DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Center for Biologics Evaluation
and Research
1401 Rockville Pike
Rockville MD 20852-1448

In reply refer to HFM-475

DEC 23 1997

Dear

By this letter, the Food and Drug Administration's (FDA's) Center for Biologics Evaluation and Research (CBER) extends until July 8, 1998, the deadline for compliance with the requirement, pursuant to 21 C.F.R. § 680.3(e), that Bermuda (*Cynodon dactylon*), Kentucky Blue (June) (*Poa pratensis*), Meadow Fescue (*Festuca elatior*), Orchard (*Dactylis glomerata*), Perennial Rye (*Lolium perenne*), Timothy (*Phleum pratense*), Redtop (*Agrostis alba*), and Sweet Vernal (*Anthoxanthum odoratum*), grass pollen extracts be standardized and have potency values determined by an approved testing procedure that measures the allergenic activity of the product.

In an April 8, 1994 letter to your firm, CBER stated that suitable testing methods were available which measure the allergenic activity of eight grass pollen extracts. This letter also stated that after April 8, 1996, new lots of these eight grass pollen extracts, introduced into interstate commerce, would be considered safe and effective and not misbranded only if the new lots were standardized and the potency values for these extracts had been determined by an approved testing method that measured the allergenic activity of the product with respect to a CBER reference standard and serum pool or equivalent CBER approved reference and serum pool. The April 8, 1996 deadline was extended until July 8, 1997, and was subsequently extended until January 8, 1998, in order to ensure an uninterrupted supply of grass pollen extracts.

As the January 8, 1998 deadline has approached, CBER has received requests from the Allergen Products Manufacturers'

Association (APMA) that the deadline be stayed, and from the American Academy of Allergy, Asthma & Immunology (AAAA&I) that the deadline be extended. Specifically, on July 1, 1997, the APMA submitted a Petition for Stay of Action pursuant to 21 C.F.R. § 10.35, requesting that FDA stay the effective date beyond January 8, 1998, of any and all requirements pertaining to the standardization of the grass pollen extracts. On December 5, 1997, members of AAAA&I met with CBER and urged that the January 8 deadline be extended, later memorializing comments on the deadline in a December 17, 1997 letter to the agency. Both the APMA and the AAAA&I raised concerns that the current January 8, 1998 deadline for cessation of manufacture and distribution of non-standardized extracts may result in an inadequate supply of standardized grass pollen extracts. The AAAA&I requested an extension of the deadline to allow for a transition period, in which standardized extracts of these eight grass pollens could be jointly distributed with the currently available non-standardized, so that physicians could be educated regarding the use of standardized grass pollen extracts, and for conversion of patients currently receiving immunotherapy with non-standardized extracts.

After consideration of the issues described above, CBER has determined that an extension of six months from the January 8, 1998 deadline is appropriate in order to allow physicians and manufacturers to address any concerns, including those raised by the APMA and AAAA&I, related to the transition from non-standardized to standardized grass pollen extracts. During the six month extension period (even after approval of a product license supplement to manufacture of standardized grass pollen extracts), manufacturers may continue to distribute non-standardized grass pollen extracts. However, on July 8, 1998, new lots of the eight grass pollen extracts, introduced into interstate commerce, will be considered safe and effective and not misbranded only if the new lots are standardized such that the product's potency has been measured under FDA-approved procedures and FDA has approved the labeling.

Again, CBER strongly suggests that you develop, in a timely fashion, a plan to phase out distribution and sale of non-standardized grass pollen extracts.

If you have any questions, please call Ms. Jennifer Bridgewater in the Division of Allergenic Products and Parasitology, 301-435-3011.

Sincerely yours,

M. Carolyn Hardegree, M.D.
Director
Office of Vaccines
Research and Review
Center for Biologics
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