VOL. 29, NO. 9 SEPTEMBER 1974

# Food Drug Cosmetic Law JOURNAL

## Legal Update Overview of Recent Judicial and Regulatory Developments in Rx and OTC Law

RAYMOND D. McMURRAY

## So Are They All—All Honorable Men A Review of the DES Revocation Cases to Date

WALTER E. BYERLEY

A COMMERCE CLEARING HOUSE PUBLICATION
PUBLISHED IN ASSOCIATION WITH THE FOOD AND DRUG LAW INSTITUTE, INC.

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.

The FOOD DRUG COSMETIC LAW JOURNAL is published monthly by Commerce Clearing House, Inc. Subscription price: 1 year, $25; single copies, $3. Editorial and business offices, 4025 W. Peterson Ave., Chicago, Ill. 60646. Printed in United States of America.

September, 1974
Volume 29 • Number 9

Second-class postage paid at Chicago, Illinois and at additional mailing offices.

FIRST CLASS
PERMIT NO. 57
CHICAGO, ILL.

**BUSINESS REPLY MAIL**

NO POSTAGE STAMP NECESSARY IF MAILED IN THE UNITED STATES

POSTAGE WILL BE PAID BY—

FOOD DRUG COSMETIC LAW JOURNAL

COMMERCE CLEARING HOUSE, INC.

PUBLISHERS of TOPICAL LAW REPORTS

4025 W. PETERSON AVE.

CHICAGO, ILL. 60646

# Subscription Order Card

*Old friends may use this card to extend their subscriptions.*

Enter our subscription to the FOOD DRUG COSMETIC LAW JOURNAL for the 12 months beginning with the current issue at $25.00 for the year.

[ ] Remittance herewith [ ] Send bill

8110—2359

**Signature & Title** .....

**Firm** .....

**Attention** .....

**No. & Street** .....

**City and State** ..... **Zip** .....

*Published by* COMMERCE CLEARING HOUSE, INC

# FOOD DRUG COSMETIC LAW JOURNAL

## Table of Contents . . . September, 1974




Volume 29 Number 9

# FOOD DRUG COSMETIC LAW JOURNAL

## Editorial Advisory Board

# REPORTS

## TO THE READER

"So Are They All—All Honorable Men—A Review of the DES Revocation Cases to Date," an article written by *Walter E. Byerley*, examines the controversy between the FDA and manufacturers over the use in animal feeds of diethylstilbestrol (DES), a hormone alleged to be a carcinogen. Mr. Byerley is a partner in the Washington law firm of Markel, Hill and Byerley. He also was Counsel of Record for two of the parties in the DES Premix Case. His article begins on page 460.

**Pharmaceutical Update IV.**—The following paper was presented at the Food Drug Law Institute's Pharmaceutical Update IV, which was held in New York City on May 22 and 23, 1974.

*Raymond D. McMurray*, a partner in the Washington law firm of McMurray and Pendergast, presents a summary of recent Supreme Court decisions which have greatly affected the pharmaceutical industry. The first landmark decision is the *Bentex* case which involved the effect NAS/NRC studies concerning the efficacy of pentylenetetrazol would have on "me too" drugs. The second case, *U. S. V. Pharmaceutical Corp. v. Weinberger, et al.*, further narrowed the applicability of the grandfather clause. The *Hynson, Westcott and Dunning* decision involved the question of a drug company's right to an administrative hearing before the FDA. Finally, the *CIBA* case reconfirmed that the FDA had the authority to determine whether a product is an old or new drug. The article, entitled "Legal Update Overview of Recent Judicial and Regulatory Developments in Rx and OTC Law," begins on page 469.

Vol. 29, No. 9 September, 1974

Food·Drug·Cosmetic Law
Journal

# So Are They All— All Honorable Men A Review of the DES Revocation Cases to Date

By WALTER E. BYERLEY

Mr. Byerley Is a Partner in the Washington Law Firm of Markel, Hill & Byerley, and Was Counsel of Record for Two of the Parties in the DES Premix Case.

ON JANUARY 24, 1974, the United States Court of Appeals for the District of Columbia Circuit rendered two decisions[1] in which it found that the Food and Drug Administration (FDA) had engaged in "palpably impermissible procedures," "scare tactics," and "illegal actions," all in furtherance of FDA's "paternalistic sagacity." How did it come to pass that FDA, long given *carte blanche* by the courts because of its reputation as "protector of the public weal," so angered the Court of Appeals as to require the use of such language?

Although the actions of FDA that aroused the Court all occurred within a nine-month period in 1972 and 1973, the genesis of the cases goes back to September 6, 1958, the date of enactment of the Food Additives Amendment[2] to the Federal Food, Drug, and Cosmetic Act.[3]

[1] *Chemetron Corporation, et al. v. HEW*, No. 72-1864, and *Hess and Clark v. FDA*, No. 73-1581.

[2] P. L. 85-929, § 4, 72 Stat. 1785.

[3] Act of June 25, 1938, 52 Stat. 1040.

## The Delaney Clause

An integral part of the Food Additives Amendment was the so-called "Delaney Clause," which provided that no food additive "shall be deemed to be safe if it is found to induce cancer when ingested by man or animal, or if it is found, after tests which are appropriate for the evaluation of the safety of food additives, to induce cancer in man or animal. . . ." The entire concept of the Delaney Clause is scientifically suspect, particularly in view of the fact that it prevents approval even of additives for which a no-effect level can be found, but that is another subject. For our purposes, it is sufficient to understand that enactment of the Food Additives Amendment placed in jeopardy the use of many substances in foods. Included among such substances was a synthetic estrogen known as diethylstilbestrol—and even better known as DES.

## Carcinogenicity of DES Questionable

DES, when administered to meat-producing animals and poultry, causes them to gain weight faster, on less food, than they would in its absence. In technical terms, DES increases feed efficiency and rate of weight gain.

Although direct proof of the carcinogenicity of DES is scanty, it is widely believed to be carcinogenic, since it is an estrogen, and some estrogens are known to be carcinogens. Therefore, under the absolute terms of the Delaney Clause, DES was banned from use in chickens and turkeys,[4] and its use in other animals was jeopardized.

## The DES Amendment

In 1962, Congress, recognizing that there should be circumstances under which a carcinogen (known or suspected) could be used in meat-producing animals, enacted the so-called "DES Amendment"[5] to the Delaney Clause. This Amendment provided that the Delaney Clause did not apply "with respect to the use of a substance as an ingredient of feed for animals which are raised for food production, if the Secretary finds (i) that, under the conditions of use and feeding specified in proposed labeling and reasonably certain to be followed in practice, such additive will not adversely affect the animals for which such feed is intended, and (ii) that no residue of the additive will be found (by methods of examination prescribed or approved by

[4] The original ban of DES (in poultry) gave rise to a hearing and, ultimately, to litigation in 1962. This case was finally decided, *sub nom. Bell v. Goddard*, 366 F. 2d 177, in 1966.

[5] P. L. 87-781, Title I, § 104(f)(1); 76 Stat. 785, 21 U. S. C. 360b(d)(1)(H).

the Secretary by regulations . . .) in any edible portion of such animal after slaughter. . . ."

Under this Amendment, use of DES in beef cattle became widespread. It did not adversely affect the animals to which it was administered, and no residues were found in edible tissues, using the "mouse uterine test" which the Secretary had prescribed.[6]

## DES Residue

When the Animal Drug Amendments of 1968[7] were enacted, the Delaney Clause, with its DES Amendment, was made an integral part of the provisions for approval of the use of New Animal Drugs.[8] Under these provisions, use of DES in beef animals continued. It was used both as an implant and as a direct additive to feeds. As an implant, it was to be implanted for a sufficient time before slaughter to allow it to be totally absorbed; as a direct additive to feed, its use was to be discontinued at least 48 hours prior to slaughter.

In 1971, the United States Department of Agriculture (USDA), which had the responsibility of monitoring meat for DES residues, began to employ a more sensitive test (gas liquid chromotography, or GLC) in its monitoring. As a result of the increased sensitivity, residues of DES began to be discovered in liver tissue and it was assumed that they had been present all the time, but at levels too low to be discovered by the prescribed mouse uterine test.

In view of these findings, in late 1971 FDA found it necessary to require that use of DES as a feed additive cease seven days before slaughter, rather than 48 hours. All manufacturers of DES for feed use complied with this label change, and, apparently, most feed-lot operators followed the new label instructions.

