

Updates on USP 797 and mixing for Allergy

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Disclosures

- ▶ Donald Accetta
 - ▶ Forensic consultant
- ▶ Deborah Pedersen
 - ▶ None relevant

Ground rules

- ▶ Don't shoot the messengers
- ▶ We are not lawyers
- ▶ Sharing ideas and best practices should help all of us to improve
 - ▶ Please share your ideas from your own practice

History of sterile compounding

- ▶ Historically unregulated
- ▶ 1990s: case reports of compounding errors
 - ▶ 4 patients die
 - ▶ 2 patients lose vision
 - ▶ Pediatric patient dies due to improper NaCl concentrate infusion
- ▶ USP 797 proposed in 2004, launched 2008
- ▶ 2012: Fungal meningitis outbreak
- ▶ 2014: USP 797 update proposed, Launched Nov 2023

Purpose of USP 797

- ▶ The intent of USP 797 is to establish practice and quality standards and prevent harm to patients resulting from contamination, variation in the strength of ingredients and chemical and physical contaminants

Allergists need to comply with USP 797 because:

- ▶ It is the law
- ▶ It is the right thing to do
- ▶ Non-compliance could result in the loss of numerous carve-outs

If you are not compliant with USP797

1. How risky is it?
2. Is it because you can't comply or is it because you don't want to comply?

USP 797 Carve out for Allergy

- ▶ 2.5 pages of specific guidelines for Allergenic Extracts in USP 797 document
- 1. Personnel Qualifications
- 2. Hygiene and garbing
- 3. Facilities
- 4. Cleaning and disinfecting
- 5. Establishing Best Used Dates (BUDs)
- 6. Labeling
- 7. Shipping and Transport
- 8. Documentation

Personnel Qualifications

- ▶ Identify immunotherapy “expert” in the practice to be supervisor
 - ▶ Demonstrate that you have gone to trainings/talks on USP797
- ▶ Initial and Annual training for all mixing staff
 - ▶ Written examination (available on College website)
 - ▶ Fingertip glove testing and media fill test - yearly
 - ▶ Evaluation of sterile technique - yearly
 - ▶ Must compound every 6 months or else need to complete competencies before mixing again

Fingertip glove test

- ▶ 3 sets (R and L hand) for initial competency and 1 set for annual competency
- ▶ Must perform hand hygiene and be fully garbed (gown, mask, hairnet, gloves) and re-do hygiene and garbing for each set during initial competency evaluation
- ▶ Cannot rub gloves with isopropyl alcohol prior to testing

- ❖ We found that having a “helper” works best.
 - ❖ Helper opens each set of plates for the person getting tested so there is as little time as possible for accidental contamination
 - ❖ Helper can also label each test
- ▶ Incubation at 30-35° C for no less than 48h, then 20-25° C for no less than 5 additional days

Media Fill Test

- ▶ Commercially available media fill kit for sterile compounding
 - ▶ Allerteq www.valiteq.com
- ▶ Complete hand hygiene and garbing
- ▶ Follow directions on kit
 - ▶ Transfer 5ml of testing solution using aseptic technique 10 times
 - ▶ Incubate both vials for 7 days at 20-25°C and then another 7 days at 30-35°C

