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Corporation

Rec'd 5/6/97

Via Federal Express

May 2, 1997

Dockets Management Branch
(HFA-305)
Food and Drug Administration
12420 Parklawn Drive
Room 1-23
Rockville, MD 20857

Re: Docket No. 96N-0417

Dear Sir/Madam:

On behalf of Rexim Degussa ("Rexim"), the following comments on the February 6, 1997 Advanced Notice of Proposed Rulemaking on Current Good Manufacturing Practice in Manufacturing, Packing, or Holding Dietary Supplements, Docket No. 96N-0417, RIN 0910-AA59, 62 Fed. Reg. 5700, are submitted.

Degussa Corporation and Rexim Degussa ("Rexim") are wholly owned subsidaries of Degussa AG, which is based in Frankfurt, Germany. Degussa Corp. is a chemicals and metals company based in Ridgefield Park, New Jersey. Rexim is a French Company that manufactures amino acids and their derivatives, which are used as dietary supplements. Degussa Corp. sells Rexim products in the U.S.

While Rexim understand that FDA does not intend nor desires to impose on dietary supplements the type of documentation and validation currently required in the manufacture of pharmaceutical products, we remain concerned that the proposed rule may impose substantial burdens on producers of dietary supplements. As proposed, the rule does not distinguish the obligations on chemical producers from those manufacturers using raw agricultural materials in their processes.

The specific comments of Rexim, organized according to the section headings of the February 6, 1997 Proposal, are attached.

Thank you.

Very truly yours,

Jayne A. Pritchard
Regulatory Compliance Attorney

Enclosure

96N-0417

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Dockets Management Branch
Food and Drug Administration
12420 Parklawn Drive, Room 1-23
Rockville, MD 20857

April 17, 1997

Ref : Current Good Manufacturing Practice in Manufacturing , Packing or Holding Dietary Supplements; Proposed rule, [Docket n°96N-0417]

Dear Sir/Madam

On behalf of Rexim / Degussa Company, I am pleased to submit comments regarding FDA's proposed rule « Current Good Manufacturing Practice in Manufacturing , Packing or Holding Dietary Supplements » 21 CFR Ch.1.
Rexim Degussa is a French Company, manufacturing *Amino Acids and their derivatives*, used especially but not exclusively as *dietary ingredients*.
Rexim understands it is not the intend or desire of FDA to impose on dietary supplements the type of documentation and validation currently required in the manufacture of pharmaceutical products. However, in some areas (contaminations, testings, standards) the proposed rule impose substantial requirements that do not necessarily concern chemical firms which do not carry out raw agricultural materials the quality of which is very poor in regards with potential contamination with microorganisms, filth, pesticides residues etc.

Changes and their rationale

Definitions, k-1- « microorganisms » :

Proposed change : suppress the word « *viruses* ».
Rationale : Including viruses in this definition implies that manufacturer is able to demonstrate there is no potential for virus in its dietary supplement. Industry does not have analytical equipment dedicated to show presence or absence of viruses.

Personnel (a) disease control :

Proposed change : The scope of this paragraph is inappropriate for chemicals, it should be limited to manufacturing, processing and handling of *raw agricultural materials*.
Rationale : Chemical processes are carried out into closed pipes and vessels. The risk for human contamination is very limited and exclusion from operations any worker suffering of wounds seems to be an extreme position.

Plant and grounds (6) :

Proposed change : The scope of this paragraph is inappropriate for chemicals, it should be limited to manufacturing, processing and handling of *raw agricultural materials*.

Rationale : Emanation of fumes and odors is currently observed in chemical processes, however most of chemicals are odorless.

Sanitation of buildings and facilities, (d) water supply :

Proposed change : The scope of this paragraph is inappropriate for chemicals, it should be limited to manufacturing, processing and handling of vegetables, ready-cooked dishes etc.

Rationale : Chemical processes implementing chemical reactions, distillation, crystallization, drying steps remove and/or inactivate microorganisms due to a broad spectrum of processing parameters like pH, osmotic pressure, temperature, pressure, solvents, etc.

Quality control and laboratory operations (a) (iii)

Proposed change : « Quality control unit » should be replaced by '*competent unit*'.

