USP 797 and Me: steps to implement the new extract mixing standards

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Executive Director of Advocacy and Governmental Affairs, ACAAI
Past President, ACAAI

Objectives

At the end of this presentation, participants:

• Should understand the requirements of the new USP 797
• Understand why it is critical to meet the USP standards
• Ensure their individual office staff and mixing areas are compliant with USP 797 requirements
Important Updates

- September 1, 2021 – Proposed revisions to <795> and <797>
- September 1, 2021 – Registration for Open Forums for proposed revisions to USP General Chapters <795> and <797>
- November 25, 2020 – USP Stakeholder Engagement on veterinary compounding (General Chapters <795> & <797>)
- September 15, 2020 – Open Forum for Beyond-Use Date (BUD) Provisions in General Chapters <795> & <797>
  - Presentation
  - Agenda
  - Roundtable summary
- July 21, 2020 – USP Stakeholder Engagement Plan on Beyond-Use Date (BUD) Provisions in General Chapters <795> & <797>
  - Registration opened for September, 15 2020 Open Forum
- May 26, 2020 – Update on stakeholder engagement activities related to beyond-use-date (BUD) provisions in General Chapters <795> & <797>
- March 12, 2020 – Appeals Panel issues decisions on the Appeals to USP <795>, <797>, and <825> (see FAQs on USP Compounding Appeals)
- September 23, 2019 – Revised General Chapter <797> is postponed until further notice. Click here for more information.
- June 1, 2019 – Publication Date of Revised <797> in USP-NF

*IMPORTANT NOTE: The currently official version of General Chapter <797> (last revised in 2008) remains official.

For more information on other compounding chapters click here.
Understanding the 2019 USP Document

- The latest USP document can be confusing
- It includes the regulations for three different classes of compounded materials
  - Compounded Sterile Preparation (CSP) 1
  - CSP 2
  - Allergen Extracts
- The regulations regarding Allergen Extracts are NOT the same as the regulations for CSP 1 and 2
  - Allergen Extracts are recognized as unique
  - Allergen Extract regulations are contained in Chapter 21 of the latest USP document

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College Solutions
The practical support you need, when you need it.

Our new Allergen Extract Mixing Toolkit has it all – instructions, checklists, assessments and more.

Ready to get started? Learn about the process with our resources:

- Get a thorough review with our easy-to-read version of Chapter 21 (Compounding Allergenic Extracts) of the final USP 797 rule.
- As you examine all of the information, get answers to frequently asked questions about mixing compliance.

Your office needs to be compliant, and the College is here to help. Start using the toolkit today! It’s free for members!

Explore all of the College’s resources for practice management and professional development.
Compounding?
Do allergists compound?

- The mixing of allergy immunotherapy kits is considered compounding by USP
- Thus, allergists and their offices fall under USP 797 compounding requirements
- Compounding language located Section 503A of Food Drug and Cosmetic Act; has always required physician compounders to comply with USP 797.
- USP 797 has contained a “carve out,” a special Allergy Section, specifically to address compounding of allergenic extracts since 2006; direct result of JCAAI (now the Advocacy Council) involvement
  - This means allergy extracts were not subject to many of the more onerous requirements for sterile compounding
USP<797> 21. COMPOUNDING ALLERGENIC EXTRACTS

- Licensed allergenic extracts are mixed and diluted into prescription sets for an individual patient.
- Because patients must be maintained on a maintenance dose of prepared concentrated allergenic extracts for a period of time longer than the Beyond Use Dates (BUDs) specified for Category 1 and Category 2, longer BUDs are required for prescription sets to achieve effective therapy.
- Allergenic extracts prescription sets must follow standards at least as stringent as those in this section.

Terminology

- CSP – Compounded Sterile Preparation
- BUD – Beyond Use Date
  - not the manufacturers expiration date
- ISO - International Organization for Standardization
- ISO Class # - lower the ISO number the cleaner the room
- AECA - Allergenic Extracts Compounding Area
- PEC - Primary Engineering Control
  - device that provides an ISO Class 5 environment for a work site – laminar flow hoods are the most common
Areas of Focus

1. Mixing facility
2. By Use Date (BUD)
3. Labeling
4. Personnel Qualifications
5. Personnel Hygiene and Garbing
6. Required Testing
7. Documentation
8. Shipping and Transport of Allergen Extracts

Facilities:

The compounding process must occur in an ISO Class 5 PEC OR in a dedicated Allergenic Extracts Compounding Area (AECA).