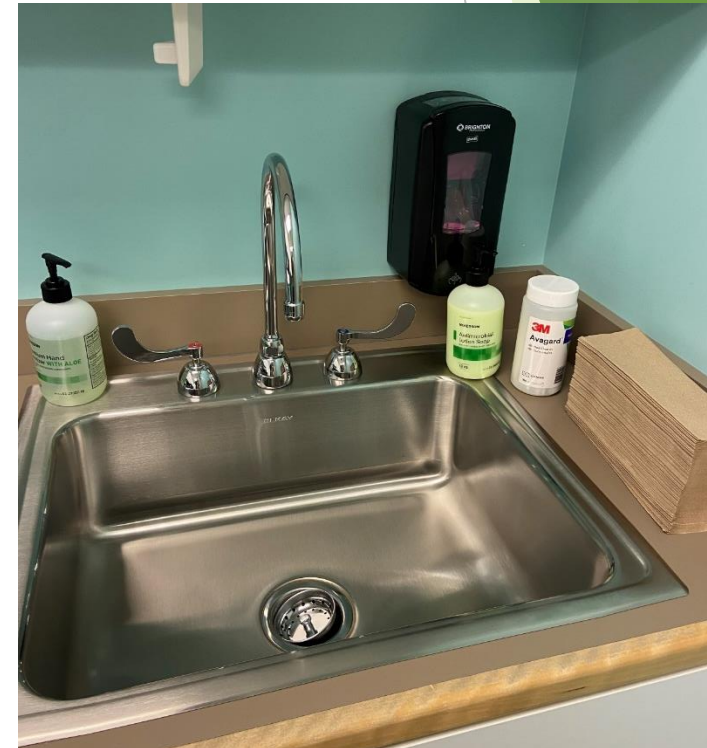
Incubation of tests

- ▶ Samples can be mailed to a company for incubation
 - ▶ Cost is per mixing person
 - ▶ Special pricing via College website
- ❖ We bought a small incubator obtained the agar plates and the Allerteq vials
- ❖ Incubation in our own office saved time and money



Hygiene and garbing

- ▶ Hand Hygiene (Box 3-1 of USP 797)
 - ▶ Use disposable nail cleaner to remove visible debris from under nails with warm running water
 - ▶ Wash hands and forearms to elbows with soap and water for 30 seconds
 - ▶ Dry hands and forearms to elbows with low lint towels



Hygiene and garbing

- ▶ Minimum garbing requirements
 - ▶ Low lint gown fitting snugly at wrists and closed at neck
 - ▶ Disposable or washable
 - ▶ Low lint disposable cover for head and facial hair if needed
 - ▶ Face mask
 - ▶ Sterile powder free gloves
- ❖ We bought washable gowns and wash them after each mixing day
 - ❖ Physicians bring home and launder them separately
 - ❖ Less hot than disposable, less \$\$\$

Facilities

- ▶ ISO class 5 PEC **OR** a dedicated allergenic extracts compounding area (AECA)
 - ▶ Away from UNSEALED windows
 - ▶ Away from restrooms, warehouses, food
 - ▶ 1 meter away from sink
- ▶ PEC must be certified every 6 months per protocols in section 5 of USP797
 - ▶ Has many specific rules

Facilities - AECA

- ▶ Visible perimeter to establish boundaries
- ▶ No other activities performed in the area while compounding
- ▶ All surfaces (walls, floors, fixtures, counters and cabinets) must be cleanable
 - ▶ No carpet!
- ▶ Surfaces should be resistant to damage by cleaning and sanitizing agents
- ▶ Prep surface must be smooth, impervious and free from cracks/crevices
- ▶ Dust collecting overhangs should be minimized and easily cleanable
- ▶ Good lighting, temp and humidity controls

AECA - visible perimeter

- ▶ Can be a room, but does not need to be
- ▶ Can be an area marked with tape on the floor
- ❖ Our AECA is defined in our mixing manual as being located in the room known as “the lab”.
 - ❖ “The AECA includes the area of the stainless steel mixing table, the refrigerator and the area 3 feet in front of the table/fridge for mixing personnel to stand”

AECA - “Cleanable” surfaces

- ▶ All surfaces (walls, floors, fixtures, counters and cabinets) must be cleanable
- ▶ What does this mean??
- ▶ Is drywall “cleanable”?
 - ❖ We went with plastic paneling

The screenshot shows a Home Depot product page for a plastic panel. The page is titled "#1 Home Improvement Retailer" and features a navigation bar with the Home Depot logo, location information (Taunton 9PM, 02780), a search bar, and icons for Shop All, Services, DIY, and My Account. The breadcrumb trail indicates the product is in the "Decorative Wall Paneling" category. The product is a "1/16 in. x 4 ft. x 8 ft. Plastic Panel" with a "Top Rated" badge, a 5-star rating from 390 reviews, and 625 questions and answers. The price is \$25.99, with a promotional offer of \$0.98 after a \$25 discount. The product covers 32 sq. ft. and is described as "Incredibly durable and easy to maintain," "Installs best with specially formulated FRP adhesive," and "Highly rated for quality and value." The Taunton Store has 60 units in stock. Delivery options are available for pickup today (free) or delivery tomorrow (75 available).

