the broadcasting of misleading representations for foods, medical remedies and health preparations. Later, it recommended establishment of liaison with the industry and support of the NBBB and others in eliminating questionable advertising for remedies sold to the public. Educating the public, through the papers they read, should be high on the priority list of professional responsibility.

4. If it has not been obvious, I recommend an aggressive public information campaign to combat quackery. Let us, in the spirit of free enterprise, compete vigorously by stimulating and producing literature for the patient, the consumer and the student which is helpful, truthful and informative. For example, more books, more potent presentations and more avenues should be developed by the AMA in company with similar agencies in a long-term program to reach the public. There are opportunities in doctors' and clinic waiting rooms, school rooms, and in shopping areas, such as drug counters and pharmacies. Television, radio, the press and films are open to present our scientific data in attractive ways. This tactic would meet the opposition on its own ground but with better and superior force. Meet their sex appeal with Rx appeal.

5. Finally, I would recommend to the medical and health profession and to those who write for it and about it, a careful study of the total environment of health writing affecting the public. The Federal interagency study, under leadership of the FDA, to understand misrepresentation which influences the public should provide some guidance. That study may tell us how and why we cling to quacks but it will be up to us to inspire responsible ways to break this grasp. We should use all means to discourage detrimental writing at the source and dam its flow when it emerges. **[The End]**

Welcoming Remarks

By FRED J. DELMORE

The Following Remarks Were Presented at the Food and Drug Law Institute—Food and Drug Administration's Tenth Annual Educational Conference at Washington, D. C., on November 28, 1966. Mr. Delmore Is the Director of the Bureau of Education and Voluntary Compliance.

SHALL OUR PART, though small in the history of these significant times, be that of executives and professionals of a great nation's largest industries and her government who merely met and talked?

To this, I say "No!" If for no other reason, there has been a consistent note of better understanding through these conferences—improvement in the relationship between the regulated industries and FDA.

But today we can go beyond mere improvement. We can deal in specifics, and we have been given a theme that can be dealt with in concrete examples.

For if we do some semantic juggling, we can transpose our theme into "giving confidence in the purity of our food and drugs." It is as simple as that—public confidence.

We must concern ourselves with public confidence because we are responsible for products accounting for 25% of all the money spent by Mr. and Mrs. John Q. Public each year. One-fourth of their income, or $103,368,000,000, is spent by American families for food, drugs, and other essentials produced by the industries represented by you and regulated by the Food and Drug Administration.

We face no easy task—and the task will not lighten in the years ahead if we remember our population is growing by leaps and bounds. The time then is NOW—for there is further erosion for every day that the upward trends of drug recalls, Salmonella, excessive chemical residues, and abuses in prescription drug advertising continue.

We have this responsibility then, to one another, and to the public—citizens have a right to safety, and that is our concern today and every day.

We can continue the good fight today, and in this conference enlarge our two-way street of communication. As Frank Depew has said, we may talk—but more importantly, we must listen to each other.

Traditionally, conferences were one-way communications and the audience passive, at hostile attention to the platform.

But times have changed, and audiences participate. That is what we have prepared today, and I assure you that your benefit will be in proportion to your participation.

Since our last meeting, Salmonella in food and health hazards arising from drug residues in the food we eat have become of paramount importance. I need not remind you that these topics have received headline attention very recently.

How do you put a price tag on public confidence? We can measure in dollars and cents the cost of a drug recall, or the recall of a microbiologically contaminated food, but confidence is a priceless thing.

The challenges then are here and now. The battle plan must be drawn. **[The End]**

DRUG MAKER LIABLE FOR FAILURE TO WARN OF SIDE EFFECTS

An arthritis victim who developed chloroquine retinopathy, a degenerative eye disorder, as the result of taking a prescription drug was properly awarded judgment for $80,000 for retinal damage against the manufacturer of the drug, the U. S. Court of Appeals in St. Louis has held.

According to the court, the evidence was sufficient to sustain the finding that the manufacturer, although it knew or should have known through medical literature that its product was causing retinal damage to some users, negligently failed to give timely warning to physicians that the drug might cause serious eye damage among a comparatively small number of persons.

Sterling Drug, Inc. v. Cornish (CA-8, Missouri),
CCH PRODUCTS LIABILITY REPORTS ¶ 5664

Salmonella—
History and Occurrence in Foods

By KENNETH R. LENNINGTON

Mr. Lennington is Salmonella Project Officer, Food and Drug Administration

THE SALMONELLAE GENUS OF BACTERIA probably poses as great a problem as any facing the public health today. Salmonella is a large and widespread group of organisms found almost everywhere that man or beast exists. There are, at the present time, over 1,200 known strains or serotypes, all of which are capable of causing infection in man and animals. Salmonellosis, or Salmonella infection, has been reported in recent years in increasing incidence throughout the world.

Early Recognition and Isolation of Salmonella

The name, Salmonella, was given this group in recognition of Dr. D. E. Salmon, the first Chief of the Bureau of Animal Industry, United States Department of Agriculture (USDA), who in 1885 isolated the first of this group of bacteria. The particular strain isolated by Dr. Salmon, *cholerae-suis,* was thought to be the cause of hog cholera at the time, but it was later demonstrated to be a secondary invader.

The role of Salmonella in producing infections in man was not recognized until about the turn of the century, though review of early reports leads one to suspect that salmonellosis was commonplace. In Paris in 1829, a blacksmith's wife prepared a cream cake for her husband, who ate the cake, was stricken with "colic," and died three weeks later. The wife was accused of poisoning her husband, was tried, found guilty and sentenced to life at hard labor. In 1902, at the Feast of St. Peter at Bordeaux, 150 persons became ill about 24 hours

after eating cream cakes. A contemporary investigator determined that preserved duck eggs had been in the cream cakes.

It was also about the turn of the century that certain Salmonella types were associated with animal disease or infection. S. *pullorum* was found to be associated with white diarrhea in poultry; S. *gallinarum* was determined to be the cause of fowl typhoid; S. *abortus-equi* in abortion in horses and, as mentioned earlier, S. *cholerae-suis* was found to be a secondary invader in hog cholera. It is interesting to note that S. *psittacosis* was isolated from an outbreak of psittacosis in Europe in 1893 and was believed to be the causative agent of that infection until 1929-30 when the responsible virus was identified. It was later found that the S. *psittacosis* isolated from the outbreak was identical to S. *typhimurium,* and as in the case of cholera, was a secondary invader.

The pathogenicity of Salmonella also has been utilized to man's advantage, though the degree of success is highly questionable. About 1892, Loeffer used cultures of S. *typhimurium* (mouse typhoid) as a means of destroying field mice. A decade later when the Russian city of Odessa was experiencing a plague epidemic, the city and surrounding areas were baited with crust dipped in broth cultures of S. *enteriditis.* No illnesses were reported in human or domestic animals, but the rat population disappeared. In the ensuing years up to the 1940's, various Salmonella cultures were marketed for rodent control purposes; however, public health officers took a dim view of baiting with a pathogen around home and factory.

The Ubiquity of Salmonella

The medical and veterinary medical literature of recent years has abounded in reports of salmonellosis in man and animals. Epidemiological studies have implicated a wide variety of birds, reptiles, and animals, domestic and wild, as hosts and carriers. Snakes, from the black mamba to the common garden snake, pet turtles, frogs and fence lizards, domestic fowl in general, birds, practically all domestic animals, including household pets, have been found to harbor and pass Salmonella. Insects, especially those associated with man such as flies, roaches, ticks, and fleas are also carriers. In recent weeks, Coccus Cacti, the cochineal insect that has been a source of red color for centuries is suspected of being a carrier or host for Salmonella.

Salmonella has been characterized as ubiquitous. The isolations and sources reported to the Communicable Disease Center (CDC) of

the Public Health Service (PHS) in recent years fully substantiate the propriety of this term. Today the Salmonellae are one of the two most common causes of food "poisoning," though technically it should be termed food-borne infection, in man.

High Incidence of Salmonella in Poultry and Eggs

Probably the most common food raw materials presenting a problem in Salmonella are poultry and eggs which have been implicated in outbreaks of salmonellosis over the past 75 years. The experience of the British with Salmonella contamination in American spray-dried eggs during the Second World War is well known, and was one of the largest factors in bringing into focus the Salmonella problem in eggs, whether dried, fresh broken, or frozen. All of you are aware of the recent regulations and requirements of USDA and Food and Drug Administration (FDA) calling for pasteurization or some type of treatment of liquid, frozen, or dried eggs to assure that they are free of Salmonella. Canada, the United Kingdom, and other countries have imposed similar requirements. In spite of the awareness of the problem and the preventive measures taken, correction has not been achieved. FDA in fiscal year 1966 examined 309 interstate shipments of domestic eggs and egg-containing foods, and found 81 or 26% of the shipments contaminated with Salmonella.

There were 90 cases of human illness due to S. *st. paul* in one of our western states during the first half of this year. Two-thirds of these cases were reported from May 1 to June 30. Epidemiological studies pointed to consumption of custard or cream-filled bakery products as the common factor. Of 81 women who attended a club luncheon, 18 became ill with diarrhea, cramps, nausea, vomiting and fever. Banana cream cake from a commercial bakery was the only food eaten by a significant number of the ill. S. *st. paul* was isolated from the stools, and from a piece of the banana cream cake which had been held in a freezer. A survey of egg packers whose products were marketed in the area revealed four firms whose products were found positive for S. *st. paul.*

In another state, an outbreak of salmonellosis occurred in midsummer affecting about 60 persons. Eight of the victims were hospitalized from two to seven days, suffering diarrhea, vomiting, abdominal cramps and fever. Two became dehydrated, requiring intensive care. Chickens, barbecued in a local market, were suspect. Washings from remaining dressed birds revealed S. *typhimurium.*

Typhimurium was isolated from stool cultures of the victims, and was recovered from remaining barbecued birds. Investigation disclosed that temporary summer help had barbecued 600 birds in one day, most of them having been grossly undercooked.

Salmonella has recently been encountered in enzymes and glandular materials of animal origins such as granulated pepsin and pancreatin.

Other Outbreaks of Salmonella

Outbreaks of salmonellosis implicating dried coconut in 1961 in England and Australia led FDA to the routine sampling of all imported lots. Incidence of contamination and the detention rate were relatively high early in the program, but through improved sanitation and pasteurization procedures, Salmonella-contaminated coconut now is a rarity.

The contamination of dried yeast with Salmonella has been sporadic and recurring over the past decade and has necessitated a number of recalls of dried yeast, yeast tablets, and special dietary preparations containing the contaminated ingredient. It would seem that the conditions under which yeast is cultured and produced are conducive to Salmonella growth once the plant becomes infected or seeded with the organism.