Nonetheless, USDA continued to find residues in about 2% of the beef livers it examined. Residues of DES were not found in any other edible portion of beef cattle. The FDA felt that even this small a finding required action on its part.

## FDA Issues Pronouncements

Thus, on June 21, 1972, FDA issued the first[9] in the series of pronouncements which ultimately resulted in the court's expressions of indignation which are quoted at the beginning of this paper.

---

[6] 21 C. F. R. 135g.26.
[7] P. L. 90-399, 82 Stat. 343.
[8] 21 U. S. C. 360b(d)(1)(H).
[9] 37 F. R. 12251.

The June 21 publication was, in form, a proposal by FDA to revoke all New Animal Drug Applications (NADA's) for the manufacture of DES premixes, and was, interestingly enough, entitled "Notice of Opportunity for a Hearing."

In the proposal, the FDA made it clear that there was no real intent to revoke the NADA's. Rather, the FDA said, though there was no problem as to safety, it was necessary to convene a hearing to discuss the DES problem, and the only lawful way to convene a hearing was to propose to revoke the NADA's. Affected parties were given the opportunity to object to the proposed withdrawal and, if they did so object, to present facts adequate to raise issues determinable at the proposed hearing. FDA listed several questions it had about the use of DES, and invited submission of facts to answer these questions.

## Manufacturers Respond

Most manufacturers of DES and DES premixes responded to the proposal, objecting to the withdrawal, demanding a hearing, and setting out facts which, at least from their viewpoint, raised issues sufficient to require a hearing. Most respondents also offered suggested answers to some or all of FDA's questions.

There matters rested until August 4, 1972. On that day a second pronouncement appeared,[10] incredible on its face, and even more incredible when viewed against the background of the June 21 proposal.

## FDA Claims "New Evidence" from USDA

The August 4 publication was a final order, denying all public hearings requested in response to the June 21 proposal and revoking all NADA's for manufacture of DES premixes. According to the order, this course of action was mandated by "new evidence" which had just come into the Commissioner's hands. This new evidence, it turned out, was a preliminary report from the USDA Research Facility at Fargo, North Dakota.[11] According to the FDA's interpretation of this preliminary report, USDA researchers had found residues of DES, even after 7 days' withdrawal, by use of a radio-

[10] 37 F. R. 15747.

[11] See document entitled "Progress Report" attached as Exhibit H to brief in support of Motion for Stay in Case No. 72-1864, U. S. Ct. of App. for the D. C. Circuit.

active tracer technique in which atoms of carbon-14 were attached to molecules of DES which was then fed to the test animals.

Oddly enough, however, the FDA's interpretation of the Fargo study did not accord with the interpretation of the USDA researchers who ran the study. The most that the USDA researchers were willing to say was that they found *radioactivity* in the animals at levels slightly higher than background. They had not then, and have not to this day, ever said that the increased levels of radioactivity necessarily meant DES residues.[12]

## Inadequate Data

Moreover, even assuming that radioactivity meant residues, the test itself was open to challenge on several grounds. Only ten test animals were used, with one control animal. Two test animals were slaughtered at 1 day, 2 days, 3 days, 5 days, and 7 days, respectively, after administration of the carbon-14 tagged DES. Residual radioactivity of various tissues, as well as excreta, was expressed in counts per minute (cpm). A "baseline" was established by burning paper, and this resulted in establishment of a background radioactivity of 46 cpm. However, the report indicates a "contamination" of the control animal of about 20 cpm, and assumes that the test animals were similarly contaminated. Therefore, any reading below 46 cpm is lower than background, and any reading below 66 cpm is suspect.

Of the edible tissue readings taken from the two animals slaughtered at 5 days, only one reading showed a cpm above 66. The liver of one steer showed 93 cpm. All other edible tissue readings ranged from 21 to 38 cpm.

Of the edible tissue readings taken at 7 days, again only one was above 66—the liver of one steer showed 121 cpm. All other readings were in the range of 18 to 45 cpm.

How much credence can be given to a preliminary report of a test using minimal numbers of animals in which the results are, at best, equivocal? Certainly, these data are not the sort of "hard" data that FDA would require in support of a New Drug Application or a Food Additive Petition. Nonetheless, FDA not only accepted this data, but stated that it mandated the ban of DES.

---

[12] As a matter of fact, a report given by the researchers to the American Society of Animal Science on August 2, 1972 differs in several significant details from the "Progress Report" relied upon by FDA.

## Ban on DES

FDA made it quite clear that the ban was mandated by the restrictions of the Delaney Clause.[13] Time after time in the August 4 order, FDA reiterated that there was no danger to public health. The Commissioner's conclusions are as follows:

"This action is required under the strict terms of sections 512(d)(1)(H) and 512(e)(1)(B) of the Act. These provisions, which contain the so-called Delaney Clause, require that there be no detectable residue. The new USDA study clearly shows residues at levels that are in the range of current detection methodology; new detection methodology is being developed that would be significantly more sensitive. Thus, under the law there is no alternative but to withdraw approval of the drug, even though there is no known public health hazard resulting from its use.

"It should be emphasized that the Commissioner has no reason to believe that use of DES in animal feed represents a public health hazard. No human harm has been demonstrated in over 17 years of use. Under the law, however, this (*sic*) continued use of the drug may no longer be permitted."

As if to underline the absurdity of FDA's position, the order goes on to state that the ban would not be fully effective until January 1, 1973, so that use of oral DES could be "phased out."

## The Controversy Continues

In form, the August 4 order was based upon the June 21 proposal and the responses to that order by affected manufacturers. Citing 21 C.F.R. 135.15(b), the regulation which allegedly empowers FDA to grant itself summary judgment, the Commissioner stated that none of the responses to the June 21 proposal raised facts sufficient to justify a hearing, in view of the progress report received from USDA.

Of course the comments did not refute the progress report. Under terms of the June 21 proposal, affected manufacturers had 30 days, or until July 21, within which to file comments. The progress report was not received by FDA until July 28 (a Friday) and was not made public until *after* the August 4 final order. The various affected parties therefore never had any opportunity at all to challenge the study and the conclusions FDA drew from it, or to adduce contradictory evidence. In short, the Commissioner granted himself summary judgment without ever giving the other side either notice of, or an opportunity to refute, or even see the "new evidence."

---

[13] It should be noted that in recent months, spokesmen for FDA have insisted that DES was not banned because of the Delaney Clause, but because of "lack of proof of safety." The reader is invited to read 37 F. R. 15747 and decide for himself the grounds of FDA's actions.

Three DES manufacturers objected to the final order, protesting against the lack of notice and lack of opportunity to refute, and demanded a hearing. The Commissioner denied these demands.

Faced with a Final Order of the FDA, with a hearing denied, these three manufacturers of DES premixes appealed to the Court of Appeals for a review of the Order[14] and requested a Stay pending that review. On November 7, 1972, the request for a Stay was denied. Thus, on January 1, 1973, use of oral DES ceased, while the parties waited for a hearing on the merits.

Meanwhile, use of DES implants continued, as they had not been involved in the Fargo study and thus were not covered by the August 4 order. However, studies were now being made on implants, using the carbon-14 method.

## Final Order Issued

These tests culminated in the issuance of a final order on April 27, 1973, banning the use of implants. Again, two manufacturers of implants appealed,[15] and requested a Stay. Although the Court of Appeals had denied oral argument on the Stay in the oral DES case, it granted argument on the Stay in the implant case.

Both in its briefs and at the oral argument on the Stay in the implant case, FDA abandoned its reliance on the Delaney Clause and attempted to convince the Court that its actions were based on considerations of safety. In view of the earlier pronouncements by FDA, this argument did not particularly impress the Court.

The Stay was granted on September 14, 1973, but was made conditional upon (1) the appellants submitting to FDA their "evidence" in opposition to the order, and (2) FDA convening a hearing during the month of October, 1973.

Appellants submitted their evidence. FDA, after reviewing the evidence, issued yet another order in the *Federal Register*,[16] stating that the evidence was insufficient and thus there would be no hearing.

On November 12, 1973, the Court of Appeals combined the implant and premix appeals for argument on the merits, and set the oral argument for December 7, 1973.

---

[14] Case No. 72-1864.
[15] Case No. 73-1581.
[16] 38 F. R. 29510, October 25, 1973.

