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E. As has been previously noted, Marasperse C is identical with Marasperse N except for the replacement of calcium ion by sodium ion in the latter. Attached to and made a part of this petition is a report on acute oral toxicity of Marasperse N and Marasperse C prepared by the Industrial Bio-Test Laboratories, Inc., for the Hercules Powder Company. Attached as well, is the authorization to use this report as a part of this petition. This report shows that both Marasperse N (sodium lignosulfonate) and Marasperse C (calcium lignosulfonate) have acute oral LD₅₀ values greater than 31.6 g./kg.

Attached as well, is written authorization from the American Cyanamid Company to use a report from the Industrial Bio-Test Laboratories, Inc. to the Napco Chemical Company on the Ninety-day Subacute Oral Toxicity of Marasperse N, as a part of this petition. This report was submitted by American Cyanamid as a part of Food Additive Petition 355. These data are submitted in support of the petition on Marasperse C since, as has been previously noted, Marasperse C is identical with Marasperse N except for the difference in the sodium-calcium ion content. The report cited indicates that feeding of lignosulfonate at a dietary concentration of 5% for 90 days was without discernible effect on rats.

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HERCULES POWDER COMPANY
INCORPORATED

HERCULES TOWER · 910 MARKET STREET · WILMINGTON 99, DELAWARE

March 30, 1962

Dr. Paul F. Cundy, Manager
Package Materials Department
Research and Development Division
Marathon,
A Division of American Can Company
Menasha, Wisconsin

Dear Dr. Cundy:

We have sent you a copy of the report from Industrial Bio-Test Laboratories, Inc. on the acute oral toxicity studies on Marasperse N (sodium lignosulfonate) and Marasperse C (calcium lignosulfonate) conducted for Hercules Powder Company. We hereby grant permission for Marathon, A Division of American Can Company, to include copies of this toxicity report in any petition on these products to be submitted by Marathon to the Food and Drug Administration.

Sincerely yours,

Robert M. Miller

Robert M. Miller,
Technical Services Administrator,
Medical Department

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Industrial **BIO-TEST Laboratories, Inc.**
1810 FRONTAGE ROAD
NORTHBROOK, ILLINOIS
Telephone Clarendon 2-3030

REPORT TO
HERCULES POWDER COMPANY
ACUTE ORAL TOXICITY STUDIES ON
MARASPERSE N AND MARASPERSE C

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REPORT TO
HERCULES POWDER COMPANY
ACUTE ORAL TOXICITY STUDIES ON
MARASPERSE N AND MARASPERSE C

I. Introduction

Samples of two materials identified as Marasperse N (Code Number NH10L-27S) and Marasperse C (Code Number CH07L-13S) were received from Hercules Powder Company for the purpose of conducting acute oral toxicity studies in rats.

II. Procedure

The general procedure employed was identical for each test material and is described below.

Healthy, young albino rats of the Sprague-Dawley strain with an average body weight of approximately 250 grams were used as test animals. The rats were divided into five groups of four animals each for dosing purposes.

All animals used were kept under observation for five days prior to experimental use, during which period they were checked for general physical well-being and homogeneity. The animals were housed

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individually in stock cages and permitted a standard laboratory rat diet* plus water ad libitum until 16 hours immediately prior to oral intubation.

On the morning of the first test day, after a 16-hour fast (water permitted), the selected dose groups of four rats each were intubated with previously calculated doses of a 25 per cent (w/v) aqueous suspension of the test material. The test material was orally intubated at five separate, graded dose levels. All doses were administered directly into the stomachs of the rats using a hypodermic syringe equipped with a ball-pointed intubating needle.

Following oral administration of the test material, the rats were returned to their stock cages and observed for the succeeding 14 days.

At the end of the observation period, all data were collected and arrangements were made to calculate the acute oral mean lethal dose (LD₅₀) of the test material using the techniques of Weil**, Thompson***, and Thompson and Weil****.

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* Rockland Rat Diet, Rockland Farms, New City, New York

** Weil, Carrol S.: Tables for Convenient Calculation of Median-Effect Dose (LD₅₀ or ED₅₀) and Instructions in Their Use. Biometrics, Sept. 1952.

*** Thompson, William R.: Use of Moving Averages and Interpolation to Estimate Median-Effect Dose. Bact. Rev., Nov. 1947.