- ISO Class 5 PEC (Primary Engineering Control)
  - Generally known as a “hood”
  - NOT required, but acceptable: if used, must be certified every 6 months
- The PEC or AECA used to compound prescription sets must be located away from unsealed windows, doors that connect to the outdoors, and traffic flow.
- Neither a PEC nor an AECA may be located where environmental control challenges (e.g., restrooms, warehouses, or food preparation areas) could negatively affect the air quality.
- The PEC or the work surfaces in the AECA must be located at least 1 meter away from a sink.

Most Allergy Practices will use an AECA
Facilities:
AECA Specific Requirements

• **Must** have a visible perimeter (tip: indicate boundaries)
• During compounding activities, **no other activity is permitted** in the AECA.
• Surfaces of walls, floors, fixtures, shelving, counters, and cabinets in the AECA **must** be cleanable.
• Carpet is not allowed in the AECA.
• Surfaces **should** be resistant to damage by cleaning and sanitizing agents.

Facilities:
AECA Specific Requirements (cont.)

• Surfaces in the AECA upon which the allergenic extract prescription sets are prepared **must** be smooth, impervious, free from cracks and crevices, and non-shedding to allow for easy cleaning and disinfecting.
• Dust-collecting overhangs such as utility pipes, ledges, and windowsills **should** be minimized. If present, they must be easily cleanable.
• The AECA **must** be designed and controlled to provide a well-lighted working environment, with temperature and humidity controls for the comfort of compounding personnel wearing the required garb.
Facilities:
PEC Specific Requirements*

• It’s much more than just having a laminar flow hood
  – All interior surfaces must be cleaned and disinfected daily
• Certification of the ISO Class 5 area including the PEC must be performed initially, and recertification must be performed at least every 6 months and must include:
  1. Airflow testing
  2. HEPA filter integrity testing
  3. Total particle count testing
  4. Dynamic airflow smoke pattern test

*USP <797> Section 5. Certification and Recertification

Disinfection Requirements

• AECA, all work surfaces in the AECA where direct compounding is occurring must be cleaned and disinfected daily and when surface contamination is known or suspected. Apply sterile 70% IPA to the horizontal work surface between each prescription set.
• Walls, doors, and door frames within the perimeter of the AECA must be cleaned and disinfected monthly and when surface contamination is known or suspected.
• Ceilings within the perimeter of the AECA must be cleaned and disinfected when visibly soiled and when surface contamination is known or suspected.
• Vial stoppers on packages of conventionally manufactured sterile ingredients must be wiped with sterile 70% IPA to ensure that the critical sites are wet and allowed to dry before they are used to compound allergenic extracts prescription sets.
Establishing BUDs

- The BUD for the prescription set **must be no later** than the earliest expiration date of any allergenic extract or any diluent that is part of the prescription set, and the BUD must not exceed 1 year from the date the prescription set is mixed or diluted.

- Example:
  - Vial being made on 7/19/2019: 1 year = 7/18/2020
  - Dust mite Expiration date 6/18/2020
  - Diluent Expiration date 12/1/2019
  - **BUD 12/1/2019**

Labeling

- USP 797 Requires the following information be displayed prominently and understandably on each vial of an allergenic extract
  - Patient name
  - Type and fractional dilution of each vial, with corresponding vial number
  - BUD
  - Storage Conditions
Compounding Records must include at least the following information:

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

Personnel Qualifications

- A designated person with training and expertise in allergen immunotherapy is responsible for ensuring that personnel who will be preparing allergen immunotherapy are trained, evaluated, and supervised.
- Before beginning to independently prepare allergenic extracts all compounding personnel must complete training and be able to demonstrate knowledge of principles and skills for sterile compounding as follows:
Personnel Qualifications

