Formulating Bulk Extract Mixes

ALK TECHNICAL MEMO
November 2018

ALK Medical Scientific Affairs

In February 2015 the FDA issued a guidance to manufacturers stating that "special mixes" can no longer be manufactured. The term "special mixes" refers to those mixes that were specially formulated for general use and not associated with a named patient. To comply, the Allergen Products Manufacturers' Association (APMA) agreed to cease all production of these "special mixes". This technical memo is intended to provide general instructions for formulating "special mixes" (referred to herein as "bulk extract mixes") within a physician's office.

Prescription Formulations – Equal and Unequal Parts

ALK-manufactured mixes had an associated prescription formulation, in which all information necessary for compounding can be found. Formulating a bulk extract mix is very similar to mixing a patient treatment vial; it is important to pay close attention to all components being included to ensure an appropriate extract mix composition and concentration. Table 1 shows an example of an equal parts bulk extract mix prescription formulation. In an equal parts mix, all components are present in the same volume.

In the example (Table 1), four components are used to generate a 10 mL vial of glycerinated, 1:10 w/v mold extract. As denoted, the four components are included at equal strengths (1:10 w/v) and equal parts (component %). Since this is an equal parts mix, the volume of each extract to be added would be calculated as follows:

Volume of individual extract =
Total volume of extract / Total number of components

Table 1: Equal Parts Mix (4 Components)

Component	Strength	Component %
Mucor	1:10 w/v	Equal Parts
Bipolaris	1:10 w/v	Equal Parts
Cladosporium	1:10 w/v	Equal Parts
Alternaria	1:10 w/v	Equal Parts

For the above example, 2.5 mL of each mold extract will be combined into a 10 mL sterile empty vial to generate the desired 10 mL volume of bulk extract mix, which can then be used for patient testing and treatment.

When mix components are not present in equal volumes, these bulk extract mixes are referred to as unequal parts mixes. The following example is an unequal parts bulk extract mix prescription formulation (Table 2). Six components are used to generate a 30 mL vial of 10,000 PNU/mL extract. As denoted, the six components are included at equal strengths (10,000 PNU/mL) and unequal parts (component %, 10-30%). Since this is an unequal parts bulk extract mix, the volume of each extract to be added would be calculated as follows:

Volume of individual extract =

(% component) x (Total volume) / 100

Table 2: Percent Mix (6 Components)

Component	Strength	Component %
False Ragweed	10,000 PNU/mL	30%
Rough Pigweed	10,000 PNU/mL	10%
Lambs Quarters	10,000 PNU/mL	10%
Russian Thistle	10,000 PNU/mL	10%
Sagebrush	10,000 PNU/mL	20%
Mugwort	10,000 PNU/mL	20%

The volume of each extract to be added would be calculated as follows:

Volume of individual extract =
Total volume x Parts for individual extract / Total number of parts in mix

For the example shown in Table 2, using either approach, 9 mL of Ragweed, 3 mL of Pigweed, Lambs Quarters and Russian Thistle, and 6 mL of Sagebrush and Mugwort extract will be combined into a 30 mL sterile empty vial to generate the desired 30 mL volume. Once combined, this mix can be used for patient testing and treatment.

Bulk Extract Mix Concentration Labeling

Mixes should be labeled according to the concentration of the components that are contained within the mix (i.e., 1:10 w/v, 1:20 w/v, 1:40 w/v, 10,000 PNU/mL, 20,000 PNU/mL, 40,000 PNU/mL). This designation applies when all extracts contained within a mix are formulated in the same manner (e.g., all extracts are 1:10 w/v, the resulting mix is labeled as 1:10 w/v). This concentration labeling is not consistent, however, if various extract formulations are used to generate a mix (e.g., 1:20 w/v extracts are combined with 1:10 w/v extracts). In these circumstances, a mix should be labeled with a 1:1 designation, denoting that various concentrations were utilized.

Bulk Extract Mix Expiration Dating

The expiration date for a mix should not exceed the expiration date assigned to the earliest expiring component contained within the mix. For example, the expiration date for a mix containing an aqueous extract expiring December 2016 and a glycerinated extract expiring December 2018 would be December 2016. The inclusion of glycerinated extracts with aqueous extracts does not extend aqueous dating.

Bulk Extract Mixes and USP 797

All safety and sterility recommendations put forth in the USP 797 allergenic extract compounding guidelines apply to the formulation of

bulk extract mixes [1, 2]. Annual media fill tests should be completed to ensure appropriate mixing technique[1]. Please contact your local Allergy Consultant for vendor recommendations. Sterility testing is not required for mixes formulated in a physician office setting.

Allergen Mixes vs. Individual Species

Individual species extracts can be utilized in place of mixes to formulate patient treatment vials, in many circumstances. This can be facilitated by careful analysis of cross-reactivity among species and a thorough understanding of allergen significance. The use of individual species negates the potential for introducing unnecessary allergens to a patient who is not sensitized to all mix components, a controversial issue that has yet to be evaluated extensively in clinical research[1]. Furthermore, with multi-component mixes, therapeutic dosing is difficult to achieve, due to significant dilution of the individual extracts. ALK Medical Scientific Affairs can evaluate current mixing protocols and formulate dosing strategy recommendations based off of individual components, rather than mixes.

ALK Commitment

ALK is committed to helping Allergy Specialists maintain uniformity of care for their patients. Please do not hesitate to contact your Allergy Consultant, Customer Service (800.325.7354) or Medical Scientific Affairs (855.782.9323, science@alk.net, or submit your scientific questions to our 24/7 online helpdesk in a support ticket at: https://alkinc.freshdesk.com) should you have additional questions or concerns regarding ALK products.

This technical memo is not intended to replace physician judgment with respect to the clinical diagnosis and treatment of patients. All decisions regarding potential patient care are solely at the discretion of the treating physician.

References

1. Cox L, Nelson H, Lockey R, Calabria C, Chacko T, Finegold I et al. Allergen immunotherapy: a practice parameter third update. *J Allergy Clin Immunol*. 2011;127(1 Suppl):S1-S55.
2. Lin SY, Houser SM, Gross G, Aaronson D. Impact of newly revised sterile medication compounding guidelines USP {797} on allergy vial preparation. *Otolaryngol Head Neck Surg*. 2008;139(1):5-6.