Last February, the CDC reported a series of salmonellosis, largely in small children, caused by S. *new brunswick*. Epidemiological studies by CDC indicated that instantized milk was a common factor and the most suspect food. Intensive sampling and bacteriological testing by FDA, USDA, and PHS led to an awareness that powdered milk, unless pasteurized in processing, and prepared under rigid sanitation control, may contain Salmonella.

This past May, a series of outbreaks of food poisoning occurred on the East Coast affecting nearly 400 people after ingestion of smoked fish. Salmonella *java* was isolated from the patients and from remaining portions of the smoked fish. Investigation at the factory by FDA, CDC, and local health officials disclosed fish in process, tables, and equipment contaminated with S. *java*. Stool cultures of employees revealed several to contain S. *java*. Numerous deficiencies in sanitation existed. Further investigation, however, revealed that the frozen fish as received at the plant were contaminated with S. *java*. Subsequent investigations by CDC and Department of National Health

and Welfare of Canada in the North West Provinces, the origin of the fish, indicated that contamination might be attributed to polluted water in which the fish were caught, and use of polluted water for washing and icing the fish. This incident awakens us to the realization that raw fish, in the round or dressed, may be contaminated through pollution, insanitary handling, storage, or distribution. This is an area that calls for further study and consideration.

Earlier I referred to Salmonella in cochineal. Cochineal, as you may know, consists of the dried female insect, Coccus Cacti Linné, which is cultivated on nopal cactus plants. One acre of plants produces approximately 100 kilos of dried insects. Peru and Madeira Islands are the principal commercial producing countries, though some comes from Mexico and Honduras. The dried insect material is brewed and steeped to extract the red coloring principle, carminic acid. The extracted carminic acid is treated to produce the alum lake, commonly known as carmine red. Recent hospital outbreaks of salmonellosis were traced to use of carmine red in capsule form, which, because of its non-toxic and non-absorbable qualities, is widely used as an indicator dye in intestinal studies. S. *cubana* was isolated from the patients involved in these outbreaks as well as from the carmine red dye. Investigation disclosed that the basic insect material is contaminated with Salmonella and that the carmine red processing operations are not such as to destroy the organism. As a result, most samples of the finished dye have been found heavily contaminated with S. *cubana*. Further investigation has revealed use of carmine red in candy coating. Examination of finished candy made from the carmine-containing coating has showed Salmonella present. Similarly, barbecue seasoning and flavorings containing carmine red as an ingredient have been positive for Salmonella.

The carmine red incident illustrates the widespread dissemination of Salmonella possible under today's complex production and distribution system. It also points up the necessity for careful bacteriological and quality control of materials used in food, drug and cosmetic production.

The battle against Salmonella is, and will continue to be, a formidable one. If progress is to be achieved, the combined efforts of our agricultural producers, industry, public health agencies, and even the housewife, will be necessary. **[The End]**

Salmonella in Food: Control in Manufacture and Distribution

By ROBERT G. RUARK

Mr. Ruark Is With the Corn Products Company.

MY SUBJECT IS POISON. It is not the deliberate, willful act of poisoning that we are discussing, but the accident, the oversight, the neglectful act. It occurs where we fail to control the malevolent side of nature to our maximum ability. It occurs when we fail to use our knowledge. And the result of this failure is tragic in terms of its consequences—all the more so, because it is often unnecessary.

My specific subject is salmonella. Salmonella infects the human body with results similar to those of other forms of contamination, which are widespread throughout the world. What we say about salmonella could very well be said about these other toxic materials, too. They are all bad and from the point of view of those poisoned or infected, all equally so. Some day, science may banish them all from the face of the earth, but in the meantime, we must exercise great care —care enough to decrease the frequency of these accidents.

This is particularly true of salmonellosis. As a problem it is strictly routine. It was discovered a long time ago as discoveries go. We know it is everywhere. We know how it cultures, how it reacts on people. We know the ways to reduce the occurrence of the problem. Yet it remains a very real problem. The reason is deceptively simple: accidents.

Accidents involving salmonella infection can occur anywhere along the food production chain. They can arise spontaneously, it

would seem, because of the ubiquitous nature of salmonella. A farm raw material may be perfectly satisfactory, but it can be contaminated from numerous sources as it progresses toward a finished food product.

So whose problem is this? I think you will agree that it is everyone's problem. Frequently food poisoning problems are laid directly at the manufacturer's door, yet nowhere in the entire chain from the farm to the table is more care exercised to keep things sanitary than in the modern food plant. Nowhere is sanitation as a science and a religion more carefully applied. Food plants have to be clean, because this is the only way to assure proper products. There is a venerable cliché that cleanliness is next to godliness. Without being irreligious I would suggest that if given his choice, the food manufacturer would place cleanliness first.

As far as my company is concerned, and I am sure this applies generally to the food industry, we are not dazzled by our sparkle or shine nor complacent about our procedures. We are vastly concerned. We apply the best procedures that are found today and we are at work along with the government in developing even better ones.

Research efforts involving heat treatment, pasteurization, sterilization, and irradiation, provide partial corrections, but it is far more desirable that properly produced salmonella-free farm products go through the entire production chain and into the home without any contamination whatsoever. To accomplish this, all segments of the food producing community must continue to work together with the government.

It is important that we understand the regulations of the federal government pertaining to salmonella. The major regulations are those promulgated by the Food and Drug Administration (FDA) and United States Department of Agriculture (USDA). They are long and appear complicated, but their essence can be stated very simply —salmonella must not be present in food ingredients or in the final food products.

Full discussion of these regulations would require days on end, and their interpretation, many more days. I am sure this is due to the fact that the final drafts were written by lawyers rather than technical people, and they might be much simpler if we followed Shakespeare's advice as given in Henry VI, namely, "The first thing we do, let's kill all the lawyers!" Seriously, however, we all recog-

nize the necessity of familiarity with the details of these regulations as they affect our respective businesses.

Many of the statements which follow repeat what government officials have said before and what food manufacturers' associations and others have published in comprehensive form. I feel, however, that repetition is merited, considering the seriousness of the salmonella problem. Need I do more to emphasize this than call your attention to the recent problems involving dried milk?

Let's consider what should be done to exercise salmonella control at every stage from the farm to the home—purchasing, storage, plant operation, and sanitation, distribution and utilization.

The Food Manufacturer's Responsibility

Food manufacturers have many opportunities to exercise salmonella control in their ingredients before they even enter the plant. Obviously one of these is at the *purchasing* stage. Specification should be tightened up to provide ingredients that are salmonella-free. The manufacturer should place requirements on his supplier to guarantee this condition and should require the supplier to provide proof that the condition has been met. In addition, checks of raw materials for the presence of salmonella should be carried out—either in the manufacturers' laboratories or in outside commercial laboratories—to assure that the supplier is meeting the specified requirements.

When packaged ingredients capable of harboring salmonella enter the plant and before *storage,* each shipment should be inspected. Damaged containers must be rejected. The acceptable raw materials should be stored under proper sanitary conditions to prevent microbial growth of any type. Prior to the entry of the ingredients into the process, individual batches, or pooled batches, should be tested. At this point, it is important to note that salmonella testing, like many other procedures to insure a sanitary operation, is difficult and lengthy. Qualified technical personnel must set them up and interpret results. The FDA-specified test for salmonella takes four to five days for completion to a presumptive stage, much too long for best operating procedures, which in the food line can show "ups and downs" in production output in response to market demand. More recent approaches to salmonella determination appear to provide answers in 24 hours, so it now remains for industry and FDA to check out such methods and to improve them.

As in all analytical operations, sampling varies from one test material to another. There is still great need for studies of sampling procedures and for statistical research to assure that the selected sampling procedure is broad enough to provide an aliquot representative of the entire batch of product. It goes without saying that the manufacturer should use each opened batch of perishable product promptly or store it under proper conditions if it is to be used at a later date.

In the *plant operation,* sanitary aspects of manufacturing start-up are most important. Equipment must readily lend itself to sanitary clean-up and should be rendered sterile or substantially sterile before operation.

It is becoming more apparent in every food company that the engineer does not dare to select or design food processing equipment without a bacteriologist by his side. The bacteriologist, who might also be the plant sanitarian, will no doubt recommend equipment which can be readily dismantled for sanitary clean-up. But the few extra dollars spent on the recommendations will repay themselves many-fold, in labor saved in regular plant clean-ups and in quality of product manufactured. New equipment should at least meet the 3A standards of the International Association of Milk and Food Sanitarians.

At the end of any given operation when the equipment goes out of service for some time, proper clean-up is mandatory. Evidence of infestation appearing in any plant operation is sufficient cause for an immediate shutdown to permit corrective measures. With salmonella-prone products, raw material containers should be promptly removed from the manufacturing area and either destroyed or thoroughly cleaned and sanitized prior to reuse.

Sanitary practices relating to personnel must be observed. Physical examinations of new personnel, prior to hiring, should include tests assuring that they are not carriers of salmonella. The initial testing is only a preliminary move, and routine repeat testing is necessary to be certain that employees, following episodes of illness, are not carriers. Indeed, some sanitarians would hold that periodic checks should be conducted on all food handlers, since some carriers may show no clinical evidence of the disease.

Plant inspections and visits by outside groups, for public relations and other purposes, tend to increase contamination hazards, and

certainly should not be encouraged, unless the plants are designed with proper barriers to prevent people from getting close to foods in process.

All of the precautions in manufacturing also apply to packaging and every step in the *distribution* chain. Obviously the finished product must be stored properly until delivered. The end products should not be stored alongside susceptible ingredients. Laboratory control methods should guarantee that manufacturing processes take into account those indices reflecting potentials for salmonella destruction, such as temperature of processing, pH, presence of preservatives if allowed, and so forth.

Right at this point I would like to interject that some of the precautions that have preceded and some that follow may seem arduous and costly. If the food manufacturer is going to stay in business, however, he must be willing to pay the price required to assure a quality product. The precautions and the regulations relating to salmonella *are* costly, but we can be certain that better products will flow to the consumer in the future by proper exercise of these precautions. This is certainly economic incentive enough for the manufacturer to comply with regulations and recommendations and to extend them.

Getting back to the distribution chain, proper storage is the most effective method of control. There is little that a handler, distributor or marketer can do of a corrective nature, but proper storage is within his ability. The marketer must not sell damaged goods under any conditions. He should promptly remove such products for return to the food processor. I can say that all of us in the food industry are most appreciative of the critical marketer who is quality conscious.