**** Thompson, William R. and Weil, Carrol S.: On the Construction of Tables for Moving Average Interpolation. Biometrics, March, 1952.

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III. Results

A. Marasperse N

1. Mortality

The results of the acute oral toxicity test are presented in Table I. As indicated, no deaths occurred at any of the dose levels tested.

TABLE I
TEST MATERIAL: Marasperse N
Acute Oral Toxicity - Albino Rats

Mortality Data

Dose g/kg	Concentration Administered*	Number Dead	Number Tested	Per Cent Dead
6.81	25 per cent	0	4	0
10.00	25 per cent	0	4	0
14.70	25 per cent	0	4	0
21.50	25 per cent	0	4	0
31.60	25 per cent	0	4	0

* Test material administered in the form of an aqueous suspension.

The acute oral LD₅₀ is greater than 31.6 g/kg.

2. Reactions

Mild generalized inactivity and slight diarrhea were noted among animals of all dose levels during the first eight hours following dose administration. All animals appeared completely normal within 24 hours after dosing. The remaining 14-day observation period was uneventful.

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B. Marasperse C

1. Mortality

The results of the acute oral toxicity study are shown in Table II. As indicated, no deaths occurred at any of the dose levels tested.

TABLE II
TEST MATERIAL: Marasperse C
Acute Oral Toxicity - Albino Rats

Mortality Data

Dose g/kg	Concentration Administered*	Number Dead	Number Tested	Per Cent Dead
6.81	25 per cent	0	4	0
10.00	25 per cent	0	4	0
14.70	25 per cent	0	4	0
21.50	25 per cent	0	4	0
31.60	25 per cent	0	4	0

* Test material administered in the form of an aqueous suspension.

The acute oral LD₅₀ is greater than 31.6 g/kg.

2. Reactions

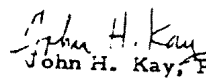
Animals in all dose groups exhibited mild generalized inactivity and slight diarrhea during the first eight hours following dose administration. All animals appeared completely normal within 24 hours after dosing. The remaining 14-day observation period was uneventful.

IV. Summary

The acute oral mean lethal dose (LD₅₀) of both test materials (Marasperse N and Marasperse C) was found to be greater than 31.6 g/kg for the albino rat.

Respectfully submitted,

INDUSTRIAL BIO-TEST LABORATORIES, INC.

Report prepared by: 
John H. Kay, Ph.D.
Associate Director

Report approved by: 
J. C. Calandra, M.D., Ph.D.
Director

March 6, 1962

OPTIONAL FORM NO. 10
5010-104

UNITED STATES GOVERNMENT

Memorandum

TO : OFFICE OF COMMISSIONER
ATTN: Mr. Alan Spiher, FA

DATE: May 10, 1962

FROM : Division of Pharmacology, Toxicology Branch

SUBJECT: Calcium lignosulfonate as a dispersing agent and stabilizer
for pesticide sprays and dips which are mixed in the field
and applied to bananas both post-and pre-harvest

FOOD ADDITIVE PETITION NO. 807
(Filing and Final)

Marathon, Division of Amer. Can Co.
Menasha, Wisconsin
(AF 15-749)

Evidence supplied with this petition indicate a residue of not more than 2.1 ppm in washed bananas. There is no reason to expect this substance to migrate from the surface of the peel so that, in terms of consumption, the residue is essentially zero.

There have been a large number of petitions related to the use of salts of lignosulfonate for such things as extenders and binders for feed pellets, salt cakes, and vitamins for livestock. In addition, there is a petition (FAP #355) for its use in paper coatings.

As early as March 9, 1960, Dr. A. J. Lehman (DP), in answer to an inquiry from Dr. P. F. Cundy of Marathon, stated, "We see no problem of safety in the use of Norlig as a binder in animal feed and that such use would be generally recognized as safe."

Since Norlig A is the first and most impure fraction of lignosulfonate derived from the paper making process it follows that the Marasperse which are purified Norlig are also GRAS for these purposes. A similar opinion was expressed by F. A. Cassidy (OC) in a telegram to Mr. R. B. Bailey of Crown Zellerbach Corp. (1-3-61) in relation to a similar lignosulfonate.

We have data on the acute oral toxicity, in rats, for both the sodium and calcium Marasperse and a 90 day chronic study in rats fed up to 5% sodium Marasperse.

