to achieve effective enforcement of the Export Administration Act of 1969.

Accordingly, it is hereby ordered,

I. All outstanding validated export licenses in which respondent appears or participates, in any manner or capacity, are hereby revoked and shall be returned forthwith to the Bureau of International Commerce for cancellation.

II. The respondent is denied all privileges of participating, directly or indirectly, in any manner or capacity, in any transaction involving commodities or technical data exported from the United States, in whole or in part, or to be exported, or which are otherwise subject to the Export Control Regulations. Without limitation of the generality of the foregoing, participation prohibited in any such transaction, either in the United States or abroad, shall include participation, directly or indirectly, in any manner or capacity: (a) As a party or as a representative of a party to any validated export license application; (b) in the preparation or filing of any export license application or reexportation authorization, or any document to be submitted therewith; (c) in the obtaining or using of any validated or general export license, or other export control document; (d) in the carrying on of negotiations with respect to, or in the receiving, ordering, buying, selling, delivering, storing, using, or disposing of any commodities or technical data in whole or in part, exported or to be exported from the United States; and (e) in the financing, forwarding, transporting, or other servicing of such commodities or technical data.

III. Such denial of export privileges shall extend not only to the respondent, but also to its agents, employees, representatives, and partners, and to any other person, firm, corporation, or business organization with which the respondent now or hereafter may be related by affiliation, ownership, control, position of responsibility, or other connection in the conduct of trade or services connected therewith. This order is applicable to Maurice J. Flexman as agent or representative of the respondent.

IV. This order shall remain in effect until the respondent provides responsive answers, written information, and documents in response to the interrogatories heretofore served upon it or gives adequate reasons for failure to do so, except insofar as this order may be amended or modified hereafter in accordance with the Export Control Regulations.

V. No person, firm, corporation, partnership, or other business organization, whether in the United States or elsewhere, without prior disclosure to and specific authorization from the Bureau of International Commerce, shall do any of the following acts, directly or indirectly, or carry on negotiations with respect thereto, in any manner or capacity, on behalf of or in any association with the respondent or any related party, or whereby the respondent or related party may obtain any benefit therefrom or have any interest or participation therein, directly or indirectly: (a) apply for, obtain, transfer, or use any license, Shipper's Export Declaration, bill of lading, or other export control document relating to any exportation, reexportation, transshipment, or diversion of any commodity or technical data exported or to be exported from the United States, by, to, or for any such respondent or related party denied export privileges; or (b) order, buy, receive, use, sell, deliver, store, dispose of, forward, transport, finance, or otherwise service or participate in any exportation, reexportation, transshipment, or diversion of any commodity or technical data exported or to be exported from the United States.

VI. A copy of this order shall be served on respondent.

VII. In accordance with the provisions of § 388.15 of the Export Control Regulations, the respondent may move at any time to vacate or modify this indefinite denial order by filing with the Compliance Commissioner, Bureau of International Commerce, U.S. Department of Commerce, Washington, D.C. 20230, an appropriate motion for relief, supported by substantial evidence, and may also request an oral hearing thereon, which if requested shall be held before the Compliance Commissioner, at Washington, D.C., at the earliest convenient date.

This order shall become effective on April 20, 1972.

Dated: April 14, 1972.

RAUER H. MEYER,
Director,
Office of Export Control.

[FR Doc.72-5990 Filed 4-19-72;8:46 am]

Office of Import Programs

NORTH CAROLINA STATE UNIVERSITY

Notice of Decision on Application for Duty-Free Entry of Scientific Article

The following is a decision on an application for duty-free entry of a scientific article pursuant to section 6(c) of the Educational, Scientific, and Cultural Materials Importation Act of 1966 (Public Law 89-651, 80 Stat. 897) and the regulations issued thereunder as amended (37 F.R. 3892 et seq.).

A copy of the record pertaining to this decision is available for public review during ordinary business hours of the Department of Commerce, at the Office of Import Programs, Department of Commerce, Washington, D.C.

Docket No. 70-00711-01-77040. Applicant: North Carolina State University, Department of Chemistry—NCSU, Raleigh, N.C. 27607. Article: Mass spectrometer, Model MS-1201. Manufacturer: Associated Electrical Industries, Ltd., United Kingdom.

Intended use of article: The article will be used for research studying the mechanism of the transmission of electronic effects in the adamantane skeleton; for a study of the solvolytic behavior of the isomeric 2-substituted compounds to attempt an elucidation of the mass spectral behavior of these compounds; and for quantitative analysis of complex gaseous mixtures.

Comments: No comments have been received with respect to this application.

Decision: Application denied. An instrument of equivalent scientific value to the foreign article, for such purposes as this article is intended to be used, is being manufactured in the United States.

Reasons: The captioned application is a resubmission of Docket No. 68-00646-01-77040 which was denied without prejudice to resubmission on December 5, 1968, due to informational deficiencies contained therein. In this application the applicant alleged that the metastable performance and analytical (quantitative) accuracy of the foreign article were not matched by the instruments which were offered by domestic manufacturers, including the Model 12-90-G manufactured by Nuclide Corporation (Nuclide). A comparison of the foreign article and the Nuclide 12-90-G discloses as to the pertinent characteristics:

Metastable performance. The Department of Health, Education, and Welfare (HEW) advises in its memorandum dated September 14, 1970, that the Nuclide 12-90-G is similar to the foreign article and should have comparable metastable characteristics. The applicant, in material attached to the application, acknowledges the physical similarity of the 12-90-G to the article but points out that a representative sample of 1-bromoadamantane was sent to the companies concerned and an adequate spectrum was received from the manufacturer of the article while Nuclide replied that a 12-90-G was not available at State College (the location of Nuclide) to evaluate the sample. In this connection HEW advises: "The test run on 1-bromoadamtane [sic] with regard to metastable performance is not very conclusive. The intensity of metastables is largely a function of the length of the drift free region in front of the magnet. Intense metastables can be the result of collision induced reactions and may thus be intense with an overloaded source."