The Housewife's Responsibility

The last problem area in the salmonella chain involves *utilization* —storage and use of the food in the home. The housewife has available a number of excellent protective measures. For example, liquid products that are to be served warm should, if possible or appropriate, be heated to a boiling temperature. In baking, sufficient time and temperature should be allowed to assure the death of micro-organisms that are present. Susceptible foods should be served promptly and eaten promptly. If portions remain that are to be used at a later time, prompt refrigeration is essential, but it should not be assumed that this is an absolute cure. Lengthy storage is certainly undesirable. Where possible, refrigerated materials should be reheated again

before use. Whenever this is impossible, and there is doubt, the wise housewife destroys the product. In short, "When in doubt, throw it out."

What I say here is not meant to imply that we want to make a bacteriologist out of the housewife. We in the food industry must accept the obligation of providing salmonella-free foods to her. However, we cannot protect her against health hazards within her own home, be they lack of general sanitation, or lack of cleanliness of family members, pets and guests, insanitary water supply and the like. We recognize that our foods might become involved in a food poisoning episode with the source of contamination arising in the home and not present in the food to begin with. Hence, we urge the housewife to take all necessary measures to protect herself and her family against health hazards. Manufacturers provide recipes, preparation and storage procedures on their labels to assure proper handling in the home but have no way to be sure that they are read or followed.

Some Effective Measures for Salmonella Destruction

It might be interesting to spend just a few moments on some of the effective measures for salmonella destruction in various industries where problems are present or are thought to be present. The FDA has expressed considerable concern over grains and feeds. Under many conditions, proper heating for proper times will solve this problem. Acidity is an excellent control. In the wet milling of corn for the production of starch and other products, the first step in the process involves steeping in an acidic medium for a period of about 40 hours at elevated temperatures. Corn passing through a steeping operation is completely saturated with the steepwater containing these acids, and complete salmonella destruction occurs in the first few hours of operation even in highly inoculated laboratory samples. Feedstuffs coming from this process are acid in nature and are salmonella-free when produced.

Obviously, starch from the same process constitutes no problem. Starch, as such, is most often used in gelatinized or cooked form, and the actual cooking provides a well pasteurized product or component.

High-moisture products prepared from starch and which are subjected to long-term storage in a non-sterile environment, must be handled with care. For example, a custard or pudding prepared in the afternoon and served at dinner, may be an excellent food. If left un-

refrigerated overnight, a homemade poison potion may result, and it might still taste good!

Certain types of foods are rendered essentially sterile in their manufacture. Mayonnaise and acidic salad dressings are examples that may be cited. It is well known that, in these dressings, salmonella are completely destroyed in a short period of time, provided the pH of the product is 4.1 or lower, and the acidity of the product is 1.4% or more in the aqueous medium calculated as acetic acid. This is an excellent example of a protective food.

We read and hear of episodes of food poisoning in food salads such as potato, meat, poultry and fish. Every one of these foods per se can support the growth of salmonella. Nevertheless, when salads of these foods are involved in an episode, these foods and the dressings for them are collectively blamed despite the safety of the dressings. Fortunately, both government and industry are working together to protect the housewife.

The egg pasteurization regulations of the Department of Agriculture, for example, were published on April 30, 1965. The regulations of the FDA were published in final form in March 1966. During this time, and particularly during 1966, FDA has been highly active in a salmonella correction program. This program has been highly publicized and the entire food manufacturing industry has responded with corrective actions. In recent weeks, FDA announced a series of salmonella control workshops to obtain further cooperation from the industries involved. Obviously, this is an excellent move paralleling FDA's other symposia on various subjects. The FDA deserves industry commendation for these educational actions. As was previously mentioned, education is most pertinent in connection with this entire program.

The actions of the Department of Agriculture and FDA, moreover, have been given wide consideration internationally. I have noticed over the past six months a continual desire on the part of food manufacturers in foreign countries to obtain better information on control, sampling, and analytical methods. With this education and with the corrective measures that are being applied throughout industry, it is obvious that progress will be made in providing better foods up to the point of home or local preparation.

There should be more education at every level—education from the farmer to the user—and I would like to lay particular stress on the local and consumer level. The efforts of government and industry must be devoted to all forms of education, particularly of those who

handle and prepare foods at the point closest to their consumption. This is the last point where positive control can be applied. This may be the local bakery, the supermarket with a barbecued chicken department, a delicatessen handling perishable products of multiple types or, finally, the home.

Summary

Summing up, I have tried to cover areas in the food manufacturer's plant and in the distribution chain where salmonella control precautions can be taken and where education should be provided—at the levels of purchasing, storage, plant operation, plant sanitation, distribution, and, finally, utilization.

By working together, the government, the food manufacturer and the distributor can certainly educate the housewife and all other handlers of foodstuffs from farm to home. The finest food in the world can be poisoned, but only through neglect or accident.

The greatest cause of accident today is ignorance, so as one final admonition—"When in doubt, throw it out!" **[The End]**

DECISION ON EXEMPTIONS FOR "COMBINATION DRUG" PRODUCTS ANNOUNCED

Combination drug products containing stimulant or depressant drug ingredients, covered by provisions of the Drug Abuse Control Amendments of 1965 but temporarily exempted from the requirements, will continue exempt until April 1, 1967, at which time the provisions will become generally applicable. However, 331 combination products will remain exempt as a result of decisions made during a 13-month review by a panel of physicians from the Food and Drug Administration and the Public Health Service. A list of the 331 exempt products appeared in the Federal Register of January 10, 1967, 32 Federal Register 197.

The review panel considered 494 requests from manufacturers to exempt specific drug formulations under law provisions permitting exemption in cases where control is not necessary for the protection of public health or where no potential for abuse exists.

Dr. James L. Goddard, Commissioner of Food and Drugs, notes that the exemptions in effect after April 1 apply only to requirements covering sales by unauthorized persons, possession restrictions, inventory and record-keeping and prescription restrictions. Wholesalers and jobbers of drugs containing stimulants or depressants must register even when the specific products are exempt.

The FDA considers the review of combination drugs a continuing process. Manufacturers and other interested persons may petition for the exemption of combination products, and determinations as to new products will be made on a product-by-product basis.

Veterinary Medical and Nonmedical Uses of Antibiotics

By HERBERT S. GOLDBERG

Mr. Goldberg Is a Member of the Department of Microbiology, School of Medicine, University of Missouri.

I. Introduction

THE IMPACT OF ANTIBIOTICS on the treatment of infectious disease and indeed on the practice of medicine is well appreciated by most individuals. However, the multiple uses of antibiotics in areas outside of human and veterinary medicine, although quite extensive, are not so well known. It is the purpose of this review to present the current status of the nonmedical use of antibiotics, revealing its past, present, and potential contribution to food and agriculture and its impact on public health.

In order to assess the relationship between antibiotics produced for nonmedical and medical (including veterinary) uses, a brief look at some figures is in order (Table I[1]). As we see, the three major nonmedical uses of antibiotics are in animal feed supplements, crop protection and food preservation. The data indicate that in 1961 more than half of the United States' antibiotic production was for nonmedical use. Over a ten-year span, 1951-1961, nonmedical antibiotic usage increased to the point where almost two million pounds were allocated for food preservation and feed and crop usage. A $45,000,000 annual industry has become a well-established part of the economy. In 1963, 2.5 million pounds of a 4.2 million total was used nonmedically.

The specific antibiotics of major concern in nonmedical usage include tetracyclines, streptomycin, penicillin and bacitracin, along with several others of lesser importance. Consequently, the antibiotics of medical importance are also the antibiotics of nonmedical importance. This fact complicates the role of regulatory agencies as they are presented with the problem of potential public health hazards such as toxicity, hypersensitivity and emergence of microbial

[1] Table I is on page 39.

resistance. The entire aspect of nonmedical usage of antibiotics thus presents itself in a complex form.

II. Antibiotics in Animal Nutrition

A. Current Status

It is generally held today that certain antibiotics are capable of stimulating the growth rate of a variety of livestock and fur-bearing animals. This was the first broad nonmedical use of antibiotics and was given impetus by the investigation of Moore *et al.* in 1946. Excellent reviews on the use of antibiotics in animal nutrition are available, and these reviews emphasize the fact that antibiotics stimulate appetite, increase food efficiency, reduce requirement for vitamins, increase survival, and, most significant of all, increase the growth rate. The evidence is clear that antibiotics are effective only in the early growing period, particularly in situations in which animals are undergoing stress. Animals that are weak or runts, reared in poor environmental conditions or on inadequate diets do much better on antibiotics than do normal animals, reared under good management and fed a complete diet.

The animal species generally accepted as requiring antibiotics for maximum production efficiency include poultry, swine, calves, lambs and fur-bearing animals. Since the effectiveness of antibiotics is limited to the early growing period, the age periods as shown in the following tabulation have been recommended for feeding (*WHO Technical Report,* 1963). (Table II[1]) It is unnecessary to feed antibiotics beyond these ages.

The antibiotics most frequently used for the purpose of animal growth are primarily penicillin, chlortetracycline and oxytetracycline, and also bacitracin, erythromycin, oleandomycin, spiramycin, streptomycin and tylosin. All of these have shown growth-stimulatory activity in the animals mentioned in the above tabulation and are used commercially for this purpose in the United States and abroad.

Even with the above facts well established, there exists current controversy over at least one aspect of antibiotics used in animal feeds. It concerns levels of antibiotic necessary to the ration.

B. Antibiotic Levels

In the early 1950's the antibiotic level used in feeds to bring about growth stimulation varied from 5-20 p.p.m. of the "total ration," which is defined as "the total daily feed intake on a dry-matter

[1] Table II is on page 39.

basis." Since then the tendency has been to increase the level of antibiotics in commercial animal feeds. Levels as high as several hundred p.p.m. and higher are currently used. Table III[1] indicates the maximum permissible levels in representative countries as of 1961. It can be readily seen that the concentration of antibiotics necessary for the growth effect has been universally exceeded. The reasons for this are not too clear and have never been satisfactorily explained on a nutritional basis.

In general, levels of antibiotic in feeds have been divided into "low-level feeding," "prophylactic feeding," and "therapeutic feeding." Unfortunately, these levels are not clearly defined, nor are they well-controlled. "Low-level feeding" is best defined as the minimum level which achieves the growth effect. In most instances 20 p.p.m. should be the maximum necessary for this result. However, the United States accepts low-level feeding as that which occurs at up to 50 p.p.m. Several investigators have judged 50 p.p.m. as being in excess of that needed for the growth effect. It is at this level that the term "prophylactic feeding" should apply. The question arises: is "prophylactic feeding" needed routinely to prevent infection, or should it be used only when needed to stop a suspected disease in a herd or flock? In the United States, the "prophylactic level" is assumed to be 100-400 p.p.m. and is used all too often in a routine feeding program. Often, still higher levels of antibiotics are used to treat disease. This use is properly carried out under veterinary control. However, up to 2000 p.p.m. can be so used, and there is some evidence to indicate that this "therapeutic level" feeding is not always used as intended by statute.

