Health Canada / Santé Canada
Health Products and Food Branch / Direction générale des produits de santé et des aliments

Therapeutic Products Directorate
Holland Cross, Tower "B"
6th Floor, 1600 Scott Street
Address locator 3106B

JAN 04 2002

00001-37

Dr. Ian Mitchell
Director, Office of Medical Bioethics
University of Calgary
Heritage Medical Research Building/Rm 93
3330 Hospital Drive North West
CALGARY. Alberta
T2N 4N1

Dear Dr. Mitchell:

Re: Clinical Trial Application for E.M.Power +

Further to my correspondence of October 11, 2001, regarding ongoing clinical trials with EM Power +, this is to inform you that the Clinical Trial Application for EM Power + has been reviewed by the Therapeutic Products Directorate and is considered not satisfactory according to Division 5 of the Food and Drug Regulations. Please see attached letter to Dr. Kaplan that outlines the concerns raised by the Therapeutic Products Directorate.

As a result of this decision, the trial must be terminated, and all study subjects must be notified. In addition, the sponsor must ensure that these subjects are assessed and their care is transferred to an appropriate professional who can place them on standard therapy.

Yours sincerely,

Robert G. Peterson, MD, PhD, MPH
Director General

c.c. Dr. Siddika Mithani
Dr. Philip Waddington

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Health Canada / Santé Canada

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Health Products and Food Branch
Direction générale de

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To Tanya	From Bonnie
Co./Dept.	Co.
Phone #	Phone #
Fax # 403-758-6073	Fax #

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ment l'expéditeur.

TO/À

Name/Nom: **Dr. Bonnie J. Kaplan, Ph.D. Professor , and Director, Behavioural Research unit, Alberta Children's Hospital**

Date: October 25, 2001

Organization/Organisme: University of Calgary

Tel./Tél.: (403)-229-7365 Fax/Télécopieur: (403) 543 - 9100

No. of Pages, including this page/N° de pages, incluant cette page: 4

FROM/DE

Name/Nom: Dr. Mona Akoury E-Mail/Courier électronique

Tel./Tél.: (613) 941-2132 Fax/Télécopieur: (613) 952-9656

TITLE		TITRE
Division/Unit	Clinical Trials and Special Access Programe	Division/Unité
Bureau	Bureau of Pharmaceutical Assessment / Bureau de l'évaluation des produits pharmaceutiques	Bureau
Directorate	Therapeutic Products Directorate / Direction Des Produits Therapeutiques	Direction
Room		Pièce
Building	Finance Building/ Edifice Finance	Édifice
Location	Tunney's Pasture/Pré Tunney	Lieu
Address Locator	0202C1	Localisateur d'adresse
City/Province	Ottawa, Ontario	Ville/Province
Postal Code	K1A 1B9	Code postal
	Website/site Web : www.hc-sc.gc.ca/hpb-dgps/therapeut	

INFORMATION REQUEST

In accordance with Division 5 of the Food and Drug Regulations, we request clarification of the points on the following page so that we can continue our evaluation of your IND / Amendment to IND:

Product: E.M Power +

Protocol No.: Bipolar Disorder clinical Study
Fibromyalgia Clinical Study

Control No.: 073990 and 073988

File No.: 9427- U0206 - 35 C

Received in the Bureau on: October 16, 2001

Please provide a complete response within 4 calendar days from the date of this request via

facsimile to the sender. If the requested information is not received within four calendar days, a Not Satisfactory Notice may be issued.

General Comments:

1. There is no scientific basis presented, or any evidence to indicate that bipolar disorder may be caused by, or is due to deficiencies in the ingredients present in the E.M Power formula. In addition, there is no scientific evidence indicating that large doses of vitamins, minerals, amino acids, boron , germanium would treat bipolar disorders. Please comment.

2. We have concerns regarding chronic toxicity due to large doses of ingredients present in this study formulation (Vitamins/minerals, amino acids, etc), In addition, ingredients such as boron and germanium have not been permitted due to safety considerations. What is the rationale for such a combination of ingredients?

   Please provide animal or human safety data justifying the large excessive daily dose proposed for each ingredient in the EM power + formulation. Please calculate the safety margin between the known animal and human toxic doses and the proposed total daily doses for each ingredient present in this formulation.