The major issue at the oral argument was whether FDA had been justified in issuing the two bans, primarily upon the carbon-14 studies, without ever giving any of the aggrieved parties the opportunity to refute those studies. Counsel for FDA argued that, under the regulations which entitle the Commissioner to grant himself "summary judgment," and in view of the dire threat to public health, the actions of FDA were not only proper, but necessary.

## Court Issues Opinion

Again, the Court was not impressed. On January 24, 1974, the Court issued its opinions. Pointing out that FDA had been consistent only in its inconsistency as to the grounds for the order, and indulging itself in several expressions like those quoted at the beginning of this article, the Court unequivocally revoked the August 4, 1972 and April 27, 1973 orders, and remanded the case to FDA to begin again the entire administrative process designed to culminate in a hearing on the matter. The Court also made it abundantly clear that it would not accept anything less than a full hearing as the basis for the next final order on DES to come out of the FDA. It also made it clear that the production, sale, and use of DES could resume, thereby indicating its unconcern over the belatedly raised safety issue.

To any objective observer, the Order of the Court would seem to require that FDA return to the *status quo* on June 21, 1972, and issue a proposal to revoke DES NADA's, setting forth a resumé of the evidence tending to show the necessity for such revocations, and providing an opportunity for affected parties to refute that evidence.

As of the date this is written, none of this has occurred. What has occurred is a new tactic on the part of FDA which appears designed to continue to avoid a full hearing on the merits.

## FDA's Subtle Protest

In the *Federal Register* of March 27, 1974,[17] FDA published a proposal to revoke the official method[18] for determination of DES residues in animal tissue. This apparently sets the stage for FDA to claim that, if there is no "method of examination prescribed or approved by the Secretary by regulation," then there can be no use of DES under 21 U. S. C. 360b(d)(1)(H), and thus no basis for use at all.

[17] 39 F. R. 11299.

[18] 21 C. F. R. 135g.26.

This, of course, would enable FDA to avoid making scientific judgments on the sufficiency of the evidence showing DES to be a carcinogen, and showing that residues of DES do, in fact, remain in edible animal tissue.

In fairness, it should be pointed out that FDA spokesmen have stated to the writer that the issues raised by the proposed revocation of the official method are issues to be added to the hearing and not to be in lieu of them. Since FDA spokesmen are all honorable men, we must assume that this is true.

### The Dangerous Powers of Government Agencies

Nonetheless, the story of DES to this point indicates the dangers inherent when any government agency—even an agency composed of honorable men—arrogates unto itself the sole authority to decide summarily the questions within its jurisdiction. FDA saw what it believed needed to be done, and proceeded to do it, posthaste, without regard for the applicable law or regulations. When challenged, FDA sought to cloak itself, as it has done so successfully before, in "protection of the public health."

It did not work this time—but they will try again. **[The End]**

---

## DISPENSING CONTAINER SPECIFICATIONS PROPOSED BY FDA

A requirement that prescription drug labeling specify the type of container in which the drug can be dispensed that will maintain its original identity, strength, quality, and purity has been proposed by the Food and Drug Administration. The FDA stated that the increase in the use of packaging materials other than glass necessitates instructions for pharmacists as to which containers will afford protection against decomposition or deterioration due to heat, light, or exposure to air or moisture. The FDA also proposed requiring that an identifying lot or control number be included in labeling so that the complete manufacturing history of the drug package can be determined.

The National Formulary and the United States Pharmacopeia are developing proposed standards and test procedures for determining the adequacy of various dispensing containers, the FDA stated. These standards are applicable to multiple-unit containers, and the information required in the FDA proposal would not be required on unit-dose packaging. The FDA has proposed that its requirements be implemented concurrently with the container standards that will be proposed by the N. F. and the U. S. P.

CCH Food Drug Cosmetic Law Reporter, ¶ 45,182

---

# Legal Update Overview of Recent Judicial and Regulatory Developments in Rx and OTC Law

By RAYMOND D. McMURRAY

Mr. McMurray Is a Partner in the Law Firm of McMurray and Pendergast, in Washington, D. C.

SINCE THE LAST PHARMACEUTICAL UPDATE (May 21 & 22, 1973), we have had an extremely important legal year. The place to start then is with the four landmark decisions of the Supreme Court handed down on June 18, 1973.

These cases involve fundamental interpretations of various contentious provisions of the federal Food, Drug and Cosmetic Act (FD&C) which had been the subject of debate among the Food and Drug Bar and directly with the Food and Drug Administration (FDA).

## Landmark Decisions of the Supreme Court

First is the *Bentex* case.[1] Here, a group of drug companies marketing pentylenetetrazol had filed suit against the FDA, alleging that their products were generally recognized as safe and effective and, therefore, not new drugs. They asked not to be subjected to the regulatory results of a National Academy of Sciences and National Research Council (NAS/NRC) panel report which had found that other companies' pentylenetetrazol, which were the subject of new drug applications (NDA's), lacked substantial evidence of efficacy. They

[1] *Weinberger v. Bentex Pharmaceuticals, Inc., et al.*, 412 U. S. 609 (1973).

also claimed to have been on the market prior to October 10, 1962. This means that the question before the court was whether a so-called "me too" drug could be subject to the NAS/NRC results even if it had never held an NDA and even if it might meet the literal requirements of the grandfather clause. The Supreme Court held that such products would be subject to the NAS/NRC results. Thus, "me too" products must meet the standards announced by the FDA for NDA'd drugs, notwithstanding any other legal arguments that the "me too" manufacturers might make. The Court held that the FDA has jurisdiction to decide, with administrative finality, the new drug status of individual drugs or classes of drugs. The FDA, according to the Supreme Court, should not be required to litigate, on a case-by-case basis, the new drug status of each drug on the market. The administrative decision as to new drug status is, of course, judicially reviewable, but the primary jurisdiction for such determination lies with the FDA.

## Narrowing the Application of the Grandfather Clause

The second case decided by the Supreme Court involved USV's bioflavonoid product.[2] There, a lower court had held that the courts had jurisdiction to determine if that product was protected by the grandfather clause, and that the FDA did not have authority to decide this question conclusively. The lower court also had held that USV's own "me too" versions of its own NDA drug were subject to the NAS/NRC decisions. The Supreme Court held that the phrase "any drug," as used in the grandfather clause, is used in a generic sense. This means that the "me too's," whether of products of the same or different manufacturers, covered by an effective NDA, are not exempt from the efficacy requirements of the 1962 law.

Thus, the grandfather clause has been further narrowed so that it applies *only* to those drugs which meet the definition in the grandfather clause *and* are not "me too's" of other drugs which did have NDA's. This latter refinement is clearly not a portion of the statutory language, but that language must now be read with this refinement in mind by reason of this decision.

## The *Hynson, Westcott & Dunning* Case

The third decision involves the important question of a drug company's right to administrative hearings before the FDA. This is

---

[2] *U. S. V. Pharmaceutical Corp. v. Weinberger, et al.*, 412 U. S. 655.

the *Hynson, Westcott & Dunning* decision.[3] In this case, a lower court had ruled that the company had presented enough evidence, in its request for a hearing following FDA's notice of its intention to revoke the company's new drug application, to entitle it to a hearing. In this decision, the Supreme Court sustained the summary judgment mechanism instituted by FDA to determine whether or not administrative hearings must be held. Under this mechanism a drug company is compelled to present, in its hearing request, substantial evidence that the drug is effective, and if FDA concludes that such substantial evidence has not been presented, no hearing is granted and the drug is removed from the market without a hearing. The Supreme Court sustained this mechanism as a valid exercise of administrative discretion.

In the event that the FDA denies a hearing, the Supreme Court decision mandates that a Court of Appeals, in reviewing this administrative denial, "must determine [that] the Commissioner's findings accurately reflect the study in question, and, if they do, whether the deficiencies he finds *conclusively* render the study inadequate or uncontrolled . . .".[4] (Emphasis added.) What does "conclusively" mean? It will take further litigation to find out. However, in the instant case, Hynson, Westcott & Dunning was granted a hearing by the device of remand to the Agency.