The basic concern over the amount of antibiotic in feed is caused by public health hazards which may occur when the antibiotic develops a tissue level and is then presented to the consumer in meat. Those levels which result in tissue residues and offer a threat to the public health are those which exceed the level necessary for the simple growth effect.

Very few publications of investigations carried out to determine tissue residues in animals fed dietary antibiotics are available. This is unquestionably a neglected area from the standpoint of evaluating any public health aspects of this use of antibiotics. It is undoubtedly true that animals are coming to slaughter with antibiotic residues in their tissues, particularly those animals which have been on prophylactic or therapeutic dosage.

[1] Table III is on page 40.

Thus far, antibiotics used as feed supplements have not been known to have led *overtly* to untoward effects in man. Residues of bacteriologically active antibiotics are not encountered in the flesh of animals that have received recommended levels of antibiotics (up to 20 p.p.m.) in feeds throughout their life span. Furthermore, detectable levels of bacteriologically active antibiotic residues in the flesh of animals fed antibiotic supplements disappear rapidly when antibiotic feeding is discontinued by recommended withdrawal times. There would seem to be little public health danger from the use of antibiotic-supplemented feed, *if feeding were discontinued after growth stimulation occurred and well before the time of slaughter.*

Analyzing the tissue residue of antibiotics used in feedstuffs has not yet been done on a large scale. Although there are data to show that high-level feeding is required to achieve tissue levels, it is not known how many animals came to slaughter following high-level (prophylactic or therapeutic) feeding.

III. Antibiotics in Plant Disease Control

Antibiotics of Importance

In a recent review (1959), Goodman listed 25 bacterial diseases of plants that are amenable to antibiotics for treatment or prevention. In addition, almost 50 fungal diseases of plants that respond similarly to antibiotics are described. In all of these cases there are only three antibiotics which play any significant role. These antibiotics are streptomycin, griseofulvin (Brian *et al.,* 1946), and cycloheximide (Whiffen *et al.,* 1946). The latter two are antifungal in their activity, while streptomycin is able to inhibit many bacterial and some fungal phytopathogens. Although streptomycin is well established as a medical antibiotic, griseofulvin and cycloheximide are less well known.

Cycloheximide is the more prominent of these two antifungal agents in phytopathology. However, now that griseofulvin is produced by large-scale fermentation as an oral antibiotic for treatment of human fungal disease, it is possible that an extension of its use in agriculture will occur.

The fundamental advantage of antibiotics over previous methods of plant disease control has been the fact that antibiotics are absorbed by the plant and are effective within the plant. That is to say, the antibiotics are systemic in their action. Prior to the advent of antibiotics, plant disease control was based upon external protectants. Such protectants were applied to surfaces, where they re-

mained until diluted, inactivated or degraded. They were "preventive" in their action. There is evidence to show that antibiotics are both protective and "therapeutic." Not only can the antibiotics prevent plant disease, they can also eradicate existing disease by virtue of their ability to act systemically and be translocated. This use of antibiotics also has a public health aspect since many plants so treated ultimately are used for food. Two problems may exist: that of the field worker in contact with the antibiotics, and that of possible antibiotic residue in the food product made from the plant.

IV. Antibiotics in Food Preservation

A. Fresh Meats and Poultry

Rather remarkable preservative powers have been evidenced in the use of tetracycline antibiotics applied to red meats and poultry. Three methods of introducing the antibiotic have been used with success. The first consisted of dipping steaks and chops in antibiotic solution; this retarded bacterial spoilage quite effectively. As many as 20 antibiotics were used, but oxytetracycline (OTC) and chlortetracycline (CTC) proved best. In a second method, the entire carcass was infused with antibiotic just after slaughter. Here again CTC was able to keep beef successfully at temperatures as high as 80° F. for several days. A third successful method utilized *ante-mortem* injection of OTC for preserving the meat of cattle, lamb and other species.

In all cases of tetracycline preservation of meat, it is quite apparent that some low-level residue will reach the consumer. Although residues of OTC are somewhat higher than those of CTC, there is actually little difference. The initial level in the raw meat ranges from 1-4 p.p.m. Following cooking, a decrease in residue occurs, but there is still detectable residue whether the meat is cooked rare, medium, or well done.

When applied to poultry, this point is somewhat different. It has been shown that the tetracyclines are the antibiotics of choice for poultry and that dipping in antibiotic solution is the preferred method. However, by limiting the dip to 55 p.p.m. concentration, the residue level in the bird is less than 7 p.p.m., and most of this is destroyed by cooking.

B. Fish and Seafood

Most work in this area has been done by Canadian, Japanese and English workers concerned with the preservation of one of the most perishable of foods. As is true with certain other foods, stability of

antibiotics is often enhanced, particularly in conjunction with fish skin. Ample studies have shown that only tetracycline antibiotics have the capability of controlling spoilage in this product. Applying these antibiotics in the form of ice or dipping fillets in antibiotic solution are both highly effective in increasing storage ability. Although much antibiotic residue is decreased in cooling, it is still necessary to consider the tetracycline residues in concentrations of less than 1.0-5.0 p.p.m. in fish treated for preservation by antibiotics. Table IV[1] sums up the current status of antibiotics permitted for food preservation in various countries.

V. Public Health Aspects of Nonmedical Uses of Antibiotics

Untoward effects of antibiotics have been described in numerous reports in the literature of clinical medicine. For the most part, these effects have appeared following therapeutic dosage and have been due to individual idiosyncrasy or specific drug action.

The untoward reactions have been emergence of antibiotic-resistant bacteria, hypersensitivity, toxicity and superinfection or overgrowth of indigenous flora resulting in a pathogenic process, that is, *candidiasis.*

The question at hand is whether or not low levels of these antibiotics are capable of producing the same effects. In most instances, the dose of antibiotic ingested from food would be 100-500 times less than a therapeutic daily dose of the same antibiotic. This can be illustrated with chlortetracycline. The level in foods preserved with CTC is 1-10 p.p.m., usually at the lower range. If an individual consumed 1-2 kg. of food per day, the total intake of antibiotic would be 5-10 mg. This is about 100-300 times less than the therapeutic daily dose of CTC.

In order to consider the effect of low levels of these antibiotics, each should be studied with regard to resistance, superinfection, hypersensitivity and toxicity rate at low levels.

One relatively unknown area involves breakdown products of the tetracyclines, such as isochlortetracycline, a heat degradation product which appears to be harmless. Studies on bone-seeking action, potential tooth discoloration and drug status during pregnancy are also needed. A new problem presents itself: that of the resistance transfer factor of multiple antibiotic resistance. This, too, must be considered.

VI. Research Needs

Because of the paucity of noncommercial laboratories working in the area of nonmedical use of antibiotics, there are many unanswered questions. It would appear, therefore, that considerable stud-

[1]Table IV is on page 40.

ies are needed to further results, protect the public health and expand the world's food supply.

The necessary public health research studies fall into three categories:

1. *Laboratory Studies:* Most needed here are acceptable standardized methods and an assay of antibiotics in all types of foods. Obviously, intelligent evaluation of residues cannot be made until such tests are available and standardized. The techniques of the Food and Drug Administration (FDA), available on request, go a long way in this direction.

2. *Animal Studies:* These must be directed to acute and chronic oral toxicity studies of the antibiotic compounds and their breakdown products. These studies should be oriented toward finding safe levels. If it is clear that levels are going to be present, what are the safe ranges toxicologically?

3. *Human Studies:* Limited studies such as those completed in Japan, Germany and the United States should be expanded and extended by more studies of human volunteers. One can take the laboratory and animal data and achieve meaningful results. However, studies of resistance, toxicity and hypersensitivity need to be encouraged in human volunteers whenever possible and should be conducted according to recent NIH (National Institutes of Health) guidelines for human experimentation.

TABLE I

Antibiotic Production For Nonmedical Uses (United States) 1951-1961

Year	Antibiotic use	Pounds	Value in millions of dollars
1951	Feed supplement	236,000	17.0
1952	Feed supplement	258,000	17.0
1953	Feed supplement	434,000	19.0
1954	Feed supplement	479,000	25.0
1956	Feed-food-crops	779,000	28.2
1960	Feed-food-crops	1,200,000	39.4
1961	Feed-food-crops	1,800,000	45.4
1961	All uses—medical and nonmedical	3,311,000	114.6

TABLE II

Animal	Age
Poultry	8-10 weeks
Swine	4-6 weeks
Calves	3 months
Beef cattle	18 months
Lambs	2 months
Fur-bearing animals	2-3 months

TABLE III

National Regulations For Antibiotic Feed Supplements

Country[a]	Antibiotics	Animals	Maximum level (p.p.m.)
Austria	OTC-CTC penicillin	Pigs-poultry	60
Belgium	OTC-CTC-penicillin-bacitracin	Calves-pigs-poultry	50
Denmark	OTC-CTC-penicillin	Young growing animals	25
Finland	OTC-CTC	Pigs-poultry-fur-bearers	50
France	OTC-CTC-penicillin-bacitracin[b]	Pigs-poultry	200
Germany	OTC-CTC-penicillin	Pigs-poultry-calves	200
Great Britain	OTC-CTC-penicillin	Growing pigs-poultry	100
Holland	Not specified	Pigs-poultry-calves	100
Norway	OTC-CTC-penicillin	Pigs-poultry-calves	50
Sweden	OTC-CTC-penicillin	Pigs-poultry-calves-mink	20
Switzerland	OTC-CTC-penicillin-bacitracin	All except dairy cattle	50
United States	OTC-CTC-penicillin-bacitracin[b]	Pigs-poultry-calves	2000

[a] Ireland, Greece, Israel, Italy, and Portugal have no restrictions.
[b] Also several other antibiotics.