The National Bureau of Standards (NBS) advises in its memorandum dated November 17, 1970, that this application does not justify a finding different from that of its previous evaluation relating to the applicant's initial submission. NBS advised as to metastable performance in its previous evaluation:

"For mass spectrometric study of metastable species, the instrument should possess, (a) extremely good resolution, (b) wide range of accelerating voltage, and (c) a suitable long path length from the point it receives its accelerating voltage to the magnetic analyzer. Assuming its other characteristics to be equal, the mass spectrometer that provides the best "metastable" performance will be a double focusing instrument.

"The subject foreign article is a single focusing instrument. Among single focusing mass spectrometers, the instrument with the highest resolution, assuming each is comparable in the features (b) and (c) should give superior metastable

performance. The Nuclide 12–90–G is considered comparable to the AEI–MS–1201 (the foreign article) for general purposes and should give equivalent metastable species detection."

NBS also advised that, with respect to type, geometry, and resolution, the foreign article and the 12–90–G are similar in that both feature a magnetic sector having a 12-inch radius and 90° deflection and both provide a resolution of 7,500 while, in the case of accelerating voltage, the article provides 8,000 volts regulated step wise and the 12–90–G provides 10,000 volts continuously adjustable.

Quantitative accuracy. Although rigid formal specifications were not sent to the manufacturers contacted, the applicant alleges that all contacted, including Nuclide, were requested to provide a maximum deviation of analytical results from the value of the component being analyzed of 1 percent, 1 percent, 5 percent, and 10 percent when the component represents 100 percent, 10 percent, 1 percent, and 0.1 percent of the sample respectively. The applicant did not indicate to the manufacturers concerned the conditions under which such accuracy was to be attained. The foreign article provides the maximum deviations requested by the applicant but the manufacturer specifies, "These values may be obtained when the MS–1201 (the foreign article) is equipped with appropriate inlet systems, precision recorder, and source temperature is allowed to equilibrate for 2 hours." According to the applicant, Nuclide's reply to the request for an instrument providing the required maximum deviations was that it did not have information available pertaining to this specification. The applicant did indicate, however, that the intended uses of the required mass spectrometer were communicated to each manufacturer concerned and that Nuclide offered to furnish an instrument for these uses, i.e., the Model 12–90–G. In this connection HEW advises that: "The quantitative analysis requirements are * * * vague and depends on the quality and size of the reservoir and leak. This figure can be increased even above that stated by proper attention to enough variables (use of balanced electrometers, etc.), not a really good test of mass spectrometer quality."

Finally, NBS and HEW advise in a joint memorandum dated December 16, 1970, that the Nuclide 12–90–G could be used to accomplish the intended purposes of the applicant and that therefore a scientifically equivalent domestic instrument is available for the applicant's intended purposes.

SETH M. BODNER,
Director,
Office of Import Programs.

[FR Doc.72–6004 Filed 4–19–72;8:49 am]

VETERANS ADMINISTRATION HOSPITAL, IOWA CITY, IOWA, ET AL.

Notice of Applications for Duty-Free Entry of Scientific Articles

Correction

In F.R. Doc. 72–5644 appearing at page 7354 in the issue for Thursday, April 13, 1972, in the fourth line of the first complete paragraph on page 7355 the word "spin" should be inserted after the word "Electron".

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Food and Drug Administration

[Desi 6499]

OTC ANALGESIC AND ANTIPYRETIC PREPARATIONS

Drugs for Human Use; Drug Efficacy Study Implementation

The Food and Drug Administration has received reports from the National Academy of Sciences-National Research Council, Drug Efficacy Study Group, for the over-the-counter drugs listed below. Pending the results of the OTC study of drugs in this class, action on these reports will be deferred in accordance with the "Proposal Establishing Status of Over-the-Counter Drugs Previously Reviewed Under the Drug Efficacy Study (DESI)" published elsewhere in this issue of the FEDERAL REGISTER.

The following analgestic and/or antipyretic drugs are included in this announcement:

1. Surfacaine Suppositories containing cyclomethycaine; Eli Lilly and Co., Indianapolis, Ind. 46206 (NDA 6–139).

2. Bufferin Tablets containing aspirin, aluminum glycinate and magnesium carbonate; Bristol-Myers Co., 225 Long Avenue, Hillside, N.J. 07207 (NDA 6–499).

3. Trigesic Tablets containing acetaminophen, aspirin and caffeine; E. R. Squibb & Sons, Division Olin Mathieson Chemical Corp., 745 Fifth Avenue, New York, N.Y. 10022 (NDA 7–289).

4. Nebs Tablets containing acetaminophen; the Norwich Pharmacal Co., 17 Eaton Avenue, Norwich, N.Y. 13815 (NDA 7–654).

5. Apamide Tablets containing acetaminophen; Dome Laboratories, Division Miles Laboratories, Inc., 125 West End Avenue, New York, N.Y. 10023 (NDA 8–188).

6. Metalid Tablets containing acetaminophen; Philips Roxane Laboratories, Division of Philips Roxane, Inc., 330 Oak Street, Columbus, Ohio 43216 (NDA 8–717).

7. Duplexin Tablets containing dihydroxyaluminum sodium carbonate, magnesium carbonate, aspirin, phenacetin, and caffeine; Whitehall Laboratories, Inc., Division American Home Products Corp., 685 Third Avenue, New York, N.Y. 10017 (NDA 9–329).

8. Nysacetol Tablets containing acetaminophen; Nysco Laboratories, Inc., 34–24 Vernon Boulevard, Long Island City, N.Y. 11106 (NDA 9–870).

9. Tylenol Elixir containing acetaminophen; McNeil Laboratories, Inc., Camp Hill Road, Fort Washington, Pa. 19034 (NDA 9–927).