## Definition of an "Old Drug"

Perhaps the most important statement in the *Hynson* decision deals with a problem other than the hearing requests problem. It had long been accepted that a drug could be an "old drug" or more precisely "a not new drug" if the drug was generally recognized as safe and effective. It was further thought that this general recognition could be based upon expert medical opinion and need not be based upon any particular type of scientific data. The Supreme Court severely narrowed this thinking by ruling that a drug is not a "new drug" if general recognition is based upon a consensus of expert opinion, but only when that expert consensus is founded upon "substantial evidence" as defined in Section 505(d). This means that a drug can be an old drug only if there is substantial evidence of efficacy by adequate and well-controlled studies which demonstrate that the product is, in fact, effective. This means clinical work akin to that necessary for NDA submissions.

---

[3] *Weinberger v. Hynson, Westcott & Dunning*, 412 U. S. 609 (1973).

[4] *Ibid*, p. 622.

## The *CIBA* Case

The final case before the Supreme Court involved CIBA.[5] Here, a lower court had ruled that the FDA had the authority, in an administrative hearing, to determine whether a product was a new or old drug. CIBA had appealed this decision. The Supreme Court held, in a manner consistent with the previous three decisions, that the Agency does have such jurisdiction, and primary jurisdiction at that.

Waiting in the wings, of course, were other cases which would be affected by these decisions. Specifically, there was the *Squibb* case[6] which was before the Third Circuit and which by agreement was deferred pending the outcome of the Supreme Court arguments. This case was on appeal from an FDA order revoking Squibb's NDA's on several drugs. Squibb had been denied an evidentiary hearing at which, the company alleged, it would have produced substantial evidence of safety and effectiveness.

## Meaningful Comparison of the Submissions

Echoing the Supreme Court's admonition in the *Hynson* case that a court, in reviewing an order of the Commissioner denying a hearing, must determine whether the Commissioner's findings accurately reflect the study in question, and if they do, whether the deficiencies he finds *conclusively* render the studies inadequate or uncontrolled in light of pertinent regulations. The Court held:

> (1) since efficacy alone was the ground for remand in *Hynson,* there remains the question whether summary proceedings are also available to questions of safety. The remand was to deal with that question and;
>
> (2) the *Hynson* submission "appears to be a matrix or benchmark against which other submissions may be assayed." The remand called for a "meaningful comparison" between the two submissions. A comparison which presumably would also be subject to court review but which was suggested could better be done in the first instance by the expert Agency.

So far there has been silence from the FDA. I am sure they are still wrestling with the "meaningful comparison" and I am also certain that they will wait until after the hearing in the *Hynson* case before doing so.

---

[5] *CIBA Corp. v. Weinberger, et al.,* 412 U. S. 640 (1973).

[6] *E. R. Squibb & Sons, Inc. v. Weinberger, et al.,* 483 F. 2d 1382 (C. A. 3, 1973).

That hearing is to be held at the FDA offices in Rockville on the morning of June 17, 1974. A notice in the *Federal Register* for Thursday, May 2, 1974[7] called for written appearances to be filed with the Hearing Clerk no later than May 13, 1974. All of which sounds very straightforward; however, a prehearing conference was also noticed in the same issue of the *Federal Register*[8] for the purposes of simplifying the issues; of obtaining stipulations, admissions of facts and documents; limiting the number of expert witnesses; scheduling the witnesses to be called; and submitting in advance all documentary evidence and other matters in aid of the disposition of the proceeding. This conference was scheduled to be held on May 15 but has been postponed (on Motion of Hynson) to June 15.[9] It is not inconceivable that between June 5 and June 17 the Commissioner, in reviewing the results of the prehearing conference, might determine that the *Hynson* submissions still do not present material issues of fact to be tried, and once again might file a Notice of Intention to Revoke, or actually revoke, especially if no new data is presented.

## Bolstering the June Decisions

Other cases, of course, came along during the last year to bolster the June decisions. *The National Ethical Pharmaceutical Association and Pharmaceutical Associates v. Weinberger, et al.*,[10] which was decided in September of 1973 in the Federal District Court in South Carolina, represents an interesting theory. Plaintiffs asked in a declaratory judgment action for the Court to declare *as a matter of law* that once a drug is found effective, and the prescribed labeling is published by FDA (in the *Federal Register* announcement), then the drug to which such labeling applies is no longer a new drug. There seemed little question that FDA has primary jurisdiction to decide whether or not a drug is a new drug and the Court so found citing *Hynson* and *Bentex*. The government moved to dismiss the complaint and this decision is a result of granting that motion. The Court said that the touchstone of "not new drug" is the general recognition of safety and effectiveness by qualified experts (presumably, though not said, as narrowed again by the substantial evidence requirement) and *not* any declaration, even by FDA, that certain administrative activities may take place, for example, the submission of an abbreviated NDA based upon label-

[7] 39 F. R. 15341.
[8] 39 F. R. 15342.
[9] Personal Communication.
[10] 365 Fed. Supp. 735 (D. C. S. C., 1973).

ing set forth in a *Federal Register* announcement. Hence, plaintiffs are directed back to the FDA as the more able arbiter of complex scientific and medical determinations.

Plaintiffs may petition FDA to determine if the drugs are still "new drugs." Following an administrative determination of that question, plaintiffs may then seek judicial review if they so desire and at that time raise the question of the impact of the prior FDA announcement.

A rather obvious decision was reached in the case of *North American Pharmaceutical Inc. v. HEW* consolidated with *Costos Pharmaceutical Co., Inc. v. FDA*[11] decided by the Eighth Circuit Court in December, 1973. A contention by manufacturers of "me too" anorectic drugs, in an action to set aside the withdrawal of approved NDA's, that "clinical studies and facts before the Commissioner were scanty and incomplete evidence" proved their own undoing. Since they had the burden of producing substantial evidence, their admission that there was none defeated their claim.

Almost as an aside, the contention that the plaintiffs lacked proper notice of impending FDA action was turned away with the observation that it was incumbent upon "me too" manufacturers to keep themselves informed of the status of the drug they had copied. It was also held that, as with new drug status, FDA must first decide the grandfather status of a drug with review in a District Court (not the Court of Appeals), if necessary, citing *Bentex*.

The proposition that new animal drugs are to be treated identically with new drugs for human use was articulated in the *Agri-Tech Inc. v. Richardson*[12] case in the Eighth Circuit in August. This case upheld the proposition that the burden of proof of efficacy was on the manufacturer, citing *Hynson*.

The world had to wait until late January before receiving some good news as a fallout from the June decisions. Two decisions came down from the Circuit Court for the District of Columbia Circuit putting something of a hobble on the high-riding Food and Drug Administration. These cases are *Hess and Clark, et al. v. Weinberger, et al.*[13] and *Chemtron Corporation, et al. v. HEW*.[14] Both cases dealt with diethylstilbestrol (DES) as a feed supplement for cattle growth.

---

[11] 491 F. 2d 546 (C. A. 8, 1973).
[12] 482 F. 2d 1148 (C. A. 8, 1973).
[13] Nos. 73-1581 and 73-1589, decided Jan. 24, 1974, — App. D. C. — (F. 2d, 1974).
[14] Nos. 72-1864 and 72-2217, decided Jan. 24, 1974, — App. D. C. — (F. 2d, 1974).

## The *Hess and Clark* Case

In *Hess and Clark,* Judge Leventhal wrote a hard-line opinion reaching the only viable conclusion where, in essence, FDA changed the ground rules in the middle of the game. A Notice of Intention to Withdraw approval of New Animal Drug Application's (NADA's) covering diethylstilbestrol (DES) implant pellets in June 1972 stated that the purpose of the notice was to trigger public hearings "to determine whether it was appropriate to withdraw approval, to institute new restrictions, or to take other action." In August 1972, the FDA banned the use of DES as an additive to cattle feed on the basis of the results of tests which revealed small amounts of DES residue in beef livers. In its order denying a hearing to the feed additive manufacturers, the FDA stated that testing of implants had recently involved a new technique employing radioactive tracers. When the FDA withdrew approval for the implants in April 1973 on the basis of results of the new tests, it also denied implant manufacturers a hearing. The June 1972 notice did not contain any of the data on which the FDA relied in withdrawing approval of the implants since results of the radioactive tests were not known at that time. The FDA contended that the August withdrawal of approval of DES as a feed additive served as adequate notice to the implant manufacturers of the new test method involved and of the FDA's intention to withdraw approval of the implant pellets. However, the FDA made no report of the results of the new tests to the implant manufacturers. The FDA's finding that insufficient evidence had been submitted to warrant a hearing was made without giving the implant manufacturers an opportunity to submit material to dispute the results of the radioactive tests. Without adequate notice communicated to the manufacturers in time for them to respond, the Commissioner's use of summary withdrawal was invalid. His order was vacated and remanded by the Court with instructions to hold a hearing.