TABLE IV

Food Preservation by Antibiotics in Different Countries

Country	Antibiotics permitted	Tolerance permitted (p.p.m.)	Used for
Argentina	Chlortetracycline Oxytetracycline	5-10	Meat, poultry, fish
Canada	Chlortetracycline	7	Poultry
	Oxytetracycline	5	Fish preservation in ice
		10	Fresh fillets in dipping tanks
Great Britain	Chlortetracycline[a] Oxytetracycline[a]	5	Raw fish
	Nisin[a]	No limit	Cheese and certain canned goods
	Nystatin	On the skin but not in the flesh	Bananas
Japan	Chlortetracycline Oxytetracycline	5	Fish preservation in ice; fish for fish pasta; salmon for canning
Norway	Chlortetracycline	250	Slaughterhouse offals for minks in the warm weather period
United States	Chlortetracycline Oxytetracycline	5	Fish preservation in ice; preservation of shrimps and scallops
	Chlortetracycline	7	Poultry preservation in slush-ice tanks
USSR	Chlortetracycline	5	Codfish preservation in ice and for transport

[a] The use of these antibiotics for the purposes and in the amount stated is a proposal only, made by the Antibiotic Panel of the Ministry of Health.

[The End]

Antibiotic Residues in Food

By ROBERT S. ROE

Mr. Roe Is Associate Director, Bureau of Science, Food and Drug Administration.

THE QUESTION OF ANTIBIOTICS IN FOOD has received considerable attention in recent months. I use the word "question" advisedly, for there are several areas where specific knowledge and data are either incomplete or lacking.

There are a number of ways in which antibiotics may gain entry into the human food supply:

1. As a direct additive.

a. At the present time, the antibiotics chlortetracycline and oxytetracycline may be used in the chilled dipping tanks used in processing poultry, for the purpose of retarding spoilage.

b. Chlortetracycline may be used for the same purpose in the ice used for packing various seafoods.

2. As an inadvertent additive. Other than those just mentioned, there are no approved uses for the direct addition of antibiotics to foods for the purpose of preservation. However, antibiotic residues in food may result from other usages of antibiotics:

a. As growth stimulants in the feeds of food-producing animals such as poultry, swine, calves and cattle.

b. For disease prevention and treatment whether administered in medicated feeds to food-producing animals or in drug dosage forms given by the oral, parenteral, aerosol, topical or intramammary routes; and

c. In crop sprays. Contamination from the last-named source should not occur in legitimate usage. When antibiotics are used as crop sprays in accordance with the required directions for use that must accompany the package, they are administered at the flowering stage or on seedling plants, and the antibiotics are

eliminated before the edible fruits or vegetables are formed. With regard to chlortetracycline and oxytetracycline as direct additives to poultry, residues of not more than 7 ppm are permitted in any part of the uncooked birds. However, experiments have shown that cooking destroys these antibiotics.

Residues of not more than 5 ppm chlortetracycline are permitted in fresh, uncooked, unfrozen fish, scallops and shrimp. In this instance, cooking does not completely destroy the antibiotic, and approximately 0.5 ppm may remain if the maximum permitted amount is originally present in the raw commodity. Actually, the use of chlortetracycline and oxytetracycline in poultry was very limited in extent, and short-lived. Practically no use has occurred in fish. The reason? Unsatisfactory results or adverse economics.

Necessary Criteria

On August 23, 1966, following a recommendation by the Advisory Committee on the Veterinary Medical and Non-Medical Uses of Antibiotics, the Food and Drug Administration (FDA) published a proposal that the regulations allowing these uses for chlortetracycline and oxytetracycline be revoked. This proposal has not been made final, pending consideration of comments by the interested parties. At present, no other antibiotics are authorized for use in food preservation. However, requests for authorization of certain antibiotics as preservatives in various canned vegetables to permit reduction in cooking times and temperatures have not been accepted by FDA, because supporting data were adjudged inadequate to establish effectiveness and safety. The Advisory Committee agreed with our conclusions in those cases and recommended criteria that the members felt should be met before any usage should be approved, including requirements that:

1. The antibiotic ideally should not be used in human or veterinary medicine, although exceptions may be justified to solve serious problems.

2. It should not cause resistant strains to arise or cause cross-resistance to other antibiotics approved for therapeutic use.

3. It should not antagonize therapeutic antibiotics.

4. It should not be used as a substitute for good sanitation.

5. It should not cause excessive effects on the body flora of people consuming it.

6. It should be safe and effective when used on a wide scale.

All of the feed uses of antibiotics for growth promotion, disease prevention, disease control and disease treatment that are described in the Food Additives Regulations have been approved on the basis of adequate tissue residue data supplied by the applicants. It is estimated that these regulations cover over 95% of the feed uses of antibiotics. There are a few antibiotics in feeds that were either covered by new drug applications or were declared to be no longer new drugs before the Food Additives Amendment of 1958 came into effect. There are few tissue residue data on these.

Tissue Residue Data Required

The regulations contemplate no residues of any antibiotic in the food products of animals treated with antibiotic-containing feeds—milk, eggs, meat—except in the case of chlortetracycline and oxytetracycline, for which the following tolerances for residues in meat have been established:

Chlortetracycline in poultry: 4 ppm in kidney and 1 ppm in muscle, liver, fat and skin.

Chlortetracycline in swine: 4 ppm in kidney, 2 ppm in liver, 1 ppm in muscle and 0.2 ppm in fat.

Chlortetracycline in calves: 4 ppm in kidney and liver, 1 ppm in muscle and fat.

Chlortetracycline in cattle: 0.1 ppm in kidney, liver and muscle.

We are attempting to decrease the concentrations of residues to below 1 ppm in all tissues by requiring appropriate withholding periods of one day or more before the animals are slaughtered.

Since 1962, no batches of certifiable antibiotic preparations intended for use in milk-producing animals have been certified unless there were adequate milking-out data to show the proper milk-withholding period. This requirement applies to all antibiotic preparations intended for intramammary infusion or parenteral injection. In the case of the intramammary ointments used for treating mastitis in dairy cows, data were required from each manufacturer on the products as made in his own plant; for the injectables, considerable latitude was allowed in approving preparations judged to be quite similar to those on which data were already available.

It is estimated that the certifiable mastitis preparations on which adequate residue data are available constitute about 90% of the mar-

keted preparations of this type. The others are not subject to certification because they are new drugs, have been declared no longer new drugs or were never considered to be new drugs. There is a paucity of data on most of the latter preparations and the available information would be considered inadequate under present requirements.

Dosage Forms

It is in the area of antibiotics administered in dosage forms that tissue residue data are particularly sparse. This category includes tablets, boluses, powders for use in drinking water, powder or liquid aerosols and injectables.

There are several such uses covered by the Food Additives Regulations, and these, of course, are supported by adequate tissue residue data:

1. Chlortetracycline in drinking water of chickens and turkeys: At 100 to 400 mg per gallon, the finite tolerances in edible tissues mentioned above are met with no withdrawal period, but at 1000 mg per gallon the poultry must be kept off the medication for at least 24 hours prior to slaughter to allow for partial elimination of the antibiotic from the tissues.

2. Chlortetracycline alone or in combination with neomycin in tablets for calves: A 24-hour withdrawal period must be observed in order that the finite tolerances will not be exceeded. When combined with sulfamethazine in tablets, the calves must not be slaughtered within five days of the last treatment.

3. Tylosin for intrasinus or drinking water use in turkeys: A five-day withdrawal period is necessary to allow the zero tolerance to be met.

4. Tylosin for drinking water use in chickens: A 24-hour withdrawal period is required.

5. Tylosin for intramuscular injection and for drinking water use in swine: Four-day and two-day withdrawal times are needed.

6. Oral tablets or suspensions of dihydrostreptomycin in combination with chlorhexidine for treating calf scours: A three-day withdrawal time is needed.

All of these authorized uses include withdrawal periods of from one to five days to insure absence of residues from tissues at the time of slaughter. It is extremely important that these requirements be observed. If investigations reveal that such requirements are not fol-

lowed, or are impracticable, it may be necessary to revoke the authorizations.

Conclusion

On August 23, 1966, the FDA published a statement of policy requiring the submission within six months of data on residues of antibiotics in the edible tissues, milk, or eggs of animals treated with antibiotics. If such data have been previously submitted, they need not be resubmitted.

It is anticipated that appropriate action will be taken on those products for which no data, or inadequate data, are submitted, including revocation of prior sanctions, suspension of new drug or antibiotic approvals, changes in the antibiotic regulations or requirements for changes in the labeling.

It is the intention of the FDA to exclude from the market those products for which tissue residue data showing absence of residues are lacking. Our goal is to insure that residues of chlortetracycline and oxytetracycline in foods will be reduced to a minimum, and that residues of all other antibiotics will be eliminated completely from the human dietary. **[The End]**

NEW FDA APPOINTMENTS MADE

The following appointments to Food and Drug Administration posts, all effective in January, 1967, have been announced:

Former Senator Maurine C. Newburger has become a Consultant on Consumer Relations to the Commissioner of Food and Drugs. In her years as a Senator from Oregon, Mrs. Newburger was actively interested in the area of consumer protection. In her new post, she will advise the Commissioner on a wide range of programs and policies involving consumer needs.

Dr. B. Harvey Minchew has been named acting deputy director of FDA's Bureau of Medicine, succeeding Dr. Robert J. Robinson, who resigned.

Weems L. Clevenger is the new director of FDA's New York District. He succeeds recently-retired Charles A. Herrman.

William V. McFarland has been selected as the first FDA Regional Assistant Commissioner; he is assigned to the Dallas Regional Office. Mr. McFarland was deputy director, serving as acting director, of the FDA Office of Federal-State Relations in Washington. Glenn W. Kilpatrick is now serving as acting director of that Office.

What FDA Expects in Prescription Drug Advertising

By WILLIAM W. GOODRICH

Mr. Goodrich Is Assistant General Counsel to the Department of Health, Education & Welfare.

THERE ARE, NO DOUBT, SOME WHO HAVE A DEEP CONVICTION that we have already said far too much about prescription drug advertising. Some, indeed, may be asking, "Why all this drum beating?" The short answer is that we need better performance by those who advertise and by those who create advertisements. Better performance is required now, not just to please government regulators, as some have suggested, but to improve the quality of patient care—to meet the needs of the sick and distressed at the end of the long line of drug distribution.

While some advertisers reacted vigorously, and negatively, to our recent efforts to make ourselves better understood, we are nonetheless encouraged by the march of events—by a new attitude of willingness to examine current promotions with us in the light of our objections. We are hopeful, at last, that we are about to see a change for the better in communicating the action and the hazards of drugs to their prescribers.

For simplicity, we can divide this subject into three headings. First, what is asked by the law and the regulations? Second, what is bothering the Food and Drug Administration (FDA) about the state of compliance? And third, what are FDA and the advertisers doing about it?

What the Law Asks

The public's interest was first drawn to Rx advertising by the Kefauver investigation into administered prices. This investigation

highlighted many excesses in drug promotion. From it, the word emerged loud and clear that there would have to be some basic changes in this phase of drug promotion. President Kennedy recommended, and the Congress enacted, provisions intended to "help assure the American people . . . that the promotional material [for Rx drugs] tells the full story . . . [the] possible bad effects as well as the good—and the whole truth about therapeutic usefulness." This is the basic guideline that controls our actions.