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Internet # 202090190 Model # 63003 St

Top Rated

1/16 in. x 4 ft. x 8 ft. Plastic Panel

★★★★★ (390) Questions & Answers (625)

Covers 32 sq.ft. (81c /sq.ft.)

\$25.99

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- Incredibly durable and easy to maintain
- Installs best with specially formulated FRP adhesive
- Highly rated for quality and value (see reviews)
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✓ 60 in stock Aisle 26, Bay 011

Pickup at Taunton Delivering to 02780

Pickup Today 60 in stock FREE	Delivery Tomorrow 75 available
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[Get it as soon as tomorrow.](#) Schedule your delivery in checkout.

1 [Add to Cart](#)

Evolution of an AECA



2013 - After NE compounding. CLEAN UP THE AREA

Evolution of an AECA



2018: Remove upper cabinets.
Remove porous work surface and
replace with stainless steel table
Move paperwork and computer away
from the mixing area

Evolution of an AECA

2023: Installation of
“Cleanable” plastic
paneling on the wall in
front of the mixing surface



Alternative locations for AECA

- ▶ If mixing happens on a less busy day in the office, could a patient exam room turn into the AECA?
 - ▶ Have a table in that room that becomes the mixing table
 - ▶ Push table to the middle of the room for mixing - walls will not need to be “cleanable”
- ▶ Is there an area in your nursing station that can be used?
 - ▶ Put tape on the floor to delineate the area
 - ▶ Cover wall with permanent or removable covering

Cleaning and Disinfecting

- ▶ All work surfaces must be cleaned and disinfected daily and when surface contamination is known/suspected
- ▶ Apply Sterile 70% IPA to work surface between each prescription set
- ▶ Vial stoppers of serums must be wiped with Sterile 70% IPA prior to being used
- ▶ Walls, doors, and door frames within the AECA must be cleaned and disinfected monthly and when contamination known/suspected
 - ❖ Checklist for cleaning personnel for monthly cleaning - initials and date
- ▶ Ceilings within the perimeter of AECA must be cleaned when visibly soiled or contamination is known/suspected

Cleanable ceiling??

- ▶ Vinyl ceiling tiles?
- ❖ Replacement of regular ceiling tiles if soiled
 - ❖ Manual: “Ceiling tiles in the AECA will be cleaned via replacement with new ceiling tiles if they are visibly soiled or if surface contamination is known or suspected”

Best Used Date (BUD)

- ▶ No later than the earliest expiration date of any extract or diluent in the prescription set
- ▶ Not to exceed 1 year from the date the prescription set is mixed/diluted
- ❖ We do not mix with extract that is less than one year from expiration - we will save for testing only or throw out so that we do not run into issues with vials expiring too soon
 - ❖ You may find another plan works for your office

Labeling

- ▶ Patient name
- ▶ Type and fractional dilution of each vial with corresponding vial number
- ▶ BUD
- ▶ Storage conditions

Shipping and Transport

- ▶ “If shipping or transporting allergenic extract prescription sets, compounding personnel must select modes of transport that are expected to deliver properly packed prescription sets in an undamaged, sterile, and stable condition. Inappropriate transport can adversely affect the quality of allergenic extract prescription sets.”
- ▶ “When shipping or transporting allergenic extract prescription sets that require special handling, personnel must include specific handling instructions on the exterior of the container.”
- ❖ We no longer ship extract due to these requirements

Documentation

- ▶ **SOPs describing all aspects of the compounding process**
- ▶ Personnel training records
- ▶ Certification reports of PEC if using (not needed for AECA)
- ▶ Temperature logs for refrigerators
- ▶ Compounding records for individual allergenic extract prescription sets
- ▶ Information related to complaints or adverse events
- ▶ Investigation and corrective actions