10. Tempra Drops and Tempra Syrup containing acetaminophen; Mead Johnson Laboratories, Division of Mead Johnson & Co., 2404 Pennsylvania Street, Evansville, Ind. 47721 (NDA 10–382).

11. Tralgon Elixir containing acetaminophen; E. R. Squibb & Sons (NDA 10–800).

12. Tylenol Tablets containing acetaminophen; McNeil Laboratories, Inc. (NDA 11–630).

13. Arthropan Liquid and Actasal Pediatric Drops containing chlorine salicylate; the Purdue-Frederick Co., 99–101 Saw Mill River Road, Yonkers, N.Y. 10701 (NDA 11–844).

14. Defencin Tablets, containing glyceryl guaiacolate, aspirin, and phenyltoloxamine dihydrogen citrate; Grove Division, Bristol-Myers Products, Post Office Box 7300, St. Louis, Mo. 63177 (NDA 12–622).

The NAS/NRC, Drug Efficacy Study Group, Panel on Drugs for Relief of Pain, made the following General Statements on Analgesic Preparations, which are applicable to these OTC analgesic products that are intended for oral use.

GENERAL STATEMENTS ON ANALGESIC PREPARATIONS

EVIDENCE FOR GENERAL ANALGESIC EFFECT

It is the recommendation of the Panel that, when a drug has been shown to be an effective analgesic in several different kinds of clinical pain, by suitable controlled trials using modern criteria, such a drug be entitled to consideration as an "all-purpose analgesic" unless special considerations indicate that this is not appropriate. In such cases, it would seem desirable to allow the drug to be marketed for the relief of most kinds of pain, thus avoiding the necessity for listing specific conditions.

ANALGESIC MIXTURES

There is increasing evidence, which has accumulated particularly within the past few years, that it is not always easy to predict the effects of adding one drug to another. Thus, drugs may merely summate in their activities, antagonize each other, or produce true potentiation. Since adequate trials on the relative efficacy of single drugs and mixtures are usually unavailable, it is hard for the Panel to be both fair and scientific in the evaluation of many of the mixtures which it has been asked to review.

Furthermore, some ingredients appear to have been added to these mixtures on the basis of a rationale that is not evident to the Panel. On other occasions, the rationale seems evident, but the reason for the particular doses chosen (especially those which seem homeopathic) is not clear.

In addition to the well-known objections that fixed-ratio mixtures do not allow flexibility in the doses of individual ingredients, one can object to many analgesic mixtures because they contribute little additional therapeutic benefit while increasing the risks of side effects, allergic sensitization, etc. One can perhaps justify the use of some of these mixtures when pain is present with some other symptom, such as a stuffy nose, and both symptoms can be handled reasonably well by the mixture. However, to promote such a mixture as an all-purpose remedy for all kinds of pain, including those which cannot possibly be aided by one or more of the ingredients, is, in the view of the Panel, to encourage bad therapeutics.

SEMANTIC CONFUSION

The words "synergism" and "potentiation" are subject to multiple interpretations, even among professional pharmacologists. It would seem desirable to avoid their use, focusing instead on a description of what actually was achieved in the clinical setting. The word "potency" also has different meanings to different persons. If one is talking simply about milligram potency, this is actually a trivial matter in the clinical setting and, therefore, the term "potency" should probably be avoided.

IRRELEVANT INFORMATION

Many package inserts contain material of no relevance to most practitioners. For example, the animal data are often not helpful, and are not always clearly identifiable as such. This material often seems to be used as a substitute for clinical data. Also irrelevant and not particularly helpful to the reader is a long list of clinical testimonials, only some of which bear on the points at issue, and most of which are uninterpretable because of defects in clinical design.

DRUG DEPENDENCE AND ABUSE

The following statement is proposed to bring uniformity to the claims made concerning the dependence-producing properties of narcotic analgesics and preparations containing narcotic analgesics. It is recognized that many of the claims concerning a lesser dependence-producing liability of specific narcotic analgesics reflect the fact that the particular agents are not commonly abused. However, it must also be recognized that the actual abuse rates do not accurately reflect dependence-producing potential. It is known that agents and preparations that have not been commonly abused in some social settings at some times, have been extensively abused in other settings at other times.

One of the major purposes of the existing laws and regulations concerning narcotic analgesics is to prevent abuse. Therefore, all agents that have been shown to produce morphine-like physiologic and subjective changes when administered chronically, that will produce morphine-like dependence, or that will substitute for morphine in morphine-dependent subjects, shall carry the following recommended warning: "(Name of agent) can produce dependence of the morphine type and therefore has the potential for being abused."

The only exceptions to this recommendation are substances specifically exempted from bearing the label "Warning—may be habit forming" required by Federal law or regulation.

RIGID DOSE RECOMMENDATIONS

The Panel believes that doctors should not be bound legally by dose recommendations in package inserts. These recommendations represent advice as to the dose at which most patients can be started, and the range at which the needs of most patients can be met. However, it is good practice to manipulate the dose in the event of a therapeutic failure, or in the event of untoward effects. Furthermore, tolerance to a drug may develop, and may require an increase in dose. It is the Panel's observation that some of the recommended doses are too low.

DEFICIENCIES OF METHODOLOGY

There is a need for additional methodology for the study of pain. Thus, for example, there is a paucity of information available on the comparative effects of analgesics given repeatedly to patients with chronic pain. The result with single doses may or may not be transferable to such situations. Another area of deficiency is the evaluation of topical ointments that produce obvious sensations of cooling or warmth. Such limitations in methodology should be kept in mind by the Food and Drug Administration when evaluating data on drugs, both old and new.

The evaluations of the National Academy of Sciences-National Research Council, Drug Efficacy Study Group, are as follows:

1. Surfacaine Suppositories containing cyclomethycaine.

This drug has been evaluated by the Panel on Drugs Used in Gastroenterology.