The only concession made for the special needs of advertising was that the drug story might be presented "in brief summary." What this calls for is information in ads that will show fairly the effectiveness of Rx drugs, along with any side-effects, contraindications, precautions and warnings, in a form that is, while brief, neither false nor misleading. The central idea is to be sure that the message to the prescriber strikes a proper balance in telling what the drug is for, what the limitations upon its usefulness are, and what hazards may attend its use.

To summarize what the law requires: every prescription drug advertisement and any other descriptive matter issued to promote sales must contain a true statement of the formula, the established name of the drug along with any trade name used, and "such other information in brief summary relating to side effects, contraindications and effectiveness as shall be required in regulations" issued by the Secretary.

Regulations

Regulations applicable to ad content were issued about three years ago, after they had been considered by both the pharmaceutical industry and the medical profession. Initially, both expressed belief that advertising was not educational, that it served only a reminder role but played no part in the physician's choice of drugs prescribed.

We took the view that if advertising does not sell drugs it will not continue to run.

The regulations were devised to deal with one of the sensitive links between those who produce drugs and those who prescribe them. We had in mind a late ad man's own words: "approximately 3 quarters of a billion dollars is spent every year by some 60 drug companies . . . to reach, persuade, cajole . . . and sell one of America's smallest markets," the nation's prescribing physicians.

The regulations themselves are simple ones. They were offered as an initial step toward public supervision of this special means of communication between the drug producer and the medical profession. They did not try to provide the details as to exactly how any drug would have to be advertised. That was left for the advertisers to develop within broad guideline regulations.

In essence, these regulations require four things insofar as the selling part of the ad is concerned:

A fair summary of the effectiveness of the drug in the conditions for which it is offered, along with all of the side effects, contraindications, precautions and warnings applicable both to the conditions for which the drug is advertised and those for which it is commonly prescribed;

A fair balance in presenting the information on effectiveness and the related information on side effects, etc.;

A reasonably close association of the information on effectiveness with the information on side-effects, contraindications, etc., together with a discussion of the adverse data to the same degree of prominence as is given to the claims of effectiveness; and

The use of only those promotional claims that have been approved in advance upon the clearance of the drug for the market as a "new drug" or certified antibiotic, or in the case of drugs that require no preclearance, the use of claims of effectiveness that are generally recognized as true or are supported by substantial evidence, consisting of adequate and well-controlled investigations or adequate clinical experience on the basis of which it can be fairly and responsibly concluded that the drug will have the effectiveness claimed.

This is not a very big order. Simply stated, drugs may be promoted only on the basis of proven effectiveness. The total advertising message must be fair and forthright in dealing with the usefulness, limitations and hazards that may attend the administration of the drug. And the "layout" of the ad must lay out the scientific data that underlies the advertising message—not gimmickry.

Following recent regulatory actions, we have heard complaints that the regulations are not specific enough, that they do not tell the advertiser, his agency, his medical director or his lawyer *exactly* what must be done and *exactly* what must be avoided. We agree that they

do not say exactly what to do. Instead, they express the ideas we consider fundamental to proper advertising; they express these ideas in terms of "fair balance," "reasonably close association," and the "same relative degree of prominence": ordinary English terms which should be readily understood.

No more inflexible words were used because we wanted to move with the drug industry and the creative people in improving drug advertising to satisfy its high purpose of telling the prescriber briefly and accurately what drugs are available for safe and effective prescription for his patients.

These general rules were elucidated by the memoranda of understanding which passed between us and the industry in October, 1963, by a statement made public in 1964 which called attention to the most common failings in drug promotion, and, more recently, by an exposition at the medical section meeting of the Pharmaceutical Manufacturers Association which described in great detail the basic premises underlying our evaluation of advertising and promotional labeling.

But to answer the complaints that the regulations should be more specific, we are preparing to incorporate some of the points in these guidelines, as well as some points that have emerged from our most recent regulatory experience, into regulations which will have a binding effect. We hope we can avoid the complaint that any new regulations are too inflexible. With this background of the state of the law and the regulations, we may turn to what is bothering FDA about the state of compliance.

The State of Compliance

Recently, *Drug Trade News* carried an item from *The London Times* expressing astonishment at the difference in ads for the very same prescription drug as they appeared in the British and the American editions of *The Lancet*. The American ads were described as "clearly superior from the doctor's viewpoint." From that, one would think that we should commend the advertisers, not criticize them.

There has, indeed, been considerable improvement in ad copy since we first began to study it a little more than three years ago. No longer do we see ads devoted wholly to telling what the drug is good for, wholly neglecting the negative information about its side effects, warnings and contraindications. On the face of the ads, except for some problems of physical fair balance, the presentations seem

to deal adequately with both the good and bad of the advertised drug. But herein lies the problem: it is the substance of the ads that is now causing us our greatest concern.

Why, we ask, must essentially every ad for an oral contraceptive, for example, claim that it is the safest, the most effective, the lowest in hormones and the least prone to cause either distressing or serious side effects, when there are no adequate scientific data to establish that any of the drugs thus far approved differ substantially from the standpoint of safety or effectiveness, and when all such drugs must share the expert evaluation that, while there is no evidence to prove them unsafe, there are some troublesome and serious side effects that must be taken into account when any prescriber orders such a drug for his patient? Why must almost every ad for a new antibiotic claim that it is for "every day" use, that it has the broadest spectrum, that it is useful against a multitude of upper respiratory bacterial infections (when most upper respiratory illnesses are viral in nature), and that it does not share the hazards, discomforts or inconveniences of some of the established antibiotics? Why must a new diuretic or anti-arthritic drug claim that it is the safest for long term therapy and that it has unexcelled effectiveness, even for conditions that do not yet yield to definitive therapy? Why must most tranquilizers and anti-depressants be offered for target symptoms, inviting prescription for such things as sadness, fatigue, sleeplessness, lack of interest, pessimism and despair—in sum, for the ordinary frustrations of daily living? Why must a best-selling combination tranquilizer and anti-depressant be advertised as useful for those who need either drug, rather than only for those who require concomitant treatment with a tranquilizer and an anti-depressant in the fixed dosage this drug can provide?

The present rules are clear in stating that a prescription drug can only be promoted on the basis of those conditions for which it has been approved, conditions that have been spelled out in great detail on the package insert. There is no uncertainty in the regulations concerning the prohibition of the type of claims that I have just outlined. There are others areas of the regulations that may be described as "grey", but the ones I have described are not among them. The problem, as we see it, is not ignorance of the ways in which the drug can be advertised, what claims are permitted and what side effects must be described. It is the failure to deal frankly and fairly with the approved prescribing information in the advertising copy.

Only recently, two of our medical officers expressed dismay at advertising copy for drugs that they had approved. Instead of advertising a fixed dose combination drug for patients who had been stabilized on the individual drug components making up the combination, patients who could be given the fixed dose safely, one advertisement offered the new combination as an anti-hypertensive together with a diuretic, which should be used to avoid any complicating edema. It was approved for use where concomitant therapy with the fixed dosage preparation would satisfy the patient's dosage needs for both drugs; it was not approved for prophylactic use in any circumstances.

Another medical officer, troubled by his difficulties in persuading a company to provide adequate warning information, commented that if the company he was dealing with were describing Hurricane Betsy in its promotional copy, she would be described as a "mild, late summer breeze."

Further Problems—Competition and Exaggeration

Another major problem with ad copy arises out of every company's need to compete. Few drugs can be sold by telling what they are for unless they can be compared favorably with existing leaders in the particular field of drug therapy. Now let me say emphatically that we are not against competition. We understand the need to compete in advertising copy. After all, that is what advertising is for. But competitive drug comparisons must be accurate and fair. These comparisons call upon the person creating or evaluating the ad, whether a company's medical director or our own medical evaluator, to make value judgments as to relative efficacy and safety. This is a delicate field of inquiry, from which the Congress spared us in providing for our responsibilities for passing on new drug effectiveness. Yet, competitive advertising has called us back into it.

Finally, we should mention the problem of handling the data without exaggeration.

We are wary of ads which offer products as "drugs of choice"—those which attempt to show that the advertised drugs will meet every level of need. When we see an ad which features a single paper, a paper by an obscure investigator, a paper that seems to be out of line with all that is known about the drug, a paper which describes a limited experience or a paper which features a unique pattern of effectiveness, we are understandably put on alert. And when we run

down the papers, sometimes being forced to the limits of the resources of the National Library of Medicine, and find that they do not say what they have been represented as saying, that they report a study with less than a dozen patients or even with essentially healthy volunteers, that they cover animal work or laboratory testing rather than clinical experience, or that the ad uses only a part of what the author of the paper has actually reported, we call that a lack of "fair balance" in presenting the drug story.

We are concerned about ads which have a high hysteria index, a low stability index, and a high entropy index, ads that are too noisy and come screaming off the page. What causes much of the problem is that the developers of ad themes often disregard the allowable claims in the approved brochure and the scientific data on which they are based; they have mounted ad programs on data which provide a sandy foundation; and, they have set out to capture a market that cannot be properly served by their particular drugs. When the pre-clinical and clinical data show that a drug has only limited usefulness, it simply will not support a dramatic promotional effort.

FDA's Program for Improvement

What then, does the FDA intend to do to improve current performance?

We will continue to seek a dialogue with the manufacturers, the creative people who devise the ads, and representatives of the media who display the ads. We are seeking this at every possible turn, at meetings, at symposia for our own people, as well as for outside groups, indeed everywhere cross-communication can be improved.

We plan to improve both our regulations and our own performance to assure better advertising and even-handed enforcement. As to the regulations, we are gathering ideas for improvement, and we welcome suggestions now and at any time whatever. The regulations are meant to serve the needs of fair advertising, not to impede them. As to our performance, we are developing techniques to provide for faster review of new promotional themes as soon as they appear. We hope the review can be carried out in part by the physicians who have cleared the new drugs, and thus should know the most about them. We are also developing better understanding among our medical and regulatory people as to the impact advertising messages may be expected to carry to their viewers.

Enforcement, no doubt, will continue to be necessary in some instances. The policy laid down by the Commissioner last June was that we would continue the use of citation and prosecution for seriously violative ads, particularly those which created hazards in the use of advertised drugs. For advertising campaigns which require immediate attention, we are following a seizure policy. It has the advantage of immediacy, and it offers the companies involved the possibility of taking the initiative, after seizure, to develop appropriately revised advertising messages. If need arises, we will plan to utilize the injunction remedy so that judicial supervision can be brought to bear on especially difficult problems.