Also, the Court held that FDA had failed to meet its burden under the general safety clause of Section 512(e)(1)(B) of the Act as a basis for denying a hearing before withdrawing approval of the NADA's.

## Burden of Proof Under General Safety Act

Even if its notice of withdrawal were defective, according to the FDA, the withdrawal order should not have been vacated because it was proper under the general safety clause. That clause permits with-

drawal of an outstanding new animal drug application, following notice and opportunity for a hearing, if new evidence indicating that such drug is not safe becomes available after the application has been approved. In this case the new evidence consisted of results of radioactive tracer tests begun months after a notice of withdrawal of approval was issued, that indicated the presence of DES in the livers of cattle after slaughter. To meet its burden under the general safety clause without granting a hearing to the manufacturers, the FDA would have to show that no material issues of fact existed concerning either the relationship between DES implants, as used in commercial applications, and the residues detected in testing, or the relationship between the detected residues and the safety of DES implants. In light of submissions by the manufacturers to the FDA subsequent to the withdrawal order, substantial issues of fact remained unresolved about both of these issues. Since notice adequate to generate these submissions prior to withdrawal would not have resolved the issues without a hearing, failure to grant a hearing would have invalidated the withdrawal even if notice were not defective.

## Reinstatement of Use Regulations

Finally, the Court *insisted* that the products continue to be sold. The Commissioner's so-called "Motion for Clarification" stated that even though the Court might enter an order vacating the FDA's withdrawal of NADA approval, the Court had no power to review the revocation by the Commissioner of the governing use regulations. Not so, said Judge Leventhal; a court order vacating the Commissioner's order of withdrawal reinstates the *status quo*. Since the Act requires the Commissioner to revoke use regulations when he withdraws approval of an NDA, it follows that the Court's vacation of his withdrawal reinstates the use regulations.

Now, about the summary judgment procedure, the Court, citing *Hynson,* said that there is no doubt of its general validity, but, said the Court, such summary judgment procedures must be applied consistently and with basic fairness, attributes which he found lacking in the instant case.

The *Chemtron* case decided the same day deals with DES feed additives (as against implant pellets in *Hess and Clark*) and arrives at the same conclusion based on similar circumstances. Again, in this case the Court specifically finds that the products can return to the market.

## Revocation of DES Residue Test Methods

In a rather sophomoric ploy, FDA on March 27, 1974 published in the *Federal Register* a proposal to revoke the test methods for determination of DES residue levels. After explaining that neither one of the presently available test methods (quantitative or qualitative) was thought to be sufficiently sensitive to find residues in edible tissues below 10 parts per billion (stating that recent studies still in the experimental stage have picked up residues of around 2 parts per billion) the Commissioner found himself impelled by the Delaney Clause to revoke the present methods even without the availability of a validated substitute method.

Most comments in response to the proposal urged deferral of the test revocation until after the DES hearing. To my mind these were eminently reasonable suggestions since FDA should not be allowed to accomplish by indirection that which it could not do directly even though wrapping itself piously in the cloak of the technical language of the Delaney Clause.

Since DES has been determined to be a known carcinogen it follows that revocation of all test methods available to take it out of the zero residue exemption to the Delaney Clause is to *de facto* nullify all NADA's dependent on such tests. There must be more to be heard on this subject in the next few weeks.

## Labeling of Hypoglycemics

Before getting to the two most recent decisions in April and early May, we should be aware of a class action suit brought by the Committee on the Care of the Diabetic: *Bradley, et al. v. Weinberger*,[15] First Circuit, decided July 31, 1973.

This case represents a unique thrust at the dragon; 178 physicians sought a preliminary injunction against FDA promulgation of regulations requiring labeling of hypoglycemics to carry a strong warning to physicians that their use was to be only after a decision that other treatments were inadvisable. The finding of a government-sponsored study that oral hypoglycemics apparently increased the danger of cardiovascular mortality was given wide publicity. The 178 doctors challenged the study in all its particulars and claimed that the "final" labeling proposed by FDA failed to reveal a substantial body of expert opinion to the contrary—in short, a lack of fair balance.

---

[15] 483 F. 2d 410 (C. A. 1, 1973).

In the first attempt, a Temporary Restraining Order (TRO) and the preliminary injunction were denied (for the usual reasons). Later, plaintiffs moved for leave to amend their complaint supported by 13 affidavits attesting to the controversy over the results of the study. New motions for a TRO and preliminary injunction were made. After hearing, the District Court granted the motions to amend and granted the preliminary injunction (as an aside it is interesting to note that plaintiffs' standing to sue was never challenged at any point).

The novel issue this time was that the proposed labeling itself was misleading and, thus, the drug misbranded if such labeling was applied to it because it failed to reveal the existence of a "material weight of contrary opinion among qualified experts."

The injunction was vacated and the case remanded to FDA to test this novel theory which was not before the Commissioner when the decision was made. There are two points to note here: (1) this is the first time the law and regulations have been turned against FDA at least insofar as fair balance is concerned and, (2) because there had been no argument on this theory before the Commissioner, the Court held that there had been no exhaustion of administrative remedies. Possibly, in order to avoid a further appeal, the Court "hoped" that the parties which had been conferring throughout the litigation would eventually work out a responsible solution.

## The Cooper Labcratories Case

In April, the Court of Appeals for the District of Columbia handed down a decision in *Cooper Laboratories, Inc. v. The Commissioner of the Food and Drug Administration.*[16] This was on appeal for review of the Commissioner's summary withdrawal of an NDA. Although the appeal was filed before the *Hynson* case, it was conceded by both parties that *Hynson* governed. Therefore, arguments against the FDA requirement for "adequate and well-controlled investigations set forth in 21 CFR Section 130.12(a)(5)" and against the use of summary action were foreclosed. The sole question was the propriety of the method used in denying a hearing.

And, strangely, the majority, while clearly stating that FDA had erred in its procedure, nevertheless did not remand. A forceful dissent was filed by Judge Leventhal.

---

[16] U. S. C. A. D. C. No. 72-1866, decided April 19, 1974. — F. 2d (C. A. D. C., 1974).

Cooper had asked for a hearing based upon several affidavits and a submission of reports of studies. The very order denying a hearing set forth the Commissioner's conclusion concerning the data submitted. There had been no opportunity for the company to rebut. Seemingly clearly within the interdictions of *Hynson*, the Court found the other way.

Here's how:

(1) Cooper is construed by the Court to have asked for a waiver of the regulation requirement as far as adequate and well-controlled studies are concerned. The fabric of this argument is that because Cooper says that the nature of the disease being treated by the drug does not lend itself to the type of double-blind cross-over study so much in favor at FDA that such allegation is in effect a petition for a waiver in favor of clinical impressions. Having come this far in tossing down its own gauntlet, the Court, "with reluctance," picks it up and accepts the "invitation" to treat Cooper's allegations as a *de facto* waiver petition. This, because the FDA does not have a set procedure for such waivers or petitions under 21 CFR Section 130.12 (a)(5)(ii)(a). Having thus set up the straw man, the Court promptly knocks him down by finding the petition for waiver deficient!

(2) The Court then proceeds to study in great detail the medical tests as controlled investigations. What it does is adopt the language and findings of the Commissioner without being critical of such findings and indeed categorizing studies, as did the FDA, as unfavorable, uncontrolled and poorly controlled. Having thus paralleled the thinking of the Commissioner, the Court states that in discussing these materials and in reaching its conclusions, the order is "artlessly drawn." Artlessly drawn but nevertheless reviewable.

The Court then indulges itself in a separate section of its opinion called "A Caveat". What the caveat says in so many words is that FDA did not follow the *Hynson* case nor did it follow its own procedural rules. It became the job of the Court to do FDA's work for it. And it did so, *post facto*—clear violation of its own rule in *Hess and Clark* and of the Supreme Court's rule in *Hynson*. The Court stated that it felt that the Commissioner clearly understood what he was about though he didn't do it correctly and therefore the Court would not demand "chapter and verse citation."