Indication: "For local anesthetic or analgesic effect, as directed by the physician."
Evaluation: Effective, but * * *.
Comments: The warning concerning sensitivity should be clarified directing the patient to consult a physician if use of the medication aggravates his symptoms.

2. Bufferin Tablets containing aspirin, aluminum glycinate and magnesium carbonate.

This drug has been evaluated by the following Panels:

a. Panel on Drugs for Relief of Pain
b. Panel on Drugs Used in Rheumatic Diseases

PANEL ON DRUGS FOR RELIEF OF PAIN

Indication: "* * * for fast, effective relief of simple headache, painful discomforts of colds, minor arthritic pain, menstrual pain, muscular aches, * * * and pain of tooth extraction."
Evaluation: Effective.
Comments: This mixture contains the known analgesic, aspirin, which at recommended dose would provide relief of pain.
Indication: For "mild temporary tension."
Evaluation: Possibly effective.
Comments: There is very little evidence that aspirin has any tranquilizing or sedative effect.

General comments. The claim is made that Bufferin is "twice as fast as aspirin." This statement is ambiguous and misleading.

While the preponderance of studies comparing blood levels of salicylate after ingestion of Bufferin and various types of unbuffered aspirin indicate that the buffered product is somewhat more rapidly absorbed from the gastrointestinal tract than plain aspirin, there is no evidence to indicate that the speed of onset of analgesic action is significantly increased.

The claim is made that Bufferin "helps prevent the stomach upset often caused by aspirin." Most of the published studies with which the panel is familiar indicate there is little difference in the incidence or intensity of subjective gastrointestinal side effects after ingestion of Bufferin or plain aspirin.

PANEL ON DRUGS USED IN RHEUMATIC DISEASES

General comments. The Panel on Drugs Used in Rheumatic Diseases recommends that certain ill-defined and vague claims be modified or deleted. The following is a list of these claims.

1. Fibrositis, myositis, arthritis, spondylitis, and torticollis.

2. Lumbago, "stiff neck," whiplash injury, rheumatism, rheumatic, and arthritides.

The claims in the first category are of such different etiologies that it would be better to specify the diseases (e.g., osteo-arthritis, rheumatoid arthritis, and ankylosing spondylitis) or modify the claims to specify the etiology. The claims in the second category are imprecise and unscientfic terms which are objectionable to the panel and should be deleted. Because these claims are vague and ill-defined, the objective criteria necessary to evaluate the efficacy of a drug is greatly compromised.

3. Trigesic Tablets containing acetaminophen, aspirin, and caffeine.

This drug has been evaluated by the Panel on Drugs for Relief of Pain.

Indication: "For the temporary relief of pain from muscular aches, simple headache and discomforts due to colds."
Evaluation: Effective, but * * *.
Comments: This combination contains the known analgesics, aspirin, and acetaminophen, which at the recommended dose would provide relief of pain. There is no reason to expect that the additional ingredient, caffeine, would detract from this effect. However, there are no specific, well-controlled, and conclusive studies on the above-mentioned conditions.

4. Nebs Tablets containing acetaminophen.

This drug has been evaluated by the following panels:

a. Panel on Drugs for Relief of Pain.
b. Panel on Drugs Used in Rheumatic Diseases
c. Panel on Neurological Drugs.

PANEL ON DRUGS FOR RELIEF OF PAIN

Indication: Relief for a variety of pains (headache throb, sinus headache, tension headache, menstrual distress, colds, flu, neuritis, neuralgia, rheumatism).
Evaluation: Effective, but * * *.
Comments: This drug is an effective analgesic, and probably capable of relieving many different kinds of pain. However, there are no specific, well-controlled, and conclusive clinical studies on the above-mentioned conditions.

Indication: Relieves fever of colds and flu.
Evaluation: Effective.

Comments: Acetaminophen is antipyretic.

Indication: "Pain-free in minutes."
Evaluation: Ineffective.
Comments: There is no evidence for lightning speed of this type.

General comments. How can a drug that has been around since 1889 be called "the most modern of pain relievers" and a product of "modern laboratory research"? This statement is "puffery" and should be removed from the insert.

The statement is made: "Unlike aspirin the active ingredient in NEBS has been shown not to irritate stomach lining. Increasingly it is being acknowledged in scientific and medical reports as safer than aspirin for many people." This claim is justifiable.

PANEL ON DRUGS USED IN RHEUMATIC DISEASES

General comments. The Panel on Drugs Used in Rheumatic Diseases recommends that certain ill-defined and vague claims be modified or deleted. The following is a list of these claims.

1. Fibrositis, myositis, arthritis, spondylitis, and torticollis.

2. Lumbago, "stiff neck," whiplash injury, rheumatism, rheumatic, and arthritides.

The claims in the first category are of such different etiologies that it would be better to specify the diseases (e.g., osteo-arthritis, rheumatoid arthritis, and ankylosing spondylitis) or modify the claims to specify the etiology. The claims in the second category are imprecise and unscientific terms which are objectionable to the panel and should be deleted. Because these claims are vague and ill-defined the objective criteria necessary to evaluate the efficacy of a drug is greatly compromised.

PANEL ON NEUROLOGICAL DRUGS

General comments. The panel finds it impossible to evaluate for efficacy any drug used in the treatment of such unqualified conditions as neuralgia, neuritis, and radiculitis, because of the multiple known and unknown causes of these conditions.

Unless specific types of disease or recognizable syndromes affecting peripheral nerves and roots are stated, reference to the use of any drug for the treatment of neuralgia, neuritis, and radiculitis should be deleted from brochures and package inserts.

5. Apamide Tablets containing acetaminophen.

This drug has been evaluated by the Panel on Drugs for Relief of Pain.

Indication: "For temporary relief of pain, such as simple headache, minor muscular aches, ordinary discomfort of the menstrual period, minor pain following dental work, and discomforts of the common cold."

Evaluation: Effective, but * * *.

