

**ALAN D. KIRSCH
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732-603-6514
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September 7, 2000

Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services
Room 1-23
12420 Parklawn Drive
Rockville, Maryland 20857

RE: Authorization to Act on Behalf of CTS Chemical Industries Ltd., Petach Tikva, Israel 61000 for Citizen Petition to Establish Safety of Echinacea Extract as a GRAS Pharmaceutical Technical Formulation Aid (Binding Agent)

Dear Sir or Madam:

Alan D. Kirsch, on behalf of CTS CHEMICAL INDUSTRIES LTD., Petach Tikva, Israel 61000, submits this enclosed Citizen Petition to Establish Safety of Echinacea Extract as a GRAS Pharmaceutical Technical Formulation Aid (Binding Agent). Attached is a letter from Ms. Sigal First, General Manager, CTS Chemical Industries Ltd., to the US Food and Drug Administration granting Alan D. Kirsch permission to act on behalf of CTS Chemical Industries Ltd. for all matters related to this Citizen Petition.

Should you have any questions, please do not hesitate to contact me via telephone or facsimile at: (732) 603-6514 or via e-mail at: akirsch973@aol.com.

Yours truly,



Alan D. Kirsch
Pharmaceutical Consultant

Enclosures

00P-1510

CPI

CTS Chemical Industries Ltd.

All correspondence to: P.O.B. 10, Tel-Aviv 61000, Israel
Head Office: 100 Jabotinsky Rd. Petach Tikva
Tel: +972-3-9373333 Fax: +972-3-9225964
Plant: 3 Hakidma St. Industrial Zone
Kiryat Malachi 83057
Tel: 08-8607600 Fax: 08-8583956



כצט תעשיות כימיות בע"מ

התכתבות אל: ת.ד. 10, ת"א 61000
משרד ראשי: דרך זבוטינסקי 100, פתח-תקוה
טל' 03-9225964 פקס: 03-9373333
המפעל: רח' הקדמה 3
אזור תעשייה קרית מלאכי 83057
טל: 08-8607600 פקס: 08-8583956



August 9, 2000

Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services
Room 1-23
12420 Parklawn Drive
Rockville, Maryland 20857

Re: Citizen Petition to Establish Safety of Echinacea Extract as a GRAS
Pharmaceutical Formulation Aid

Dear Sir or Madam,

CTS Chemical Industries Limited grants Mr. Alan D. Kirsch permission
to act on our behalf for all matters related to this Citizen Petition.

Sigal First
General Manager

CTS Chemical Industries Ltd

Signature: _____

CTS Chemical Industries Ltd.

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September 7, 2000

Dockets Management Branch
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12420 Parklawn Drive
Rockville, Maryland 20857

RE: Citizen Petition to Establish Safety of Echinacea Extract as a GRAS
Pharmaceutical Technical Formulation Aid (Binding Agent)

Dear Sir or Madam:

CITIZEN PETITION

The undersigned submits this petition under 21CFR§10.20 and 10.30(b) of the Federal Food, Drug and Cosmetic Act to request the Commissioner of Food and Drugs to issue a regulation to classify echinacea extract as a GRAS ingredient for use as a technical formulation aid (binding agent) in the preparation of certain pharmaceutical solid dosage formulations.

A. Action Requested

CTS Chemical Industries Limited (CTS Ltd.), with offices at 100 Jabotinsky Road, Petach Tikva, Israel, requests the US Food and Drug Administration to issue a regulation that grants GRAS (generally recognized as safe) status to echinacea extract for use as a binding agent during the formulation of certain solid dosage form pharmaceutical products. Proposed language of the regulation follows:

Echinacea

Echinacea (extracted from the following plant species: *Echinacea purpurea*, *Echinacea pallida* and *Echinacea augustifolia*) as described in this section has demonstrated binding properties and may be safely used in certain pharmaceutical products as a technical formulation aid (binding agent). The quantity of any substance employed to effect such modification shall range from 3 to 30 mg per dosage unit and not exceed the amount reasonably required to accomplish the intended physical or technical effect, nor exceed any limitation prescribed. To insure safe use of echinacea extract, the label of the pharmaceutical product shall bear the name of the additive "echinacea extract" in addition to other information required by the Act. Final labeling will be submitted when available.