The opinion then goes on to state that "in future, however, we shall apply a stricter rule of construction to administration orders associated with summary action." In other words, the next litigant in

Cooper's position, given similar facts, will find that his case will be remanded to FDA for further proceedings consistent with the law. However, Cooper was denied that which future litigants will be granted. This inherent inconsistency and unfairness in the application of the law and the misapplication of the *Hynson* and the *Hess and Clark* decisions was the burden of Judge Leventhal's dissent. The case is now on petition for rehearing with a suggestion for *en banc* review by the total circuit panel. In its present posture, Cooper is and must be distinguished on its facts and it also must be considered an aberration as far as the uniform and even-handed administration of justice is concerned.

## The *Allevaire* Case

Now we come to the *Allevaire* case which was decided on May 2. This is *Sterling Drug Inc., et al. v. Weinberger*[17] in the Second Circuit.

Here is a case, like *Hess and Clark*, in which FDA shifted the basis for denying a hearing and withdrawing certain NDA's in midstream. In fact, in this case, FDA shifted at least twice. First, in the initial notice claiming that the drug, as stated by the NAS/NRC panel, was no better a muco-evaculant agent "than water." The companies holding the appropriate NDA's met this statement with studies and when FDA withdrew the NDA without hearing, stating the studies were not adequate and well-controlled, an appeal was taken. In *that* appeal (before argument) FDA moved the Court to remand to it, conceding that FDA had failed to consider relevant material in petitioners' submission. Motion was granted. There evidently was reconsideration and a full 14 months later a second order denying a hearing and revoking the NDA's was filed using the same ground, that is: not adequate and well-controlled studies, but adding the criticism that water was not a proper control, stating that a proper control would be Allevaire without the active ingredient tyloxapol.

Petitioners asked FDA to reconsider its order offering extensive rebuttal. Things being what they are at FDA, they also took the precaution of appealing to the Second Circuit Court to set the order aside. At the very last minute, FDA again did a turnabout *and* terminated the order *and* reinstated the NDA's, stating that the request for hearing should be re-evaluated. FDA moved to dismiss the appeal pending against that order. But even before *that* motion could be argued, FDA issued still another order withdrawing the NDA's

[17] — F. 2d — (C. A. 2, 1974).

without hearing, and this time abandoning all the other grounds. It based the order on the assertion that Allevaire was a fixed combination drug not meeting the published requirements for fixed combinations, and all the previously submitted material was irrelevant to that issue. Petitioners again appealed from that order. In the meantime, FDA's motion to dismiss the appeal from the earlier order was denied and it was consolidated with the appeal from the later order.

In stating its position that the earlier order, being moot, should not be the basis for an appeal, FDA's brief (quoted by the Court) contains this incredible language: "We confessed error in that order (the earlier one) before this Court . . . and petitioners objected. We again confess error with the hope that petitioners will not look a gift horse in the mouth a second time."

The Court, in fact, goes on to dismiss the earlier appeal as moot *but* takes the Agency to task for switching the rules and if not stating outright, at least implying that petitioners should have guessed at the new grounds and met them too. No such guesswork can be required; the Agency must specifically announce its grounds and provide an opportunity for rebuttal. After discussing *Hess and Clark* as applicable and stating that the question of whether or not Allevaire was indeed a combination drug was not for decision at this appeal, the Court upheld the petitioners and reinstated the NDA's. The ball is now in FDA's court.

## Effects of the June Decisions

In summary, the fallout thus far from the June decisions seems to be pretty much as follows:

FDA is the prime arbiter for initial decisions as to the new drug status of a compound and its grandfather status. The summary proceedings engaged in to avoid hearings have judicial approval but FDA must give full, fair and clear notice of its objections and respondents must be given an opportunity to rebut these contentions prior to a finding by the Commissioner that no issue of fact exists and on that score denying a hearing. Also, what is good for human medicine is also good for animal medicine; the same principles applying. There is still that minor note left as a legacy in the *Squibb* case that the submissions in *Hynson* must act as a matrix against which all other submissions are to be compared. I would judge that something will have to be done about that.

In order to meet its obligations and to implement the Supreme Court decisions in *Hynson, CIBA, Bentex* and *USV*, the FDA published in the *Federal Register* for December 21, 1973 proposed regulations on the Requirements of Notice of Opportunity for Hearing, Request for Hearing and Grant or Denial of Hearing. The final regulations, with the usual preamble, were published on March 13, 1974. The order became effective on April 12, 1974.

In general, there seems to be a genuine attempt on the part of FDA to meet the Supreme Court requirements while at the same time giving itself the widest latitude in which to deny a hearing.

## Two Types of Notices for Hearings

The regulation continues to impose the burden of proof on the applicant or respondent once a Notice of Intention to Withdraw is published. That notice can either be general or specific and in either case shifts the burden of proof. Thus, there are two types of Notice of Opportunity for Hearing which carry with it the summary judgment procedure. The first type of notice the preamble states is comparable to a general complaint filed in a Court which only summarizes in a general way the information leading the FDA to issue the notice. It is sufficient to initiate a hearing but is not sufficient immediately to initiate summary disposition of the case against a person requesting a hearing. However, the use of the general type of notice does not absolutely preclude later summary disposition of the matter. If the Request for Hearing indicates that there may be a lack of any genuine issue of fact, however, it would not be proper to enter summary judgment at that point. Instead, the proposed Denial of the Hearing would be required to be furnished to the person requesting the hearing who would then have an opportunity to demonstrate that a genuine issue of fact does exist. In effect, the proposed Denial of the Hearing would be comparable to a summary judgment motion filed with the Court and would provide the other party with an opportunity to controvert it and thus, would fully comply in the eyes of FDA with the elements for summary judgment set out in the *Hess and Clark* decision. The regulation provides for mailing to the respondent or the person asking for a hearing notice of the specific findings which he would then have a chance to controvert. If at that time, in the judgment of the Commissioner, there was still no genuine issue of fact, summary judgment would be entered without hearing which the respondent could then have reviewed judicially.

The second type of notice which FDA compares to a summary judgment motion filed in a Court specifies with sufficient particularity the precise issue on which FDA proposes to take action and informs the affected party that summary judgment may be entered in the case unless that party demonstrates that there is a genuine issue of fact sufficient to justify a hearing. This is broken down to provide that the notice may be given in two different ways. First, the notice itself may contain the detailed description and analysis of the facts which have led to the proposed action. This is an attempt specifically to meet the *Hess and Clark* decision. Secondly, the notice may refer to detailed requirements specified in the controlling statute and regulations in lieu of analyzing all of the facts in detail and may state that because those specific requirements have not been met, the action specified is proposed to be taken. This is evidently the type of administrative summary judgment procedure which received approval in the *Hynson* case. Regardless of which type of notice or which type of procedure is used, the burden of coming forward with sufficient data or information to demonstrate the existence of a genuine issue of fact then falls upon the affected party. Once again, if the Commissioner finds that the submissions do not raise a genuine issue of fact, summary judgment may be entered at that point.

## GMPs

In August in *United States v. An Article of Drug . . . White Quadrisect,*[18] the Seventh Circuit upheld Good Manufacturing Practices (GMPs), stating that they were not a constitutionally vague standard. The District Court found violations such as failure to keep basic production records, inadequate testing of active ingredients before use and insufficient tests of the finished products prior to shipment. These findings were not contested, so a pure test of the statute and regulations insofar as due process is concerned was able to be had. Defendant attacked the meanings of "current" and "good" which the Court held were adequate in the context of the statute and regulations to notify defendant that its conduct was prohibited. The Court held that the Good Manufacturing Practices provision is "as precise as necessary under the circumstances." That is, the defendant could find the meaning of the phrase within the relevant context without strain.

[18] 484 F. 2d 748 (C. A. 7, 1973).

## Vitamins and Dietary Supplements

When the Dietary Supplement regulations were published everyone knew that there would be court challenges of all or parts of it. A couple of cases in that area are worth looking at for their rather interesting findings. In July of last year the Eighth Circuit Court in *United States v. An Article of Food . . . Nuclomin*[19] upheld a District Court finding that the mere inclusion on the label of a dietary supplement of ingredients with either no nutritional value *per se*, or in quantities so minute as not to enhance the nutritional value of the product, was false and misleading, subjecting the product to seizure. The point was that such a label could persuade a purchaser that the product possessed greater nutritional value than it actually had.

