The above constitute the general policies involved in drafting the respective monographs for NF sterile solids. Exceptions may be made on an individual basis for justified reasons. I am enclosing with this letter a tabulation of NF XII sterile solids and NF XIII sterile solids, which may be of interest to you. The NF XII sterile solids do not include the content uniformity test because this was newly introduced in the case of this dosage form in NF XIII. There is only one inconsistency in this NF XII tabulation, in that Chlordiazepoxide Hydrochloride for Injection should be entitled Sterile Chlordiazepoxide Hydrochloride. As initially marketed, this article included diluents. By the time the monograph was completed, however, the article available contains no added substances but has separate diluents. Consequently, the monograph title should have been revised accordingly, although the monograph definition and the content of the monograph is all satisfactory. In the case of NF XIII sterile solids, the articles are all consistent with our policies with the apparent exception of the monographs Sterile Chymotrypsin and Hyaluronidase for Injection. However, there are special circumstances pertaining to each of these articles which require them to be exceptions to the general policies. These revolve about the fact that both are enzyme products, with peculiar problems associated with the non-homogeneity of enzymes. You will note that in each case (NF XIII page proof, page 169 and page 347), the Assay directives call for conducting the Assay on individual vials of the article rather than pooled samples. As a consequence, weight variation tests are meaningless and the Assay itself amounts to content uniformity.

I trust that the information provided above will be helpful to you in revising your specifications. My principal desire has been to indicate the basis for the NF approach to these monographs and to point out that the approach followed not only provides adequate assurance of suitable standards and specifications, but that the standards and specifications for this type of dosage form are consistent with other dosage forms such as tablets and capsules.

In particular, we find the proposed wording under item 86.4.2. to be especially objectionable and would recommend that appropriate changes be incorporated. We would further recommend that comparable changes be incorporated in section 86.4.3 of the proposed amendment to Federal Standard No. 1d2a be considered.

Sincerely yours,

Edward G. Feldmann, Ph.D.
Director

EGF:pal
Enclosure