B. Statement of Grounds

Echinacea extract, as a technical formulation aid, has binding properties that can be utilized in pharmaceutical formulations that are equivalent to and can be substituted for commonly used chemicals such as povidone, polyethylene glycol, starch, etc. Based upon experimentation, wet and dry extracts of echinacea can be used to formulate various solid dosage forms. In addition, several different types of manufacturing technologies can be employed to produce solid dosage forms of desired physical characteristics. Among the types of technologies that can be employed are: granulations (wet and dry), direct compression and microgranules application. Refer to Attachment #1 entitled "Citizen Petition to Establish Safety of Echinacea Extract as a GRAS Pharmaceutical Formulation Aid – CMC Section" for more detailed information concerning the types of experiments conducted to demonstrate the utility of Echinacea Extract.

Several monographs describing the characteristics and specifications for echinacea plant species were published in the May – June, 2000 issue of the Pharmacopeial Forum. These monographs appear in Appendix A to Attachment #1. Manufacturers of echinacea extracts must meet these specifications and fully comply with current Good Manufacturing Practices of the US Food and Drug Administration.

A comprehensive search of the scientific literature has been conducted to evaluate the biochemical actions, pharmacology, toxicology, regulatory status, safety and efficacy of echinacea extracts. The search revealed that echinacea extract is considered a safe herb that is well tolerated in infants, children and adults. The extract has been shown to positively impact individuals with respiratory infections and specifically enhance the immune response. A review of the literature along with references is appended as Attachment #2. This review is entitled "Assessment of the Pharmacology, Toxicology, Safety and Efficacy of Echinacea Species".

Labeling for herbal supplement products containing echinacea extracts warns the consumer not to use the product for more than eight (8) consecutive weeks. The dosage of echinacea in these products is approximately 150 to 300 mg per dosage unit. The literature search has revealed no scientific justification for this use restriction. Further, there are also no references that explain the rationale for this restriction. Some reports have stated that continuous intake of echinacea extracts impairs the immune function. However, no well-controlled scientific studies have identified impairment of the immune response. Incidents of reported adverse events have been rare, transient in nature and mild in severity. There are also no known toxicities.

Despite the lack of conclusive evidence that echinacea extracts impair the immune response, CTS Ltd., proposes to prohibit the formulation of pharmaceutical products with echinacea used on a chronic basis. Instead, CTS Ltd., proposes several different types of products that can be formulated with up to 30 mg of echinacea per dosage unit for short-term use. Among the types of products that would meet this categorization are: antibiotics, over-the-counter products such as cough / cold remedies, antidiarrheal agents, analgesics, and certain other products.

C. Environmental Impact

In accordance with 21CFR§25.24(b)7, CTS Ltd., requests an exclusion from the requirement to conduct an environmental assessment of the impact of echinacea on the environment. Data available to the agency do not establish that, at the expected levels of exposure, the substance may be toxic to organisms in the environment. Further, echinacea is commonly found in numerous nutritional herbal supplements.

D. Economic Impact

An economic impact statement will be submitted only when requested by the Commissioner following review of the petition.

E. Certification

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

(Signature)

(Name of petitioner)

Alan D. Kirsch

Representing CTS Chemical Industries Ltd.

(Mailing address)

16 Woodrow Wilson Drive

Edison, New Jersey 08820

(Telephone number)

732-603-6514

Attachments

1. Citizen Petition to Establish Safety of Echinacea Extract as a GRAS Pharmaceutical Formulation Aid – CMC Section
2. Assessment of the Pharmacology, Toxicology, Safety and Efficacy of Echinacea Species