Conclusion

What we really expect from the prescription drug industry today is that it will take a fresh hard look at its advertising practices. We expect the advertising media to reexamine the copy they receive, to test it, not only against the law, the regulations and the scientific data, but also against their own published principles of advertising policy.

What is happening here is that FDA now is examining an increasing volume of advertising copy. We are measuring it against the underlying scientific data which allowed the drug to enter the market through our New Drug Applications and antibiotic clearance procedures. And we are taking actions to bring the ads into compliance with the principles on which we stand: that the ad must tell the prescriber fairly and adequately how the drug may be safely and effectively used, what limitations on usefulness he should bear in mind, and what side effect or other adverse experience must be taken into account in prescribing it. We will watch especially the new ads for oral contraceptives to see how companies perform within agreed promotional guidelines.

This may well signal the start of a new era in responsible prescription drug advertising. We want these ads to enjoy high believability, as well as high visibility. **[The End]**

Assuring Integrity Through Teamwork

By PAUL RAND DIXON

Mr. Dixon Is Chairman of the Federal Trade Commission.

THE TEAMWORK demonstrated by the Food and Drug Administration (FDA) and industry today is hard to beat. However, I thought it would be helpful to discuss another example of teamwork —the horizontal teamwork between the Federal Trade Commission (FTC) and FDA.

The 1954 working agreement was intended to prevent duplication and overlapping of effort. It simply assigned primary responsibility for labeling to FDA and that for advertising to FTC. It served its intended purpose well, but it became apparent that something more was needed if these two agencies were to serve the public interest fully and carry out the mandate of Congress in meaningful fashion.

It is becoming increasingly clear that we must ensure—especially in the vital field of public health—that the total statutory authorities and procedures, and the manpower and other resources, are so employed as to afford maximum protection to the consumer. This means joint planning of coordinated programs, and exchange of information and evidence, to the extent permitted by law, by the staffs of both agencies in appropriate undertakings, and the careful selection of the procedure of either agency (or simultaneous selection) promising greatest benefit to the public.

Categories of Drugs

In approaching the subject of liaison as it relates to the advertising of over-the-counter drugs, we are cognizant that from a regulatory viewpoint such drugs fall into several categories:

(a) Post-1962 drugs which the FDA has reviewed under the New Drug Applications (NDA) procedure, and for which a determination with respect to both safety and efficacy has been made;

(b) Post-1938 but pre-1962 drugs which the FDA has reviewed under the NDA procedure for safety but not for efficacy;

(c) Pre-1938 drugs and those post-1938 drugs which are not subject to the NDA procedure and which the FDA has not otherwise formally evaluated as to safety or efficacy; and

(d) Drugs whose safety, efficacy or both have been determined by the FTC or FDA in a proceeding other than the NDA procedure. This category would include, for example, efficacy determinations resulting from Federal court litigation under the Federal Food, Drug and Cosmetic Act, and proceedings brought under the Federal Trade Commission Act. It would also include, when completed, the efficacy review of category (b) drugs now in progress.

Principles Governing Liaison

With respect to the advertising of drugs, we are working with the following guiding principles governing inter-agency liaison:

A. For pre-1938 drugs and those post-1938 non-prescription drugs to which the NDA procedure is not applicable, and which the Administration has not evaluated for safety and efficacy, liaison fully employing the scientific and legal staffs of both agencies will attempt to determine how best to proceed against any practices raising questions of law violations subject to the jurisdiction of both agencies. Particular consideration will be accorded determinations resulting from legal proceedings by either agency, bearing in mind the relative degrees of proof necessary to support, and the differing remedies provided by, seizure actions and injunctions under the Federal Food, Drug and Cosmetic Act, the FTC cease and desist orders, and the possible applicability of the doctrine of *res adjudicata.*

B. For products subject to NDA or certification procedures, the Commission staff ordinarily will accept the Administration's determinations and will attempt corrective action under the Federal Trade Commission Act with respect to claims in advertising which are inconsistent with such determinations. Examples are:

(a) Safety and efficacy claims for post-1962 over-the-counter drugs;

(b) Safety claims for post-1938, pre-1962 over-the-counter drugs which were handled as new drugs during that period; and

(c) Claims for over-the-counter antibiotic preparations certified under the provisions of Section 507 of the Federal Food, Drug and Cosmetic Act.

C. With respect to prescription drugs, statements in advertising relating to the name, the declaration of ingredients, the side effects, contraindications and effectiveness are the responsibility of the FDA.

Three Levels of Development

In order to implement this understanding, we are developing liaison at three levels:

1. Immediate liaison on routine questions, normally by telephone;

2. Regular meetings, on the order of one each month, for discussion of matters of general interest; and

3. Conferences, as appropriate, by members of the scientific and legal staffs of the two agencies to share and discuss information about matters of specific interest.

These are not empty words. For example, Dr. Goddard and I spent an afternoon within the past week planning a coordinated enforcement program covering both the labeling and advertising of several proprietary drugs, and also planning our action under the Fair Packaging and Labeling Act. You can expect to begin to see some results of this teamwork within the near future. **[The End]**

CLOSING DATES OF PROVISIONALLY LISTED COLOR ADDITIVES EXTENDED

The closing dates for the provisional listing of color additives for food, drug, and cosmetic use, under Reg. § 8.501, have been extended from January 1, 1967, to dates varying from May 1, 1967 to December 31, 1967, with a requirement that a progress report be supplied on or before July 1, 1967.

In addition, calcium carbonate and riboflavin were deleted from the provisional listings, and iron oxide was added to the listing. CCH Food Drug Cosmetic Law Reports ¶ 6801

Safe and Effective Prescription-Drug Advertising

By IRVING H. JUROW

Mr. Jurow Is Vice President and General Counsel
of the Schering Corporation, Bloomfield, N. J.

IN THE CONTEXT OF THIS CONFERENCE'S THEME—"Assuring Integrity of Food and Drugs"—I have been asked the rather innocent-sounding question: What does the industry need in drug promotion and advertising?

I should have thought, after the cascade of words on the subject of prescription-drug advertising with which we have been inundated in recent months, that we are more than ready to cry out, as Macbeth suggested, "Hold, enough!" Nevertheless, this was indeed the year, as one Administration official has put it, when prescription-drug advertising really came into view. So we continue the dialogue in the hope that out of it will come a rational and practical—and even mutual—resolution of the differences thus exposed.

But first a disclaimer: I have no mandate from the industry to speak for it. Being part of it, however, I believe I am privy to some of the things it would, or should, want. To the extent my observations coincide with those of industry spokesmen, I may indeed be speaking for it; to the extent they do not, they must stand on their own.

Next: it must be obvious to us all that advertising and promotion have much to do with the *integrity* of drugs. I think we all agree there is more to integrity than good manufacturing practices and superior quality control; these assure the *physical* integrity of our drug products. Accuracy and completeness in product labeling, truthfulness and honesty in advertising and promotion, are essential if the drug product *in actual use* is to fulfill its promise.

Finally, a frame of reference: Before the Drug Amendments of 1962, the Food and Drug Administration (FDA) had little, if any, jurisdiction over prescription-drug advertising as distinguished from

labels and labeling. With the help of the courts, however, it was not long before this frustrating void was filled. By construing the word "accompanying," in the statutory definition of "labeling" (21 USC 321(m)), to embrace written, printed, or graphic material, even though it did not physically go along with the drug—by adopting a *functional* rather than a *physical* test—the difference between labeling and advertising was substantially narrowed.[1]

Lacking express jurisdiction in the FDA over drug advertising, it was not altogether surprising that the courts adopted this expanded meaning of "labeling," thus providing the Administration with the means for enforcing its seizure powers. The hard factual cases which the Administration brought to the court, however, may well have produced, as lawyers are fond of saying, "bad law." Indeed, the *Alberty* case[2] provides an interesting contrast. There the court *refused* to treat the advertising as "supplementing" the otherwise inadequate label in order to save the product from being misbranded. Though not concerned with prescription drugs, these cases established applicable precedents and hardened regulatory thinking.

Confusion Between "Labeling" and "Advertising"

It may have been desirable prior to 1962 for the Administration to urge that promotional material be treated as "labeling," in order to obtain jurisdiction and thereby to require such material to include what we have come to describe as a "full disclosure." However, when, in the 1962 Drug Amendments, the Congress expressly vested in the FDA control and jurisdiction over prescription-drug advertising (21 USC 352(n)), it seems to me it eliminated the need to characterize such promotional material as "labeling" for the purpose of effectively regulating it, and in the process destroyed the realistic differences between these two media of information.

Moreover, the Congress clearly recognized, in Section 502(n) of the Act, both the purposes and the limitations of advertising, as distinguished from labels and labeling, by providing that the information relating to side effects, contraindications, and effectiveness were to be included in "brief summary." (Other instances of Congressional advertence to this same distinction may be found in Sections 301(l) and 301(n) of the Act.) I think it significant that the Congress expressed itself ever so plainly. To make doubly sure its meaning was clear, it indulged, you will recall, in a bit of tautology, requiring

[1] *Kordel v. U. S.*, 335 U. S. 345 (U. S. S. Ct., 1948); *U. S. v. Urbeteit*, 335 U. S. 335 (U. S. S. Ct., 1948).

[2] *Alberty Food Products v. U. S.*, 185 F. 2d 321 (CA-9, 1950).

not just a "summary," but only a "brief" summary. Obviously, it must have meant something less than "full disclosure." And, to further emphasize this distinction, it provided that the special requirements of Section 502(n) were not to be made applicable to any printed matter which the Administration concluded was "labeling" as defined in Section 201(m).

With this clear statutory authority over advertising and promotional material in the prescription-drug field, surely the need was gone for stretching the meaning of the term "labeling" to envelop so broad an area as had been attempted before the 1962 amendments. Given express statutory power, indirection, through the so-called "squeeze play" or the extension of the coverage of "labeling," became unnecessary.

However, recent pronouncements and, more to the point, recent actions on the part of the FDA suggest that it is not prepared to relax the pre-1962 concepts by which it extended the frontiers of "labeling" to embrace far more than one would ordinarily have assumed to be included in that term—concepts which serve in practical application to equate almost all advertising and promotion with "labeling." It is difficult, indeed, to envisage what, under recently announced requirements for promotional material, is left of advertising.

Moreover, despite the difference accorded by the Administration in the regulations dealing with "labeling" requirements (21 CFR Sections 1.104, 1.106), and in those dealing with prescription-drug advertising (21 CFR Section 1.105), the distinction becomes all but superficial and meaningless as the perimeter of "labeling" is expanded, the acceptable encompassment of advertising contracted, and "brief summary" is equated with "full disclosure."