Rationale : The scope of this paragraph, directly transferred from Pharmaceutical cGMP, is inappropriate for chemicals, dietary supplements and ingredients. Chemical and dietary firms do not have the same organization that pharmaceutical ones. The quality control unit does not have the responsibility for reviewing manufacturing records, evaluating errors committed in the manufacture of a product and authority to determine if errors may be corrected. This is the full responsibility of the process manager and do works very satisfactorily.

Production and process controls (a) (1) :

Proposed change : The master production and control record shall be prepared ... and shall be reviewed and approved by *a competent unit* (instead of 'quality control unit').

Rationale : Same comment as for the previous item.

Production and process controls (7) (iv) :

Proposed change : Add « when applicable » into the following sentence : « Such tests may include any appropriate test with sufficient specificity to determine identity, including chemical and laboratory tests, *and when applicable* gross organoleptic analysis, microscopic identification or analysis of constituent markers. »

Rationale : These tests are not applicable to Amino Acids as dietary ingredients.

Production and process controls (9) :

Proposed change : This paragraph should be completed by « *when applicable* ».

Rationale : Chemicals carried out in the manufacturing process of Amino Acids for instance are not necessarily adversely affected by contact with air, heat or other conditions.

Warehousing, distribution and post-distribution procedures, (g) defect action levels :

Rationale : The paragraph mentions natural or unavoidable defects that at low levels are not hazardous to health.

Question : Do they correspond to specifications defined into FCC monographs for Amino Acids ?

If so, we do not have any problem with the proposed rule.

1st Request for comments : need to develop specific defect action levels :

For Amino Acids the FCC monographs are well established and recognized and we feel there is no need for other development.

2nd Request for comments : appropriate testing for plant material :

Production of Amino Acids is not concerned by this item.

3rd Request for comments : standards to be met for certifying dietary products are not contaminated :

* *by filth; harmful contaminants and pesticides residues* : dry crystallized Amino Acids are not concerned by these items → evaluation should be done considering the raw material(s) origin and the manufacturing process of the dietary product.
Testing pesticides residues and harmful contaminants could be avoided when there is no potential for them to be present and, if tested, dietary products will comply with established standards, in the same spirit than for Organic Volatile Impurities in the USP.

* *and is microbiologically safe* : what is the definition of safe? Probably not « sterile ».
If it means « free of objectionable microorganisms » for human consumption, evaluation of origin of raw materials and manufacturing process should be enough to define whether the dietary ingredient is potentially contaminated or not.
The level of potential microbiological contamination has also to be taken into consideration : the risk for wet food from natural origin is heavily higher than for dry ingredients from chemical origin
Microbial testing could be avoided for dry dietary ingredients obtained by chemical process for instance, or at least after demonstrating the materials are free of objectionable microorganisms by testing a sufficient number of representative lots of material.

4th Request for comments :

Procedures are established to assure compliance of finished materials to standards and specific training assures the personnel follows them. If procedures are not implemented by the personnel, manufacturing and analytical processes are not under control and many lots of finished materials are out of standards.
Requirement for procedure to document that the procedures prescribed for the manufacturer of a dietary product are followed would not demonstrate they are followed.
Therefore we propose to cancel this proposed rule.

6th Request for comments :

The supplier of a dietary ingredient does not know the use of its material by customers. Except some basic scientific information on the safety of its material the supplier has not to develop more research in this line, that is the responsibility of dietary supplement customer considering potential interactions with other components of its finished dietary product.

7th Request for comments :

Specific controls for computer controlled or assisted operations have to be evaluated and then adapted considering the risk for the compliance of the finished dietary product with established standards.

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8th Request for comments :

The scope of this proposal should be limited to the dietary firms processing, packing or holding materials from botanical, agricultural or sea origin. The risks for contamination, of dietary ingredients from chemical origin, by pests, insects, filth, microorganisms, pesticides and other agrochemical residues are either not applicable or not so severe than for the previous ones; therefore there is no necessity to extend it to the chemicals manufacturers.

9th Request for comments :

Considering our analysis of the proposed rule, we suggest to establish rules for particular segments of the dietary products industry.

Our company is waiting with interest for further evolution of these proposed rules.

Yours sincerely,

Etienne VILT
Quality Manager

p/c