Disregard the fact that because the product was properly labeled in compliance with 21 CFR 125.3(a)(2) and 125.4(a)(2) concerning the statement of ingredients and their need in human nutrition, it thereby did not violate Section 403(j) and 21 CFR 343(j) dealing with the misbranding of special dietary supplements. However, it *did* violate the general misbranding provision in Section 403(a) of the Act which bars false and misleading labeling in *any* particular.

The offending ingredients were choline, inositol and paraaminobenzoic acid (PABA). The case gave further credence to the proposition that proof is not required that the public was misled. Also, the fact that a product may be safe and harmless is of no consequence if the labeling is false and misleading.

Of somewhat more interest is the maneuvering of certain plaintiffs who are attacking the dietary supplement regulations. In *National Nutritional Foods Association and Solgar Co., Inc. v. Weinberger, et al.*[20] the Southern District Court of New York, in September, 1973, denied a motion for preliminary injunction against enforcement of that part of the regulations requiring preparations containing Vitamin A and Vitamin D, in excess of 10,000 International Units per dose and 400 International Units per dose respectively, be sold only on prescription. The contentions were: (1) vitamins are foods and the Commissioner exceeds his authority by regulating food as drugs; (2) even if vitamins are drugs they can't be defined as Rx drugs, and (3) toxic doses are substantially higher than those set forth in the

[19] 482 F. 2d 581.

[20] 366 Fed. Supp. 1341 (D. C. SDNY, 1973).

regulations by the Commissioner. Plaintiffs lost on all three counts because: (1) the Commissioner was not arbitrary and capricious, he was acting within his statutory authority in ruling that vitamins are food only so long as they are used within their recommended doses (presumably within the proposed RDA's) in excess they fit the definition of a drug and may be regulated as such; (2) any potential for harmful effect as outlined in 21 USC § 353 gives the Commissioner the necessary authority to classify certain units of vitamins as prescription drugs; and (3) the Commissioner is not compelled to set the highest limits but may in his discretion provide a substantial margin of safety. This was confirmed by the Second Circuit Court in December, 1974.

These same plaintiffs sought to take the deposition of Commissioner Schmidt to inquire into the manner in which he had reviewed the materials prior to signing the order only a very few days after he took over as Commissioner. They claimed that he had not had time for sufficient review and therefore the statutory requirement was not met. The government moved to vacate the notice of deposition and for summary judgment. Judge Frankel granted both motions. In so doing the Court made abundantly clear the proposition that Section 701(a) regulations, though dubbed interpretive (or indeed no matter how dubbed), have the full force and effect of law. Citing *Hynson* and the *Bentex* case, I think it is interesting to listen to what the Court had to say:

"Wherever the legislative history alone might leave us, the Commissioner's position finds solid support in Section 701(a) of the Act, 21 USC § 371(a), and judicial as well as administrative constructions of this provision. Section 701(a) empowers the Commissioner, as delegatee of the Secretary of Health, Education and Welfare, 21 CFR § 2.120 (1973), 'to promulgate regulations for the efficient enforcement of' the Act.... Plaintiffs argue this is authority for mere 'housekeeping' provisions, and they contrast subsection (e) with subsection (a) of Section 701 to buttress the argument. But the contention is not only at war with a considerable body of administrative practice; it is also contrary to controlling judicial authority. *Weinberger v. Hynson, Westcott & Dunning*, 412 U. S. 609 (1973), sustained the FDA's authority under Section 701(a) to create an 'administrative summary judgment procedure' (p. 617) having the drastic consequence, in cases to which it applied, of withdrawing approval of new drug applications without an evidentiary hearing. The administrative action was upheld as a valid instance of 'particularizing standards through the rulemaking process,' deemed necessary and proper to prevent the 'paralysis' of the administrative process which 'would result if case-by-case battles in the courts were the only way to protect the public against unsafe or ineffective drugs,' p. 626. Equally enlightening, if not technically 'square' authority, is the pronouncement in *Weinberger v. Bentex Pharmaceuticals, Inc.*, 412 U. S. 645, 653 (1973), that the agency's power to determine 'new drug' status in its own administrative proceedings was 'implicit in the regulatory scheme' though 'not spelled out in *haec verba* . . .'

Again, the construction was powerfully influenced by the recognition that a different view 'would seriously impair FDA's ability to discharge the responsibilities placed on it by Congress.' *CIBA Corp. v. Weinberger*, 412 U. S. 640, 643 (1973).

"Our Court of Appeals has recognized similarly that 'the Commissioner has the power to issue binding interpretive regulations', citing another example of the authority sustained under Section 701(a), *Abbott Laboratories v. Gardner*, 387 U. S. 136 (1967), and observing that 'the particularization of a statute by rulemaking is not only acceptable in lieu of protracted piecemeal litigation . . . but is the preferred procedure . . .' *CIBA-Geigy Corporation v. Richardson*, 446 F. 2d 446, 468 (1971). This principle, applied in the instant case, implements our duty to treat the statute, with its paramount concern for life and health, "as a working instrument of government and not merely as a collection of English words." *United States v. Dotterweich*, 320 U. S. 277, 280 (1943); see also *United States v. Bacto-Unidisk*, 394 U. S. 784, 798 (1969); *United States v. Sullivan*, 332 U. S. 689, 696 (1948); *Permian Basin Area Rate Cases*, 390 U. S. 747, 776 (1968)."

As far as the motion to depose the Commissioner was concerned, the Court found the record clear and unambiguous and solidly in support of the Commissioner's ruling—stating that "the Commissioner's rational is sufficiently articulated to allow for meaningful review of any necessary finding in the summary judgment disposition." So much for the decided cases.

An overview would not, of course, be complete without a look at some of the more important regulations promulgated or proposed during the last year. My candidates for the two most important in the last year are the Proposed Dietary Supplement Regulation published in August, and presently being litigated, the Requirement of Notice of Request for Hearing and Grant or Denial of Hearing for New Drugs and Antibiotic Drugs published in March. The former is not appropriate for a full analysis here and the latter has been discussed in brief.

## OTC Review

The present posture of the Over-the-Counter (OTC) Review is essentially as follows: (1) all requests for data have been published; (2) all panels except the Miscellaneous Internal Products and Miscellaneous External Products panels have been assembled and have had at least one meeting; and (3) the first final monograph was published in the *Federal Register* for June 4, 1974 (39 F. R. 19862ff); and (4) the Antimicrobial I Panel, which had its last meeting in March, 1974, has a proposed monograph in the works reported to run well over 300 pages. Reports due in 1974 include: Cough-Cold Allergy and Broncho-Dilator Panel due in July but it is running late; Contracep-

tives and other Vaginal Drug Products Panel due in December; Dentifrices and Dental Care Agents was due in November, but it is rescheduled to February 1975; Hemorrhoidal Products due in September; Internal Analgesics due in August but it is running late; Laxatives and Anti-Diarrheal, etc. Panel due in October but it seems to be running early; Sedative, Tranquilizer, etc. Panel due in July; and the Topical Analgesic Panel due in August. Whether the final Antacid Monograph will be challenged legally is a matter of some speculation.

Other than the ongoing panel meetings leading to monograph recommendations, there was an important *Federal Register* publication concerning OTC drugs published Monday, November 12, 1973. A new Section 130.302 was added to Title 21 of the Code of Federal Regulations setting forth "General Conditions" for any OTC drug in order for it to be generally recognized as safe and effective. There are 10 of these conditions, which range from insisting on the application of GMP's and the manufacture of products in a registered plant, through monograph and advertising requirements, to those conditions which are perhaps the two most important ones. These important conditions are: *First,* that the labeling must contain (with a provision for exemption where appropriate upon petition) the general warning: "Keep This and All Drugs Out of the Reach of Children. *In Case of Accidental Overdose, Contact a Physician Immediately,*" and *second,* that any drug for which an applicable monograph requires a drug interaction warning, the labeling must contain the following: "Warning: Do Not Take This Product Concurrently With a Prescription Drug Except on the Advice of a Physician."

At the Antacid Monograph hearing which was held in January, it was clear that at least one consumerist group, The Health Research Group, was opposed to the inclusion, within the Antacid Monograph, of the so-called Alka-Seltzer provision. A provision which allowed a combination of an antacid product with an analgesic if the label clearly states that the product is for the treatment of both conditions and not one of them alone. There is also still some contention that a monograph should be published as an interpretive rather than as a substantive regulation, but I think that this controversy is fast becoming moot in light of recent litigation discussed previously.