Unless the Administration views the distinction in terms of reality and practicality, the day is near when we shall learn that there is no such thing as prescription-drug advertising—that all promotion of prescription drugs is "labeling." Some of us, in fact, suspected the Administration had started down that road when it defined as "labeling," in Section 1.105(1) of the prescription-drug advertising regulations, such items as "price lists," "catalogs," and "house organs."

Reappraisal and Proper Accommodation

What then is to be the proper accommodation between industry and government, between "labeling" and "advertising"?

Our starting point, as always, must be the statute. You are all familiar with the requirements of Section 502(n): the established name, the quantitative formula, and "such other information in brief

summary relating to side effects, contraindications, and effectiveness" as shall be required by regulations of the Administration. You are equally familiar with the regulations. Section 1.105 (21 CFR Section 1.105) tracks the language of the statute in requiring the inclusion of a "brief summary relating to side effects, contraindications, and effectiveness" (1.105(e)) in any prescription-drug advertisement which provides information regarding indications or dosage recommendations. It calls for a "fair balance" in presenting the information on effectiveness and that on side effects and contraindications. Moreover, the latter information is required to appear "in reasonably close association" with the former and to have "the same relative degree of prominence" (1.105(i)).

"Brief summary," "fair balance," "relative degree of prominence," "reasonably close association"—these may indeed all be "words of ordinary English." They nevertheless reflect imprecise criteria; they define by the *objective,* not measurable by a slide-rule. It is not surprising, therefore, to find that they command subjective reactions, and that reasonable men may very well honestly differ as to the proper application of these criteria to any given piece of promotional material.

Fundamental to the current confrontation is the apparent divergence in attitudes toward the role of advertising, resulting from the failure, I suggest, on the part of the Administration either to recognize or to accept fully the function of advertising in the promotion of prescription drugs in a highly competitive economy, to a skillful and learned audience, which has readily available to it the totality of information in the product brochure approved by the FDA.

What is needed, it seems to me, is a reappraisal of the role and function of prescription-drug advertising, a more valid distinction between it and "labeling," and a re-examination, in that context, of the rules to be applied to each.

In this reappraisal and re-examination, however, we must avoid overburdening the function of prescription-drug advertising and, in turn, avoid depreciating the function of labeling; and it is equally important not to ignore the realities of our audience, its expertise, the information otherwise available to it, and finally the structure of our very economic system.

The Function of Advertising

Obviously, Congress did not intend, and could not have meant, that "full disclosure," as required in "labeling," should occur also in prescription-drug advertising, even in a restricted form. Advertising and promotional material is informative, but it is not the totality of

information in the sense that labeling performs this function, as, for example, in the product information insert. To serve its purpose and its function, advertising must do less. Let's be practical. To get the drug product used by the patient, it must be sold; to get it sold, it must be prescribed; to get it prescribed, it must be brought to the attention of the physician so as to encourage him to investigate it and to use it. To require that advertising give him the complete "full disclosure" story is asking too much of it.

Just as we demand that our drug products be safe and *effective,* so should their advertising be *effective* as well as safe. Safety is achieved by honest, fair, nondeceptive, and nonmisleading advertising; effectiveness is achieved by utilizing the techniques implicit in good advertising to obtain reader attention, reader interest, and reader investigation. Unless advertising is *effective,* as well as safe, it is useless.

To be sure, the current regulation provides for "reminder advertising." As defined by the Administration, however, this is all but meaningless. "Reminder advertising," in the Spartan form acceptable to the Administration, may do for the physician who is fully informed and needs only the stimulus of the name of the product. To the physician who has yet to know the product, so bare an advertisement means nothing. Unless the allergist is at least told the product will help his allergic patients, why should his interest be aroused? Nevertheless, under current Administration dicta, even so casual an observation and characterization of the drug product in advertising is an "indication" requiring "full disclosure."

If advertising is to reflect something other than "labeling," if "brief summary" is to have any meaning other than "full disclosure," if promotion is to serve its proper function, then it is obvious that there must be in the promotional material a subjective selection and omission from the approved labeling, and it is in this area of subjective selection and omission that our differences arise.

Advertising is less a science than an art. By its nature, it is open to a variety of interpretations. I can conceive of no hard and fast method to provide for every individual to view the same advertisement in the same way, any more than a temperance worker and an alcoholic would see a bottle of whiskey through the same eyes. The temperance worker might describe it as half full; the alcoholic would see it as half empty. The government official and the industry representative share the same dilemma.

At the risk of being accused of misplaced humor, let me illustrate the point with the story of the two Missouri farmers. One of them

sold the other a mule, with the assurance that it was a most obedient animal. "He does what he is told and he does it fast." Two days later the buyer was back with the mule. "That cantankerous animal won't do a thing," he complained, "just stands there, stubborn as all get out." "Can't understand it," said the first farmer. With that, he picked up a heavy log, struck the mule a sharp blow on the nose and hollered, "Gee." The mule took off like a streak of lightning. "You see," said the farmer, "first you've got to get his attention."

Audience Appraisal

There is a second factor that needs to be considered in our reappraisal. We need to recognize that the audience to which prescription-drug advertising is addressed consists of members of a learned profession in which a high degree of morality and ethical conduct has been ingrained for centuries. Men and women of intelligence, skill, and sophistication, they reflect a rare homogeneity because of the discipline they share. Promotional material prepared for them cannot be compared with advertising intended for the consuming public, which includes a vast variation in experience and intellectual capacity, from the moronic to the genius.

I, for one, refuse to accept the thesis that the large, large majority of the medical profession does not investigate thoroughly the full recital of facts set forth in the product information insert—that they prescribe with less than a full understanding of the drugs they are using—any more than I would expect a reputable lawyer to rely on "headnotes" instead of reading in full the court's decisions.

If we insist that the physician is indeed the only one with the skill and the knowledge to prescribe prescription-drugs, why do we downgrade his intelligence and his ability to understand and accept the contemporary characteristics of advertising and to distinguish between the advertisement in the medical journal and the "full disclosure" labeling on or in the package?

Moreover, we should recognize that we live in a sophisticated society. Communication in every field, not excluding the government itself, is built on the dramatic. It is naive to assume that even so knowledgeable and worldly-wise an audience as the medical profession is wholly immune to the contemporary scene. If only subliminally, they, like all of us, have become somewhat indifferent to the ordinary, the undramatic. In a world dominated by singing commercials and neon lights, Beatles, beatniks and bikinis, miniskirts and topless barmaids—the world, may I suggest, of Dr. Marshall McLuhan

—how can you expect to attract attention to *any* message if you clothe it in dull, eighteenth-century garb?

This does not mean that an attractive, attention-getting message need be misleading or fraudulent; but it is equally unrealistic to ignore the basic rules of effective advertising and to compel it to function in a manner which is other than attention-getting and appetite-whetting. By the ad, the doctor is provoked, if you will, into investigating the drug for his patient and using it as described in the approved labeling.

Effect on the Public

Finally, I think it self-evident that the government cannot ignore the rationale for advertising and promotion, in our modern economy, for successful marketing, even in so highly scientific a field as that of prescription-drugs; and it cannot disregard the need for even this industry to live by the rules which an economy, highly sensitive to competitive marketing and promotion, demands.

Against these considerations, what public interest is served by the rash of seizures which have recently characterized the Administration's attack on the advertising of prescription-drug products? From the information available in the press, it would appear that in none of these was there any question as to the integrity of the drug itself.

In each, it appears the particular advertisement or promotional material may have warranted editorial correction; in many, this represented but a difference of viewpoint in expressing a thought or in the placement of a phrase. Surely, a better procedure for achieving an accommodation between two points of view is needed than the seizure procedure which, I submit, unnecessarily and unwisely subjects the public to widespread fear and confusion as to the safety or the effectiveness of the product itself.

The recent exchange of recriminations, resulting in the wholesale cancellation of all journal advertising by two of the most prominent companies in the industry, is hardly a sound procedure or solution. Whether the action of the companies is, in the words of the Administration, "nonsense" or not, the spectacle of this public airing of the differences between the government and industry—in what could be described as a "grammatical quibble"—serves neither the government nor the industry nor, more importantly, the public.

I think it is high time to find a different and a better solution to the advertising "problem," if indeed there is one. Surely, it should be possible for prudent and reasonable men, whether in government

or in industry, to arrive at a rule of reason concerning prescription-drug advertising rather than a per se rule of illegality.

The opportunity is at hand for a resolution of the current impasse, and for a cooperative effort toward a greater perceptiveness of the public interest implicit in this "problem." This was the motivation of the organized ethical pharmaceutical industry in establishing a distinguished committee to devise an even more precise and disciplined basis for advertising conduct on the part of its membership. Hopefully, a meaningful dialogue will be possible between government and this industry group.

After all, even so efficient an administration as the current one cannot possibly supervise all the advertising and promotional material produced by the prescription-drug industry for the very practical and simple reason that the job is too enormous. As it has for a great many years, the government must rely on the integrity of the industry and the demonstrated willingness of the manufacturers to police themselves. But the guidelines vital to making this system work must be rational, logical, understandable, and practical. Otherwise, faced by the prospect of continued use of seizure—a rather violent form of sanction—the industry contemplates equally unhappy alternatives. There will be a complete paralysis on the part of those who prepare its advertising and promotional material, or our jails will be filled with unwitting violators. If the government believes that *laissez-faire* needs to be corrected, surely it should not substitute *laissez rien*!

Above all, the reappraisal and reexamination I refer to must be done in an atmosphere of mutual respect and with something less than arm's length negotiating techniques. This industry is not devoid of a sense of responsibility and a dedication to the public interest; it has every intention and every desire to comply voluntarily with all the laws and the regulations applicable to it and to exercise a high degree of self-discipline. Despite the high level of criticism to which it has been subjected, it retains an abiding sense of decency and honesty, and is responsive to the public interest. If for no interest other than self-interest, it must act with integrity—for it serves a company nothing if, instead of orders and customers coming back, the goods come back. It does not deserve to be treated like a pack of Carthaginians, who were described in these words by the historian Polybius: "At Carthage," he wrote, "nothing which results in profit is regarded as disgraceful."

Let's be fair; government does not have a monopoly on rectitude.

[The End]

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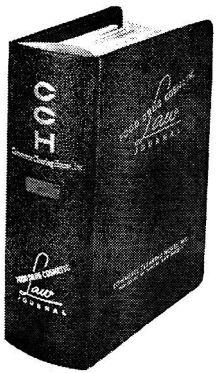

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