SOPs & Training Records

- ▶ Practice should have written available SOPs for all aspects of the training, cleaning and mixing process.
 - ▶ College and Academy have good examples.
 - ❖ Ours is about 20 pages long and is very similar to what is found from the College with edits where needed to make it “ours”
 - ▶ Make sure that you **FOLLOW** your SOPs
- ▶ College also has sample paperwork to document training
 - ❖ We fill this out and photograph our fingertip glove tests, etc.
 - ❖ We keep this paperwork in the personnel files of mixing personnel

Refrigerator temperature logs

- ❖ We have 2 ways of monitoring temperatures
 1. Temperature monitor with audible alarm on the refrigerators
 - ❖ Staff documents temp daily on log sheet attached to each refrigerator
 2. WiFi connected temperature monitor
 - ❖ Sends text alerts if temp is abnormal
 - ❖ Works well as long as there is electricity and WiFi!

- ❖ Sump pump alarm
 - ❖ Attached to largest fridge (with all prescription vials)
 - ❖ Sends a text if power is interrupted

Compounding records for individual prescription sets

- ▶ Name, concentration, volume, manufacturer/vendor, lot number and expiration date for each component
- ▶ Date and time of preparation of allergenic extract
- ▶ Assigned internal identification number
- ▶ A method to identify the individuals involved in the compounding process and verifying the final CSP (compounded sterile preparation)
- ▶ Total quantity compounded
- ▶ Assigned BUD and storage requirements
- ▶ Results of QC procedures (e.g. visual inspection, verification of quantities)

Compounding records: Can this be streamlined for your practice??

- ▶ Likely highly individualized plan
- ▶ Copying lot number and expiration date for each extract difficult
- ▶ And you need to make sure you know how to track this information
 - ▶ Imagine a manufacturer calls with a recall of an extract in 6 months, how do you figure out which patients have that extract in their vials???

FIGURE 1. EXAMPLE – ALLERGEN IMMUNOTHERAPY EXTRACT PRESCRIPTION (blank form available in Appendix)

Patient Name: Mary Wheeze		Prescribing Physician: Dr. Allergist	
Patient Number:		Address:	
Birth Date:		Telephone:	
Telephone:		Fax:	

Allergen Extract Name: R, Dm, C, G		Maintenance Concentrate Prescription Form			
Bottle Name Abbreviations		Prepared by: Great Nurse	Date Prepared: 11/01/2019	Time: 10 a.m.	
Tree: T	Mold: M	Dates of subsequent dilutions from maintenance concentration with expirations dates:			
Grass: G	Cat: C	Vial _____ From Vial _____ on ____/____/____	Expiration date: ____/____/____		
Weed: W	Dog: D	Vial _____ From Vial _____ on ____/____/____	Expiration date: ____/____/____		
Ragweed: R	Cockroach: CR	Vial _____ From Vial _____ on ____/____/____	Expiration date: ____/____/____		
Mixture: Mx	Dust Mite: Dm	Vial _____ From Vial _____ on ____/____/____	Expiration date: ____/____/____		

Antigen Number	Extract Name Allergen or Diluent (Common name of Genus/species)**	Concentration and Type Manufacturer's Extract (AU, BAU, W/V, PNU)/ (50%, G, Aq, Ly, AP)	Volume of Manufacturer's Extract to Add	Extract Manufacturer	Lot Number	Expiration Date
1	Short Ragweed	1:10 w/v G (350 mcg Amb a1)	0.25 ml	Greer	11111	12/25/2021
2	<i>D. farina</i>	10,000 AU/ml G	0.5 ml	Allermed	22222	12/26/2021
3	<i>D. Pteronyssinus</i>	10,000 AU/ml G	0.5 ml	Antigen labs	33333	2/7/2022
4	Cat	10,000 BAU/ml G	2 ml	Hollister-Stier	44444	12/5/2021
5	Timothy Grass	100,000 BAU/ml G	0.4 ml	ALK	55555	12/3/2021
6						
7						
8						
9						
10						
Diluent	HAS		1.35 ml	ALK	66666	12/5/2021
Total Volume						