In both studies a toxic level was not reached (see FAP 752 for studies).

Discussion:

1. lignosulfonates have GRAS status for many direct uses in animal feeds.
2. Toxicity data available indicates a relatively innocuous substance.

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FAP No. 807


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3. Residues to expected from the present request should be extremely small.
4. There is no reason to expect that lignin and/or cellulose should be absorbed by humans.

CONCLUSION:

This requested use of calcium lignosulfonate is without hazard.

This petition is suitable for filing and final regulation.


H. Blumenthal
H. Blumenthal

OPTIONAL FORM NO. 10
5010-104

UNITED STATES GOVERNMENT

Memorandum

TO : FAPCB (Mr. Spither)

DATE: May 29, 1962

FROM : Division of Food

AF 15-749

SUBJECT: FAP #807--Calcium lignosulfonate as pesticide adjuvant.

The Marathon Division of American Can Company proposes a regulation covering the safe use of calcium lignosulfonate as a dispersing agent and stabilizer in pesticide spray and dip formulations prepared by mixing in the field and applied to bananas both pre- and post-harvest.

Identity

Marasperse C is the calcium lignosulfonate for which the regulation is proposed. The manufacture and composition of Marasperse C are adequately described. The product contains about 82% mixed calcium and sodium lignosulfonates. Marasperse, unlike other lignosulfonates, is said to be free of low molecular weight lignosulfonates, and certain sugars and sugar derivatives. Marasperse N, the corresponding sodium salt, is reported to contain as impurities, 0.1 ppm mercury, 0.1 ppm lead, and 0.8 ppm arsenic.

Use

Marasperse C is used with pesticides, primarily fungicides, on bananas. It is added to fungicidal suspensions to improve the physical characteristics of the sprays and dips. Use with Bordeaux mixture and maneb is mentioned.

In pre-harvest use with fungicides to control leaf spot, dosages of Marasperse C are 0.25-0.8 lb per acre. In post-harvest fungicidal dips to control crown rot, the concentration is given as 0.1 lb Marasperse C per 100 gal.

Residues

The petition gives a method for residues on bananas, but it appears to be unreliable. It is based on measurement of the ultraviolet absorption of dilute hydrochloric acid washes or extracts of the bananas. Extremely high blanks

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FAP #807

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(about 5000 ppm) were obtained on banana pulp, rendering the method unworkable on the pulp. Blanks from acid washes of the outside skin of untreated control bananas were about 2.5 ppm (based on weight of whole banana). Similar blanks on open market bananas were 2.5-8 ppm. Correcting for the 2.5 ppm blank, values obtained on commercially washed bananas treated pre-harvest with Bordeaux mixture plus Marasperse C were about 2 ppm. Because of the high blank, and based on other more reliable estimates, we consider the 2 ppm value too high.

A copper analysis was made of the bananas treated with Bordeaux plus Marasperse. Based on this analysis and on the highest proportion of Marasperse to be used, we calculated that the bananas from this pre-harvest treatment may have had about 0.02 ppm Marasperse.

A perhaps more reliable estimate can be made from the data in PP #270 dealing with maneb on bananas. Pre-harvest use of maneb at 5 lb per acre on bananas gave maximum residues of about 2 ppm. Post-harvest dips containing 8 lb maneb per 100 gal gave maximum residues of about 12 ppm. Assuming a direct proportion between residues of maneb and Marasperse, the maximum pre-harvest use of 0.8 lb Marasperse per acre would give residues of about 0.3 ppm, and the post-harvest use of 0.1 lb per 100 gal would give about 0.2 ppm. From these calculations the maximum Marasperse residue on unwashed bananas from both pre- and post-harvest use would be about 0.5 ppm. The usual commercial washing would be expected to remove most of this residue.

From the foregoing we conclude that residues of Marasperse will not exceed 0.5 ppm on unwashed bananas, and on washed bananas will probably be less than 0.1 ppm. All of this residue is expected to be on the outside of the banana, there is no reason to expect migration of Marasperse to the edible pulp.

Because of the negligible residues involved the regulation should be based on safe use as proposed; no analytical method for enforcement will be required.

FAP #807

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Recommendations

It is recommended that the petition be filed.

Before making a final recommendation, consideration should be given to the relationship between the proposed regulation and the more general clearance of pesticide adjuvants under Section 408 requested by NACA.


H. A. Jones