Comments: This drug is an effective analgesic, and probably capable of relieving many different kinds of pain. However, there are no specific, well-controlled, and conclusive clinical studies on the above-mentioned conditions.

6. Metalid Tablets containing acetaminophen.

This drug has been evaluated by the following panels:

a. Panel on Drugs for Relief of Pain.

b. Panel on Drugs Used in Rheumatic Diseases.

c. Panel on Neurological Drugs.

PANEL ON DRUGS FOR RELIEF OF PAIN

Indication: Relief of minor aches and pains of simple headache, neuralgia, arthritis, and rheumatism.

Evaluation: Effective, but * * *

Comments: The drug is an effective analgesic, and probably capable of relieving many different kinds of pain. However, there are no specific, well-controlled, and conclusive clinical studies on the above-mentioned conditions.

PANEL ON DRUGS USED IN RHEUMATIC DISEASES

General comments. The Panel on Drugs Used in Rheumatic Diseases recommends that certain ill-defined and vague claims be modified or deleted. The following is a list of these claims.

1. Fibrositis, myositis, arthritis, spondylitis, and torticollis.

2. Lumbago, "stiff neck," whiplash injury, rheumatism, rheumatic and arthritides.

The claims in the first category are of such different etiologies that it would be better to specify the diseases (e.g., osteo-arthritis, rheumatoid arthritis, and ankylosing spondylitis) or modify the claims to specify the etiology. The claims in the second category are imprecise and unscientific terms which are objectionable to the Panel and should be deleted. Because these claims are vague and ill-defined, the objective criteria necessary to evaluate the efficacy of a drug is greatly compromised.

PANEL ON NEUROLOGICAL DRUGS

General comments. The panel finds it impossible to evaluate for efficacy any drug used in the treatment of such unqualified conditions as neuralgia, neuritis, and radiculitis, because of the multiple known and unknown causes of these conditions.

Unless specific types of disease or recognizable syndromes affecting peripheral nerves and roots are stated, reference to the use of any drug for the treatment of neuralgia, neuritis, and radiculitis, should be deleted from brochures and package inserts.

7. Duplexin Tablets containing dihydroxyaluminum sodium carbonate, magnesium carbonate, aspirin, phenacetin, and caffeine.

This drug has been evaluated by the following panels:

a. Panel on Drugs for Relief of Pain

b. Panel of Drugs Used in Rheumatic Diseases

c. Panel on Neurological Drugs

PANEL ON DRUGS FOR RELIEF OF PAIN

Indication: Pain of headache, neuritis, neuralgia, cold distress, arthritis, rheumatism, cold discomforts, and muscle aches.

Evaluation: Effective, but * * *.

Comments: This combination contains the known analgesics, phenacetin and aspirin, which at the recommended dose would provide relief of pain. There is no reason to expect that the additional ingredients would detract from or add to this effect.

This combination is probably capable of relieving many different kinds of pain. However, there are no specific, well-controlled, and conclusive studies on the above-mentioned conditions.

Indication: Pain of mlid migraine.
Evaluation: Ineffective.
Comments: Since this is an OTC or nonprescription drug, the Panel objects to its use by the lay public for such a serious condition, which requires medical advice and diagnosis.

General comments. The claim is made: "An advance over either plain or ordinary buffered aspirin." This is an unjustifiable statement. No evidence exists that "APC" as compared to aspirin has better analgesic effect.

Claims such as "reduces muscular tensions," "calm jumpy nerves that exaggerate pain," and "soothe swollen tissues that aggravate pain" are too vague and should be deleted. It would be proper for the company to mention the antiinflammatory properties of aspirin.

There should be justification and supportive data for the inclusion of antacids in this combination.

PANEL ON DRUGS USED IN RHEUMATIC DISEASES

General comments. The Panel on Drugs Used in Rheumatic Diseases recommends that certain ill-defined and vague claims be modified or deleted. The following is a list of these claims.

1. Fibrositis, myositis, arthritis, spondylitis, and torticollis.

2. Lumbago, "stiff neck," whiplash injury, rheumatism, rheumatic, and arthritides.

The claims in the first category are of such different etiologies that it would be better to specify the diseases (e.g., osteo-arthritis, rheumatoid arthritis, and ankylosing spondylitis) or modify the claims to specify the etiology. The claims in the second category are imprecise and unscientific terms which are objectionable to the Panel and should be deleted. Because these claims are vague and ill-defined, the objective criteria necessary to evaluate the efficacy of a drug is greatly compromised.

PANEL ON NEUROLOGICAL DRUGS

General comments. The panel finds it impossible to evaluate for efficacy any drug used in the treatment of such unqualified conditions as neuralgia, neuritis, and radiculitis, because of the multiple known and unknown causes of these conditions.

Unless specific types of disease or recognizable syndromes affecting peripheral nerves and roots are stated, reference to the use of any drug for the treatment of neuralgia, neuritis, and radiculitis, should be deleted from brochures and package inserts.

8. *Nysacetol Tablets* containing acetaminophen.

This drug has been evaluated by the Panel on Drugs for Relief of Pain.

Indication: For the relief of minor aches and pains due to colds.

Evaluation: Effective, but * * *.

Comments: This drug is an effective analgesic, and probably capable of relieving many different kinds of pain. However, there are no specific, well-controlled, and conclusive clinical studies on the above-mentioned conditions.

9. Tylenol Elixir containing acetaminophen.

This drug has been evaluated by the following panels:

a. Panel on Drugs for Relief of Pain

b. Panel on Neurological Drugs

PANEL ON DRUGS FOR RELIEF OF PAIN

Indication: "Useful in mild upper respiratory infections (tonsillitis, common cold, 'grippe'), headache, myalgia, postimmunization reactions, posttonsillectomy discomfort, and gastroenteritis."

Analgesic in bronchitis, pharyngitis, tracheobronchitis, sinusitis, pneumonia, otitis media, cervical adenitis, and viral infections.