A busy legal year. Next year should see the resolution of some of the currently doubtful issues. **[The End]**

## STANDARDS FOR SPECIAL DIETARY FOODS STAYED BY COURT OF APPEALS

The U. S. Court of Appeals for the Second Circuit has stayed the effective date of various provisions of regulations promulgated by the Food and Drug Administration relating to vitamin and mineral supplements sold as foods. The regulations were generally sustained but the Court wanted to provide an opportunity to companies who want to file an application with the FDA seeking increases in the dosages of vitamin C and vitamin B complex supplements and increases in other meritorious cases. The regulations were stayed until six months after the judgment in this case or June 30, 1975, whichever is later.

One regulation, 21 C. F. R. Part 125—Label Statements Concerning Dietary Properties of Food Purporting to Be or Represented for Special Dietary Uses, replaced corresponding parts of a regulation issued in 1955. The other regulation, 21 C. F. R. Part 80—Definitions and Standards of Identity for Food for Special Dietary Uses, invoked the FDA's power to prescribe a standard of identity under § 401 of the Federal Food, Drug, and Cosmetic Act for many vitamins and minerals and for many vitamin/mineral combinations. Both were published in the *Federal Register* on August 8, 1973 and were to become fully effective January 1, 1975.

### U. S. RDA LIMITS

In reviewing the regulations, the Court of Appeals determined that two sections in Part 125 may not be enforced because it is not "reasonable," within the terms of § 401, to ban particular vitamins and minerals essential to human nutrition from "addition to general purpose foods or dietary supplements of vitamins and minerals" just because no Recommended Daily Allowances for them have been set by the FDA. Enforcement of section 125.1(c), which lists the vitamins and minerals so prohibited, was enjoined. Also, the Court said that the FDA's decision to deem as drugs all vitamin and mineral products containing more than the upper limits of the U. S. RDAs did not take into account the fact that such higher-dosage vitamin and mineral products might still be used for nutritional purposes. Section 125.1(h), which requires the drug classification for such products, was held invalid.

### LABELING

Labeling requirements under § 125.2(b) are all sustained with the exception of § 125.2(b)(2), which prohibits a label stating or implying that a balanced diet of ordinary foods cannot supply adequate amounts of nutrients. The court said that the provision does not take into account the fact that it is very difficult for women of child-bearing age and for children to obtain an adequate supply of iron, even from a balanced diet. It is suggested that the FDA insert a qualification to this section to cover iron.

### FRUITS AND VEGETABLES

The enforcement of the regulations under Parts 80 and 125 dealing with fresh fruits and vegetables is enjoined because § 401 rules out any standard of identity for most fruits and vegetables and allows the establishment of standards for citrus and several other fruits only as to maturity and the effects of freezing.

*National Nutritional Foods Assn. and Solgar Company, Inc., et al. v. FDA, et al.*, CA-2
CCH Food Drug Cosmetic Law Reporter, ¶ 41,191

*Here's Help You'll Need on The . . .*

# PENSION REFORM ACT OF 1974

This far-reaching private pension reform measure, promising super benefits for workers, headaches for employers, and generous pension-related tax breaks for self-employeds, is ready—*are you?* You urgently need to know how you'll be hit by: —Mandatory rules for coverage and vesting, which features a 3-way option. Minimum funding standards backed by sharp excise tax teeth. Tight fiduciary rules, *audited* annual financial statements. A Pension Benefit Guarantee Corporation to collect insurance premiums from employers and pay benefits when plans fail. IRS administration and enforcement, with help from Labor and Commerce Departments.

Get the help you need from these CCH publications, all now ready for immediate delivery . . .

1. **PENSION REFORM ACT OF 1974, Law and Explanation** (4892). The law in full text plus a clear CCH explanation of its requirements and new features. About 352 pages, 6" x 9", heavy paper covers, topical index. Price, $4.50 a copy. (Pub. Sept. 1974)

2. **EXPLANATION OF PENSION REFORM ACT OF 1974** (4891). All CCH explanation, no law text. Shows who's affected, when and how—and what to do about it. About 96 pages, 6" x 9", heavy paper covers, topical index. Price, $2.00 a copy. (Pub. Sept. 1974)

3. **NEW TAX SAVING PLANS FOR SELF-EMPLOYED** (4890). Helpfully explains the special new tax rules and new benefits for self-employeds. Concise but vital highlights. 32 pages, 6" x 9", heavy paper covers, topical index. Price, $1.50 a copy. (Pub. Sept. 1974)

4. **NEW 1974 PENSION REFORM HIGHLIGHTS** (4348). Capsule coverage of major law provisions in easy-to-understand language. About 48 pages, 2⅝" x 4", heavy paper covers. Price, 2 for $1.00 (minimum order). (Pub. Sept. 1974)

5. **THE 1974 PENSION REFORM ACT—A NEW CHALLENGE** by Sidney Kess—New Audilex cassette to help comply with the new reform law. Includes "Explanation of Pension Reform Act of 1974" and a Quizzer booklet, prepared in accordance with the guidelines on continuing education approved by the AICPA (successful completion should qualify the listener for 1 hour continuing education credit). Price, $15.00. (Pub. Sept. 1974)

### Order Now for Prompt Delivery

To get your copies of these timely guides to the Pension Reform Act, just use the handy order card attached to this cover. You'll receive your copies promptly.

FOOD DRUG COSMETIC
LAW JOURNAL

PUBLISHED BY
COMMERCE CLEARING HOUSE, INC.
PUBLISHERS OF TOPICAL LAW REPORTS
4025 W. PETERSON AVE., CHICAGO, ILL. 60646
RETURN POSTAGE GUARANTEED

SECOND CLASS POSTAGE PAID
AT CHICAGO, ILLINOIS AND
AT ADDITIONAL MAILING OFFICES

---

Here's Right-Now Help on the Massive New . . .

# PENSION REFORM ACT OF 1974

SEE INSIDE FOR DETAILS

FOOD DRUG COSMETIC
LAW JOURNAL

# ORDER FORM

## MAIL TODAY!

**CCH:**

Rush publications indicated below at prices quoted. To save postage, handling and billing charges, you may elect to send remittance with order. Include sales tax where required.

☐ Remittance herewith ☐ Send bill

1. . . copies of *Pension Reform Act of 1974* (4892). Prices: 1 copy, $4.50; 2-9, $4.10 ea.; 10-24, $3.75 ea.; 25-49, $3.40 ea.

2. copies of *Explanation of Pension Reform Act of 1974* (4891). Prices: 1-4 copies, $2.00 ea.; 5-9, $1.80 ea.; 10-24, $1.70 ea.; 25-49, $1.50 ea.

3. copies of *New Tax Saving Plans for Self-Employed* (4890). Prices: 1-4 copies, $1.50 ea.; 5-9, $1.30 ea.; 10-24, $1.20 ea.; 25-49, $1.10 ea.; 50-99, $1.00 ea.

4. copies of *New 1974 Pension Reform Highlights* (4348). Prices: 2-9 copies, $0.50 ea. (min. order of $1.00); 10-24, $0.40 ea.; 25-49, $0.36 ea.; 50-249, $0.32 ea.

5. sets of *The 1974 Pension Reform Act—A New Challenge* (4411). Price, $15 per set.

☐ Send information on special low prices for larger quantities to distribute with our own imprint.

**Signature** .....

**Firm** .....

**Attention** .....

**Street & No.** .....

**City & State** ..... **Zip** .....

*Subscribers for the following CCH Reporters receive items noted and should order only for extra copies: Pension Plan Guide—1 & 3; Standard Federal Tax Reports—1; Current Law Handybooks—1; Federal Tax Guide Reports and Federal Tax Guide Reports—Control Edition—2; and Professional Corporations Handbook—1.*

**Please Indicate Your CCH Account No.**

.....

4892—2651

**BUSINESS REPLY MAIL**

No Postage Stamp Necessary if Mailed in the United States

POSTAGE WILL BE PAID BY–

**COMMERCE CLEARING HOUSE, INC.**

PUBLISHERS of TOPICAL LAW REPORTS

4020 W. GLENLAKE AVE.

CHICAGO, ILL. 60646

ORDER
CARD

MAIL TODAY!

FIRST CLASS
PERMIT NO. 57
CHICAGO, ILL.