1. **Must** complete training and demonstrate knowledge and skills for sterile compounding
2. **Must** pass written or **electronic testing** before they can be allowed to compound, and then pass annual test of knowledge.
3. **Must** successfully complete **gloved fingertip and thumb sampling**
   - *Initially* on both hands no fewer than 3 separate times. Each fingertip and thumb evaluation **must occur after** performing separate and complete hand hygiene and garbing procedure
   - *at least* every 12 months thereafter.
4. **Must** successfully complete Media Fill Test initially and then annually

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Personnel Hygiene and Garbing

- Remove all hand, wrist, and other exposed jewelry including piercings that could interfere with the effectiveness of garbing (e.g., the fit of gloves, cuffs of sleeves, and eye protection) or otherwise increase the risk of contamination of the CSP. Cover any jewelry that cannot be removed.
- Not wear earbuds or headphones.
- Not bring electronic devices that are not necessary for compounding or other required tasks into the compounding area.
- Keep nails clean and neatly trimmed to minimize particle shedding and avoid glove punctures. Nail products (e.g., polish, artificial nails, and extenders) must not be worn.
- Wipe eye lenses, if worn.
- *The designated person(s) may permit accommodations as long as the quality of the CSP and environment will not be affected.*
Gloved Fingertip Sampling (new)

- Compounding pharmacists have been doing this since at least 2006.
- Done after personnel has completed hand hygiene and garbing
- Must be done 3X initially, and then annually

Media Fill Test

- Must be done annually
- Common in pharmacies
- Aseptic technique focus
- Sterile media (not allergen extract)
- New requirements for incubation
One Stop Shop for College Members Only

- Everything you need shipped in a temperature-controlled cooler that includes:
  - The media fill kit(s)
  - Gloved fingertip-thumb sampling plates
  - Detailed instructions
  - Incubation and reporting services
- Receive a detailed report with the results to demonstrate your adherence with USP.
- 15% discount.

Documentation

- All facilities where allergenic extract prescription sets are prepared must have and maintain written or electronic documentation to include, but not limited to, the following:
  - SOPs describing all aspects of the compounding process
  - Personnel training records, competency assessments, and qualification records including corrective actions for any failures
  - Certification reports of the PEC, if used, including corrective actions for any failures
  - Temperature logs for the refrigerator(s)
  - Compounding records for individual allergenic extract prescription sets
  - Information related to complaints and adverse events
  - Investigations and corrective actions
Shipping and Transport of allergenic extract prescription sets

• Inappropriate transport can adversely affect the quality of allergenic extract prescription sets.
• **Must** select modes of transport that are expected to deliver properly packed prescription sets in an undamaged, sterile, and stable condition.
• If sets require special handling, **must** include specific handling instructions on the exterior of the container.

Thank you!
2021 11 07: Immunotherapy: The Compliant Mixing Room

Bryan L. Martin, DO, MMAS, FACAIA, FAAAAI, MACOI, FACP
Past President: ACAAI
President Elect: WAO
Professor and Chief of Allergy Immunology

Disclosures

- Dr. Martin has no relevant financial relationships to disclose.
- This presentation will not include any non-FDA approved or investigational uses of products or medical devices.
Objectives

- Encourage Patient safety from the patient’s perspective
- Use current guidelines to improve the safety and effectiveness of immunotherapy in the office
- Differentiate between systems problems & individual error

Early Reports

- 1819: Dr. John Bostock describes (his own) symptoms and calls his case “hayfever”
- 1872: Dr. Morrill Wyman reports ragweed to be the cause of “autumnal catarrh”
- 1873: Dr. Charles Blackley recognized pollen grains as causative agent
- 1906: Dr. Clemens Von Pirquet coins the term “allergy”
- 1911: Drs. Leonard Noon and John Freeman inject patients with grass pollen extracts in order to desensitize them.
Immunotherapy: the beginning

- In 1911 Leonard Noon first used the technique of specific immunotherapy.
- First two publications:
- Noon dies of tuberculosis in 1913.