Evaluation: Effective, but * * *.

Comments: This drug is an effective analgesic, and probably capable of relieving many different kinds of pain. However, there are no specific, well-controlled, and conclusive studies on the above-mentioned conditions.

Indication: Antipyretic in bronchitis, pharyngitis, tracheobronchitis, sinusitis, pneumonia, otitis media, cervical adenitis, and viral infections.

Evaluation: Effective, but * * *.

Comments: Acetaminophen is antipyretic. However, there are no specific, well-controlled, and conclusive clinical studies on the above-mentioned conditions.

PANEL ON NEUROLOGICAL DRUGS

General comments. The panel finds it impossible to evaluate for efficacy any drug used in the treatment of such unqualified conditions as neuralgia, neuritis, and radiculitis, because of the multiple known and unknown causes of these conditions.

Unless specific types of disease or recognizable syndromes affecting peripheral nerves and roots are stated, reference to the use of any drug for the treatment of neuralgia, neuritis, and radiculitis, should be deleted from brochures and package inserts.

10. Tempra Drops and Tempra Syrup containing acetaminophen.

These drugs have been evaluated by the panel on Drugs for Relief of Pain.

Indication: Relieves "discomfort due to colds, simple headaches, minor aches and pains."

Evaluation: Effective, but * * *.

Comments: This drug is an effective analgesic, and probably capable of relieving many different kinds of pain. However, there are no specific, well-controlled, and conclusive clinical studies on the above-mentioned conditions.

11. Tralgon Elixir containing acetaminophen.

This drug has been evaluated by the Panel on Drugs for Relief of Pain.

General comments. No insert was available. See comments on Trigesic Tablets.

12. Tylenol Tablets containing acetaminophen.

This drug has been evaluated by the following panels:

a. Panel on Drugs for Relief of Pain

b. Panel on Drugs Used in Rheumatic Diseases

c. Panel on Neurological Drugs

PANEL ON DRUGS FOR RELIEF OF PAIN

Indication: "Tylenol provides effective analgesia in a wide variety of arthritic and rheumatic conditions involving musculoskeletal pain, as well as in other painful disorders such as headache, dysmenorrhea, myalgias, and neuralgias."

"Analgesic in diseases accompanied by discomfort and fever, such as the common cold and other viral infections."

Evaluation: Effective, but * * *.

Comments: This drug is an effective analgesic, and probably capable of relieving many different kinds of pain. However, there are no specific, well-controlled, and conclusive clinical studies on the above-mentioned conditions.

Indication: Antipyretic in diseases accompanied by discomfort and fever, such as the common cold and other viral infections.

Evaluation: Effective, but * * *.

Comments: Acetaminophen is antipyretic. However, there are no specific, well-controlled and conclusive clinical studies on the above-mentioned conditions.

General comments. Under "Advantages," the claims are made that Tylenol is "unusually free from side effects" and "safe for long-term use." These claims are justifiable only for short-term use, but no evidence exists for "long-term use."

Under "Advantages," the claim is made: "Nonirritating. Tylenol is not likely to cause gastric irritation often encountered with aspirin or other salicylates." This statement is justifiable.

PANEL ON DRUGS USED IN RHEUMATIC DISEASES

General comments. The Panel on Drugs Used in Rheumatic Diseases recommends that certain ill-defined and vague claims be modified or deleted. The following is a list of these claims.

1. Fibrositis, myositis, arthritis, spondylitis, and torticollis.

2. Lumbago, "stiff neck," whiplash injury, rheumatism, rheumatic, and arthritides.

The claims in the first category are of such different etiologies that it would be better to specify the diseases (e.g., osteo-arthritis, rheumatoid arthritis, and ankylosing spondylitis) or modify the claims to specify the etiology. The claims in the second category are imprecise and unscientific terms which are objectionable to the panel and should be deleted. Because these claims are vague and ill-defined, the objective criteria necessary to evaluate the efficacy of a drug is greatly compromised.

PANEL ON NEUROLOGICAL DRUGS

General comments. The panel finds it impossible to evaluate for efficacy any drug used in the treatment of such unqualified conditions as neuralgia, neuritis, and radiculitis, because of the multiple known and unknown causes of these conditions.

Unless specific types of disease or recognizable syndromes affecting peripheral nerves and roots are stated, reference to the use of any drug for the treatment of neuralgia, neuritis, and radiculitis, should be deleted from brochures and package inserts.

13. Arthropan Liquid and Actasal Pediatric Drops containing choline salicylate.

This drug has been evaluated by the following panels:

a. Panel on Drugs for Relief of Pain.

b. Panel on Drugs Used in Rheumatic Diseases.

c. Panel on Neurological Drugs.

PANEL ON DRUGS FOR RELIEF OF PAIN

Indication: Relief of minor pains of arthritis, rheumatism, simple headache, and discomfort of menstrual cramps.

Evaluation: Effective, but * * *.

Comments: Choline salicylate is an effective analgesic. There is bibliographic support of the claims for arthritis and rheumatism but no acceptable and controlled studies for simple headache or menstrual cramps.

Indication: Reduce inflammation.

Evaluation: Probably effective.

Comments: Salicylates have been shown to reduce inflammation, however, there is no documentation for this formulation.

General comments. The claims are made:

a. "Faster-Acting, Long-Lasting Pain Reliever."

b. "Taken on an Empty Stomach, Starts Acting 5 Times Faster Than Aspirin."

c. "Reaches Peak of Action 12 Times Faster Than Aspirin."

d. "For Quicker, Gentler, More Convenient Temporary Relief of Minor Pains of Arthritis, Rheumatism, Simple Headache, Menstruation."