**Components of mixes listed on a separate sheet.

Specific Instructions:	
Prescribing Physician's Signature	Date

Volume to add = $\frac{\text{Maintenance Concentration}}{\text{Conc. of Manufacturer's Extract}} \times \text{Total Volume}$

Maintenance concentration and subsequent dilutions reported as volume/volume (v/v) dilutions with maintenance concentrations-1:1 v/v

BAU-Bioequivalent Allergy Unit, AU-Allergy Unit
 PNY-Protein Nitrogen Unit
 W/V-Weight per Volume Ratio
 G-50% Glycerinated
 Aq-Aqueous, Ly-Lyophilized
 AP-Alum precipitated, AcP-Acetone precipitated

By Use Date _____

Storage Requirements _____

Results of Quality Control (e.g. visual inspections, second verification of questions) _____

*Adapted from Allergen immunotherapy: A practice parameter second update. *J Allergy Clin Immunol* 2007;120: S77.

3 Affix one sticker for each patient on this paper on the date of mixing

4

5 MIXING Date: _____ Initials: _____

6

7 Extract	Lot	Manufacturer	Exp date
8 Ash 1:20	344952	Greer	9/29/2021
9 Birch 1:20	345907	Greer	9/29/2021
10 Cat 10,000 BAU	E1900705	JHS	7/2/2022
11 Dock-sorrel 1:20	362196	Greer	8/3/2022
12 Dog	363924	Greer	11/18/2022
13 Elm 1:20	353167	Greer	11/11/2021
14 Std Grass Pollen: Greer Grass Mix #7 100,000 BAU	370590	Greer	3/3/2021
15 Hickory 1:20	346923	Greer	9/29/2021
16 Horse 1:20	354154	Greer	2/18/2022
17 Maple 1:20	348350	Greer	9/29/2021
18 Mite Df 10,000 AU	E1900248	JHS	6/5/2021
19 Mite DP 10,000 AU	E1900220	JHS	10/8/2021
20 Mold Mix 1:20	366989	Greer	8/18/2022
21 Oak: 1:20	363884	Greer	8/3/2022
22 Plantain: 1:20	350748	Greer	9/29/2021
23 Poplar 1:20	366634	Greer	8/3/2022
24 Rabbit 1:20	354373	Greer	2/18/2022
25 Ragweed Mix 1:20	362594	Greer	11/28/2021
26 Sycamore 1:20	361346	Greer	11/18/2022
27 Timothy 100,000 BAU	358827	Greer	8/11/2021
28 GS 3 Weed Mix 1:20	350238	Greer	9/29/2021
29 Willow 1:20	352094	Greer	12/19/2021
30			
31 Diluent (HSA)	360981	Greer	1/31/2023
32			
33			
34			
35			

1

2

3 **VIAL SHEET FOR MIXING**

4 Print one sheet per mixing day

5	LOT NUMBER		EXP. DATE
6 5cc Red top empty vial	4503084	Greer	4/1/2027
7 5cc Yellow top 4.5ml fill vial	420419	Greer	3/1/2027
8 5cc Blue top 4.5ml fill vial	419152	Greer	2/1/2027
9 5cc Green top 4.5ml fill vial	419914	Greer	2/1/2027
10			
11 10cc silver top 9ml fill vial	403054	Greer	2/1/2026
12			
13			
14			
15			
16 Affix patient sticker below Note only if New or dilutions made			
17			
18			

Summary

- ▶ Lots of information in 2.5 pages
- ▶ Designate your AECA and work to make it compliant
- ▶ Write SOP tailored to your practice and follow it!
- ▶ Use resources available
 - ▶ College: <https://college.aaaai.org/toolkits/allergen-extract-mixing-toolkit/>
 - ▶ Academy: <https://education.aaaai.org/compounding-corner/compoundingcorner>
 - ▶ Colleagues!

If you are not compliant with USP797

1. How risky is it?
2. Is it because you can't comply or is it because you don't want to comply?

