3/18

NIH → Fauci: Interested in variety of approaches to AIDS
Interruption of transmission → one of many strategies

ACTG (Aids Clinical Trials Group) committee: Comm. that decides high/low priority on pre-clinical data NIH development → then go to protocol committee for clinical, then human trial → data review

CHR: Call FDA → FDA still putting together evaluative procedure.
① "Herpes model" Irritatability
Test tube: AIDS

New person in: (he'll call)
What will she require?
① Male to female (heterosexual) transmissions → no good animal models for male to male testing
② Male to male

May 23-24
Major Conf.: late May
"Virocides" ???

1) 6 wks to do next steps
2) 30 days or longer
3)

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Vice President and General Manager
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DEPARTMENT OF HEALTH & HUMAN SERVICES

Chief of Staff

Washington, D.C. 20201

MEMORANDUM

To: Carol Rasco

From: Kevin Thurm KT

Re: Meeting with Stephen Enterprises, Inc.

AIDS Fauchi

Dr. Anthony Fauci and Dr. Steven Sehnittman, both from the National Institutes of Health, will be attending the 3:00 meeting in your office with Stephen Enterprises, Inc.

David Dodd
Wyeth-Ayerst

Bob Allen - Scientific Director

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892
Building: Solar
Room : 2A02
(301) 496-8213

June 1, 1992

J. T. Stephens, Jr.
Chairman and C.E.O.
ExOxEmis, Inc.
Suite 1770
One Union National Plaza
Litte Rock, AR 72201

Dear Mr. Stephens:

Thank you for your interest in AIDS treatment research. Outlined below are the additional data needed to review your purified myeloperoxidase compound pursuant to our telephone conversation on May 29th. As the Executive Secretary of the NIH AIDS Clinical Drug Development Committee (ACDDC), I am responsible for reviewing submitted information on promising agents for AIDS that require further clinical development. The Committee was established by Dr. Anthony Fauci, Director, National Institute of Allergy and Infectious Diseases (NIAID), to advise the Division of AIDS (DAIDS) regarding agents to be studied in clinical trials sponsored by the AIDS Clinical Trials Group (ACTG) and by the Community Programs for Clinical Research on AIDS (CPCRA).

The ACDDC is composed of both Government and non-Government experts. Non-Government experts include ACTG and CPCRA investigators, thus providing continuity and enabling speedier movement of drugs into clinical trials. Drugs may be submitted to the Committee by sponsors in industry, academia, and/or Government. Following a thorough review of data on each drug, the Committee assigns it a priority rating. The criteria for evaluation include a rationale, laboratory evidence of activity, safety information in animals and demonstration of *in vivo* efficacy. The DAIDS decides which drugs will enter clinical trials it sponsors, taking into account the recommendations of the Committee.

Because of the large number of suggestions proffered by individuals and organizations regarding treatment of this disease as well as the substantial time and effort required to review the relevant data, it has become necessary to limit review of suggested therapies to those which have demonstrated scientific merit. The ACDDC has established suggested guidelines for the submission of data for review in order to analyze a potential therapeutic candidate in a rational and objective scientific manner which will assure optimal use of federal funds and patient resources. We strongly encourage the inclusion of the requested data (listed below) in your submission. Material which is imprecise will be of limited value to the Committee in fairly evaluating your purified myeloperoxidase compound as a potential therapeutic approach to AIDS.

Please submit five (5) complete copies of the data to be reviewed (suitable for photocopying); however, if your proposal contains colored charts and/or tabs we request that you submit 50 copies. This information is for the exclusive use of the AIDS Clinical Drug Development Committee and the Division of AIDS staff, each of whom recognizes the confidential nature of the submission and his or her obligation to restrict the use of this information to the deliberations of the Committee and the Division of AIDS staff. A copy of our confidentiality policy is enclosed for your information.

Please limit the packet of information that you send us to no more than 50 - 55 pages. If any of the submitted data have been published, the specific references should be indicated where the data are presented in the body of the submission, as well as providing a separate bibliography. You are encouraged to submit reprints.

The information submitted should include a brief summary of:

1. Theoretical background

   A brief description of why your purified myeloperoxidase compound should be a) effective, b) safe, and c) feasible. For what condition is the compound proposed? What is the purported specific mechanism of action? For example, if the agent has anti-HIV activity, does it inhibit reverse transcriptase/uptake, prevent release of virus from infected cells, etc.? Similarly, if the agent is an immunomodulator, specify the effect(s) on the immune system.

2. *In vitro* documentation of efficacy

   Ideally, data from two independent laboratories should be submitted. Please provide details of how the summarized studies were performed: the specific assays used, reagents, cell lines, isolates employed, parameters used to determine a positive or negative result (eg. the background level in a laboratory doing reverse transcriptase activity assays), positive and negative controls. Please identify the laboratories where the testing was performed. If you have been unable to obtain such testing we may be able to arrange for screening of compounds for antiretroviral activity by the NIH or one of its contractors.

3. *In vivo* documentation of efficacy

   Data from animal studies, if any, indicating the safety, tolerance, and efficacy of the proposed compound in conditions possessing some similarities to AIDS. Again, in your summary of these data, please provide details that will enable us to evaluate the agent: study design, species, dose, route and duration of administration, relevant pharmacokinetic data, length and frequency of observation, measurable parameters used to define outcomes.

4. Preclinical pharmacokinetics and toxicology

   Briefly summarize acute, subacute, and chronic toxicology studies; results of mutagenicity and teratogenicity studies; single and multiple dose pharmacokinetics in animals.

5. Results of Phase I pharmacokinetic studies

   Single and multiple dose studies; safety and tolerance. Describe patient population(s) studied and how outcome measurements were made.

6. Results of clinical trials (Phase IB or later studies)

   Summarized data should include: a) description of patient population, b) eligibility criteria, c) study design, d) objective parameters for both laboratory and clinical improvement, e) toxicity, f) concomitant therapies allowed and utilized, and g) patient status at the conclusion of the trial and at later follow-up, if done. Emphasis should be on measurable, quantitative parameters that can be summarized in tables and clearly-marked graphs. Be specific. Generalities such as "symptoms were reduced", "antiviral activity was seen", "opportunistic infections were reduced", or "lesions of Kaposi's sarcoma were reduced" are of limited value.

7. Product formulation and availability

   Data about the structure, formulation, stability-indicating assay, shelf-life, and availability should be provided to assist in determining the feasibility of conducting clinical trials with the proposed agent.

8. Cover letter delineating your overall development plan for the proposed therapy including the extent of AIDS Clinical Trials Group (ACTG) participation anticipated.

Your compliance with these guidelines will expedite the evaluation of your purified myeloperoxidase compound and will be greatly appreciated by the Committee. Information should be sent to me at the address below:

Mary Anne Luzar, Ph.D.
Executive Secretary
AIDS Clinical Drug Development Committee
Division of AIDS, NIAID
Control Data Building, Room 2A02
6003 Executive Blvd.
Rockville, MD 20852