These claims assert that choline salicylate acts sooner, last longer, and reach a peak of action faster than aspirin. Adequate studies show that blood salicylate levels after choline salicylate administration are five times as high in 12 minutes and twice as high in 30 minutes as a comparable dose of aspirin. However, there are no clinical studies available to show that the onset of analgesic action is sooner, greater, or more prolonged than with aspirin. Various studies suggest that choline salicylate has analgesic activity equivalent to corresponding doses of aspirin, but these studies were not truly double-blind, in that the liquid form of choline salicylate was compared with the tablet form of aspirin. No studies were done to compare choline salicylate with sodium salicylate. Therefore, the panel finds the above claims unjustified.

The statement is made: "Arthropan Liquid does not irritate the stomach, as does aspirin in many people. As a result, Arthropan Liquid may often be taken in required doses without stomach discomfort—even by people who have a history of stomach sensitivity to aspirin." There are some clinical studies to show that choline salicylate is less irritating to the stomach.

The statement is made: "Arthropan Liquid represents an advance in temporary relief of minor pains of arthritis, rheumatism, simple headache, and menstrual cramps. It is preferable for relief of such pains because it is much less likely to irritate the stomach than aspirin." The panel dislikes the use of the word "advance" because there is doubt that the drug really offers quicker, more prolonged, or safer action than aspirin.

PANEL ON DRUGS USED IN RHEUMATIC DISEASES

General comments. The Panel on Drugs Used in Rheumatic Diseases recommends that certain ill-defined and vague claims be modified or deleted. The following is a list of these claims.

1. Fibrositis, myositis, arthritis, spondylitis, and torticollis.

2. Lumbago, "stiff neck," whiplash injury, rheumatism, rheumatic, and arthritides.

The claims in the first category are of such different etiologies that it would be better to specify the disease (e.g., osteo-arthritis, rheumatoid arthritis, and ankylosing spondylitis) or modify the claims to specify the etiology. The claims in the second category are imprecise and unscientific terms which are objectionable to the panel and should be deleted. Because these claims are vague and ill-defined, the objective criteria necessary to evaluate the efficacy of a drug is greatly compromised.

PANEL ON NEUROLOGICAL DRUGS

General comments. The panel finds it impossible to evaluate for efficacy any drug used in the treatment of such unqualified conditions as neuralgia, neuritis, and radiculitis, because of the multiple known and unknown causes of these conditions.

Unless specific types of disease or recognizable syndromes affecting peripheral nerves and roots are stated, reference to the use of any drug for the treatment of neuralgia, neuritis, and radiculitis, should be deleted from brochures and package inserts.

14. Defencin Tablets containing glyceryl guaiacolate, aspirin, and phenyltoloxamine dihydrogen citrate.

This drug has been evaluated by the following panels:

a. Panel on Drugs for Relief of Pain.

b. Panel on Drugs Used in Rheumatic Diseases.

c. Panel on Neurological Drugs.

d. Panel on Drugs Used in Allergy.

PANEL ON DRUGS FOR RELIEF OF PAIN

Indication: Relief of pain.

Evaluation: Effective, but * * *.

Comments: This combination contains the known analgesic, aspirin, which at the recommended dose would provide relief of pain. There is no reason to expect that the additional ingredients would detract from or add to this effect.

Indication: Temporary symptomatic relief of minor pain of neuralgia, arthritis, rheumatism, and simple headache.

Evaluation: Effective, but * * *.

Comments: This combination contains the known analgesic, aspirin, which at the recommended dose would provide relief of pain. There is no reason to expect that the additional ingredients would detract from or add to this effect.

This combination is probably capable of relieving many different kinds of pain. However, there are no specific well controlled, and conclusive studies on the above-mentioned conditions.

Indication: For minor muscle aches and pains due to fatigue, overexertion, exposure.

Evaluation: Effective, but * * *.

Comments: This combination contains the known analgesic, aspirin, which as stated in the first two indications would provide relief of pain. The panel, however, objects to vague and ill-defined conditions such as "fatigue, overexertion, and exposure," which may not be associated with pain. It would be better to delete these conditions.

General comments. Whether the addition of phenyltoloxamine and glyceryl guaiacolate contributes anything to the management of the clinical entities "neuralgia, arthritis, rheumatism" is not known.

The drug is advertised as a "new and different analgesic for more effective pain relief" and contains in addition to aspirin an antihistamine and an expectorant. The panel considers this unjustifiable in that there is no valid evidence of "more pain relief" and the drug is not "new" or "different."

Under "What you can expect of Defencin," the statement is made: "Clinical studies have shown that most patients who use Defencin had no side effects. Among the remainder, the principal side effects were minor stomach and intestinal irritation similar to those from aspirin alone." This may be true, but also glyceryl guaiacolate may cause stomach irritation.

Two tablets every 3 or 4 hours are recommended. This means 25 mg. phenyltoloxamine every 3 hours, i.e., presumably enough to cause drowsiness. In the light of this side effect, the panel objects to the other statements made by the company: "Defencin has been found to be sufficiently free of undesirable side effects—so safe—that it is sold without prescription. In fact, because Defencin is safe, you can use it repeatedly."

PANEL ON DRUGS USED IN RHEUMATIC DISEASES

General comments. The Panel on Drugs Used in Rheumatic Diseases recommends that certain ill-defined and vague claims be modified or deleted. The following is a list of these claims.

1. Fibrositis, myositis, arthritis, spondylitis, and torticollis.

2. Lumbago, "stiff neck," whiplash injury, rheumatism, rheumatic, and arthritides.

The claims in the first category are of such different etiologies that it would be better to specify the diseases (e.g., osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis) or modify the claims to specify the etiology. The claims in the second category are imprecise and unscientific terms which are objectionable to the Panel and should be deleted. Because these claims are vague and ill-defined, the objective criteria necessary to evaluate the efficacy of a drug is greatly compromised.

PANEL ON NEUROLOGICAL DRUGS

General comments. The panel finds it impossible to evaluate for efficacy any drug used in the treatment of such unqualified conditions as neuralgia, neuritis, and radiculitis because of the multiple known and unknown causes of these conditions.