1911-2011
100 years of Immunotherapy
If Dr. Noon Walked into your mixing room…

- He would be familiar with much of what being done.
- The issue of standardization was identified as early as 1916
  - Dr. R.A. Cooke established standardization by the nitrogen unit

X-ray room: 1910
USP 797: Allergen extracts as Compounding Sterile Preparations

USP General Chapter <797>
Pharmaceutical Compounding – Sterile Preparations

Links for Supplemental Resources
- Information on USP General Chapter <797>
- USP General Chapter <797> FAQs
- USP General Chapter <797> Education Courses
- Sign up for USP Updates

This text is a courtesy copy of General Chapter <797> Pharmaceutical Compounding – Sterile Preparations, intended to help provide quick and comprehensive tool and resource only. Please refer to the current edition of the USP if for reference.
What Would Mickey Do?

What is the primary focus of every cast member at Disney?

- Nothing at Disney is more important than guest safety.
- “…drop everything you are doing and stop that potentially hazardous activity….”

Immunotherapy the Disney Way

- Four areas of constant quality focus at Disney (in order):
  1. Safety
  2. Courtesy
  3. Show (sensory impression)
  4. Efficiency


What Would Mickey Do?

- Nothing at Disney is more important than guest safety.
- “…drop everything you are doing and stop that potentially hazardous activity….”

1. Safety
2. Courtesy
3. Show (sensory impression)
4. Efficiency

Perceived Risks

- Medical errors are in the public perception
- 42% of the public report they have experienced an error in medical care
  - Themselves
  - Family member

Blendon et al, NEJM, 2002;347:1933-40

Medical Errors

- Individual (human) error
- Systemic or systems-based errors
  - Recognized in Graduate Medical Education literature
  - Six ACGME competencies
    - Systems Based Practice
    - Practice Based Learning and Improvement
    - Patient Care
    - Interpersonal and Communication Skills
    - Professionalism
    - Medical Knowledge
Immunotherapy Clinic

- Are our immunotherapy clinics a particular risk?
- Personalized Health Care
  - Individually compounded medication
    - Allergist devises based on his/her testing
  - Allergist and team responsible for mixing
  - Allergist and team responsible for delivery of medication
  - Allergist and team responsible for monitoring
    - Both pre and post injection

Allergy Shot Room Risks

- JCAAI survey of 1717 allergists
  - Know of an incorrect injection administered within the past 5 years in their office
    - Incorrect dose: 74%
    - Some one else’s injection: 58%

Don Aronson, MD, JD
Past President ACAAI
(1988-1989)

Aronson and Gandhi, JACI, 2004; 113(6):1117-1121
1655 Total Reactions

<table>
<thead>
<tr>
<th>Reaction</th>
<th>No. Reported</th>
<th>%</th>
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<tbody>
<tr>
<td>Local Reaction Only</td>
<td>1128</td>
<td>68</td>
</tr>
<tr>
<td>Systemic: No hospital care</td>
<td>443</td>
<td>27</td>
</tr>
<tr>
<td>Systemic: ED care</td>
<td>59</td>
<td>4</td>
</tr>
<tr>
<td>Systemic: Hospitalized</td>
<td>24</td>
<td>1</td>
</tr>
<tr>
<td>Death</td>
<td>1</td>
<td>0.006</td>
</tr>
</tbody>
</table>

Adapted from: Aronson and Gandhi, JACI, 2004; 113(6):1117-1121

Near-Fatal Reactions to IT

- 273/646 responding allergists reported a NFR
  - Respiratory compromise and/or hypotension
  - 68 of these confirmed and evaluated using a 105-item questionnaire.