3. We have received complaints on the EM Power + formulation, regarding the quality of the capsules, the mega doses, and its interactions with other medications such as lithium. We have been informed that a child had been hospitalized following administration of this product.
   In addition, we have also, received information indicating that the Schizophrenia Society of Ontario is concerned about the safety issues surrounding the EMPower+ formulation.

   Please provide any information available to you regarding possible safety concerns in patients that have been taking EM Power +. This should include all safety reports that have been sent to you.

The Bipolar Disorders Study:

With respect to the bipolar disorder study, the following must be considered:

1. Patients under 18 years of age must be excluded from the study. The safety and efficacy of this formulation in treating bipolar disorders should be first established in adults before experimenting on children.

4- The patient diagnosis of bipolar disorder must be confirmed by a physician.

5- Only the newly diagnosed patients with bipolar disorder may be included in the study.

6- Patients with suicidal tendency or previous suicide attempts must be excluded from the study.

7- It is understood that symptomatic, moderate, and severe bipolar disorders patients will be included in the study. It is recommended that these patients be hospitalized and not to be released from the hospital until their condition has been stabilized ,either on the test drug or another standard , recognized therapy. Patients who deteriorate or do not respond to the test drug should be placed on standard, approved therapy, before released from the hospital.

8- Would patients enrolled in this trial receive counseling therapy? Please advise.

9- Please provide information regarding the frequency of patient assessment by the physician in this clinical trial. Consideration must be given to frequent assessments until the patient is stabilized.

10- Please provide a clear description of the patient withdrawal criteria.

11- Please define the criteria for patient improvement and worsening of the disease condition. Please define your criteria for treatment failure.

12- Rescue medications must be allowed in the study. Please identify the rescue medication you would administer to the patient in the study, its dose, and duration of use. Would you consider giving the patients benzodiazepine as a rescue medication?

13- What are the concomitant medications that would be allowed in this study.

14- How will the placebo patients be managed in the study?

15- Please define the study duration, the duration of treatment and drug administration, the date of the start/onset of the study, and the anticipated termination date.

16- It is our understanding that patients are currently enrolled in this trial. Please provide information on how many patients are currently enrolled in the study, how many are still required to be enrolled, and the status of this clinical trial.

17- Please define the anticipated adverse effects, and the patients risk involved. How would the adverse effects be managed in this study? What are the safety measures that will be built in the study to protect the patients from the risk involved?.

18- **Patient's/Guardian's Information Consent form:**
It should be expanded to include a 24 hour telephone , direct , access number to the treating physician, in case of an emergency or any adverse drug reaction.

It should also, be expanded to explain to the patients of the risk of not treating bipolar disorder with standard approved therapy.

The patient should be made aware that we do not have any scientific or evidence to indicate that the EM Power+ formulation could be of benefit in bipolar disorders.

The risk of chronic toxicity due to the large doses should be explained in the consent form.

Please note that with respect to this point, we would only be considering patients ≥18 years

Fibromyalgia Clinical Study:

18- There is no scientific basis for the proposed hypothesis that the formulation EMPower+ would be of any benefit for fibromyalgia patients. What is the rationale for conducting this study?

20- Please identify the single and the total daily doses and the mode of administration of the formulation.

21- Please define the study duration, the duration of treatment and drug administration, the date of the start/onset of the study, and the anticipated termination date.

22- How will the placebo patients be managed in the study?

23- How many patients are currently enrolled in the study and receiving the treatment drug?. How many more patients will be enrolled in the study?.

24- Please define the anticipated adverse effects, and the patients risk involved. How would the adverse effects be managed in this study? What are the safety measures that will be built-up in the study to protect the patients from the risk involved?.

25- Please provide a clear description of the patient withdrawal criteria.

26- Please define the criteria for patient improvement and worsening of the disease condition. Please define your criteria for treatment failure.

27- Rescue medications must be allowed in the study. Please identify the rescue medication you would use, its dose, and duration of use.

28- What are the concomitant medications allowed?

29- Patient's Information Consent form:
It should be expanded to include a 24 hour telephone , direct, access number to the treating physician, in case of an emergency or any adverse drug reaction.

The patient should be made aware that we do not have any scientific or evidence to indicate that the EM Power+ formulation could be of benefit in bipolar disorders.

The risk of chronic toxicity due to the large doses should be explained in the consent form.

Nina Akowuah