Unless specific types of disease or recognizable syndromes affecting peripheral nerves and roots are stated, reference to the use of any drug for the treatment of neuralgia, neuritis, and radiculitis should be deleted from brochures and package inserts.

PANEL ON DRUGS USED IN ALLERGY

Indication: Relief of common cold symptoms, such as runny nose and sneezing.

Evaluation: Possibly effective.

Comments: Phenyltoloxamine, in the experience of the panel, is only weakly active as an antihistamine. Several carefully controlled studies, in which different antihistamines were tried, disclosed no alleviation of symptoms or shortening of the duration of symptoms of colds. When allergic rhinitis is mistaken for a cold, antihistamines may be of benefit; but allergic rhinitis is being treated in that instance, not an upper respiratory infection.

This indication was subsequently reevaluated as ineffective as a fixed combination with the following additional comments:

The evidence presented by the manufacturer that the addition of glyceryl guaiacolate improved the overall preparation was totally unconvincing. Its effectiveness in controlling runny nose, sneezing, and as a sedative was not documented.

The studies purporting to demonstrate that phenyltoloxamine improved the action of aspirin through its sedative effect was not convincing; although by inference with other studies, theoretically possible.

It has not been proven that the antihistamine contributes to the relief of cold symptoms which is provided by this combination. The majority of carefully controlled studies that have been performed with antihistamines disclosed no alleviation of symptoms or shortening of the duration of symptoms of colds. When allergic rhinitis is mistaken for a cold, antihistamines may be of benefit, but allergic rhinitis is being treated in that instance, not an upper respiratory infection.

Indication: Relief of cough.

Evaluation: Effective, but * * *. Subsequently reevaluated as ineffective as a fixed combination.

Comments: Glyceryl guaiacolate is an effective expectorant that is helpful in relieving nonproductive coughs. There is no evidence that the antihistamine or aspirin contributes significantly to this effect.

A copy of the Academy's report has been furnished to each firm referred to above. Communications forwarded in response to this announcement should be identified with the reference number DESI 6499, directed to the attention of the appropriate office listed below, and addressed to the Food and Drug Administration, 5600 Fishers Lane, Rockville, Maryland 20852:

Requests for the Academy's report: Drug Efficacy Study Information Control (BD-67), Bureau of Drugs.

All other communications regarding this announcement: Drug Efficacy Study Implementation Project Office (BD-60), Bureau of Drugs.

This notice is issued pursuant to provisions of the Federal Food, Drug, and Cosmetic Act (secs. 502, 505, 52 Stat. 1050–53, as amended; 21 U.S.C. 352, 355) and under the authority delegated to the Commissioner of Food and Drugs (21 CFR 2.120).

Dated: April 13, 1972.

SAM D. FINE,
Associate Commisisoner for Compliance.

[FR Doc.72-5978 Filed 4-19-72;8:47 am]

[DESI 1875]

CERTAIN OTC ANTACID PREPARATIONS

Drugs for Human Use; Drug Efficacy Study Implementation

The Food and Drug Administration has received reports from the National Academy of Sciences-National Research Council, Drug Efficacy Study Group, for the over-the-counter drugs listed below. Pending the results of the OTC study of drugs in this class, action on these reports will be deferred in accordance with the "Proposal Establishing Status of Over-the-Counter Drugs Previously Reviewed Under the Drug Efficacy Study (DESI)" published elsewhere in this issue of the FEDERAL REGISTER.

The following OTC antacid drugs are included in this announcement.

1. Chooz Chewing Gum Tablets containing calcium carbonate and magnesium trisilicate; Pharmaco, Inc., Galloping Hill Rd., Kenilworth, N.J. 07033 (NDA 1–875).

2. Kamat Tablets containing atropine sulfate, aluminum hydroxide, magnesium trisilicate, and kaolin; Cole Pharmacal Co., Inc., 3715–31 Laclede Ave., St. Louis, Mo. 63101 (NDA 1–952).

3. Amphojel Tablets containing aluminum hydroxide; Wyeth Laboratories, Division American Home Products Corp., Post Office Box 8299, Philadelphia, Pa. 19101 (NDA 2–436).

4. Gelusil Liquid containing magnesium trisilicate and aluminum hydroxide; Warner-Chilcott Laboratories, Division Warner-Lambert Pharmaceutical Co., 201 Tabor Road, Morris Plains, N.J. 07950 (NDA 2–545).

5. Endo-Magsal Suspension containing magnesium trisilicate and aluminum hydroxide; Endo Laboratories, Inc., 1000 Stewart Avenue, Garden City, Long Island, N.Y. 11533 (NDA 3–807).

6. Gelusil Tablets containing magnesium trisilicate and aluminum hydroxide; Warner-Chilcott Laboratories (NDA 4–380).

7. Alglyn Tablets and Alglyn Magma containing dihydroxyaluminum aminoacetate; Brayten Pharmaceuticals Co., 1715 West 38th Street, Chattanooga, Tenn. 37409 (NDA 5–668).

8. Alzinox Tablets and Alzinox Magma containing dihydroxyaluminum aminoacetate; Smith, Miller & Patch, Inc., 401 Joyce Kilmer Avenue, New Brunswick, N.J. 08902 (NDA 6–547).

9. Carmethose Suspension containing sodium carboxymethylcellulose; and

10. Carmethose with Magnesium Oxide Tablets containing sodium carboxymethylcellulose and magnesium oxide; and

11. Carmethose-Trasentine Tablets containing sodium carboxymethylcellulose, adiphenine hydrochloride, and magnesium oxide; Ciba Pharmaceutical Co., Division of Ciba Corp., 556 Morris Avenue, Summit, N.J. 07901 (NDA 6–738).

12. Resinat Capsules and Tablets containing polyaminemethylene resin; Merrell-National Drug Co., Division of