Amin et al, JACI, 2006, 117(1): 169-175
Near Fatal Reactions

- Contributing Circumstances
  - Injections at height of season 46%
  - Dosing errors 25%
  - Asthma control issues 10%
  - Previous systemic rxn to IT 9%
  - Concomitant medication 3%
  - Premature departure 3%

Amin et al, JACI, 2006, 117(1): 169-175

Immunotherapy Opportunities for Error/Improvement

- Ordering of Immunotherapy
  - Mixing of Immunotherapy Vials
- Providing Immunotherapy Injection
- Monitoring patient Pre-Post injection
USP General Chapter <797>
Pharmaceutical Compounding – Sterile Preparations
Reprinted from USP 42–NF 37

Links for Supplemental Resources:
- Information on USP General Chapter <797>
- USP General Chapter <797> FAQs
- USP General Chapter <797> Education Courses
- Sign up for USP Updates

Healthcare Law Insights

USP Finalizes Revisions to Sterile Compounding Standards

By Wook R. Tresser, Renee Zerbonia & Isaac Kicilov on July 2, 2019
POSTED IN: COMPLIANCE, PHARMACEUTICALS AND PHARMACY, SPECIALTY PHARMACY, UNCATCATEGORIZED

On June 1, 2019, the United States Pharmacopeial Convention (“USP”) published the final revisions to its pharmaceutical compounding standards (“chapter <797>”). Chapter <797> sets forth standards for the preparation of compounded sterile medications to help ensure products are safe and effective and reduce risks such as contamination or incorrect dosing. The most recent revisions implement new standards and revise existing ones based on recent scientific and technological developments. The chapter <797> revisions also incorporate stakeholder input raised during the July 2018 to November 2018 public comment period, much of which concerned allergens, beyond use dating, and the general ambiguity throughout the chapter.

The USP’s most recent revisions to chapter <797> are extensive, and those who prepare compounded sterile products (“CSPs”) are advised to familiarize themselves with the new standards. Significant changes include:

- Scope of chapter <797>: USP has changed the scope of the chapter by excluding the management of medication and involving sterile

USP 797: Sterile Compounding

Chapter is designed to deal with compounding pharmacies which may look something like this.

Why Allergen extracts have an exception or “carve out”

The chapter DOES cover compounding in the allergist’s office.
USP: Who are these guys???

A. The guys who deliver packages in brown trucks
B. A federal regulatory agency
C. A consortium of state regulatory agencies
D. A non-governmental regulatory entity
E. The PDR publishers

USP: United States Pharmacopeia

- Who are these guys?
  - Around for over 100 years
  - Originally founded by physicians
  - Preceded PDR producing a drug compendium
  - Now serves as an independent regulatory organization
  - Multi-million dollar Global Non-profit organization
  - Receive some grants from Congress
  - Now focused on compounding, among many other issues

- Why are they important?
  - Federal & State laws require compliance with their rules
  - Generally the House prefers USP to regulate, the Senate prefers FDA
  - Joint Commission expects compliance with USP revisions
Compounding?
Do allergists compound?

- The mixing of allergy immunotherapy kits is considered compounding by USP
- Thus, allergists and their offices fall under USP 797 compounding requirements
- Compounding language located Section 503A of Food Drug and Cosmetic Act; has always required physician compounders to comply with USP 797.
- USP 797 has contained a “carve out,” a special Allergy Section, specifically to address compounding of allergenic extracts since 2006; direct result of JCAAI (now the Advocacy Council) involvement
  - This means allergy extracts were not subject to many of the more onerous requirements for sterile compounding

USP 797 Allergy Section

- National legislation requires allergists to comply with the USP 797 Allergy Section as current national standard (replaces any prior guidance on formulation of patient-specific allergenic extracts)
- While USP 797 Allergy section more stringent than prior guidelines, allows for less onerous measures than apply to other sterile compounding
- Most states have laws requiring compliance with USP 797
The TROUBLE begins: New England Compounding Center

- May 2012: Unusual infections identified: fungal meningitis, localized spinal or para-spinal infections, also infections associated with peripheral joint injections
- Sept. 2012: CDC traced fungal infections to 3 lots preservative-free methylprednisolone acetate for injection, from the Framingham, MA based New England Compounding Center (NECC)

Source: www.cdc.gov

Background: New England Compounding Center

- Additional contamination in other NECC preservative-free products subsequently uncovered
- 64 deaths in 20 states, with > 700 infected (deadliest fungal meningitis outbreak in U.S. history)
- After the New England Compounding Center produced mold contaminated products, Congress felt need for legislation to regulate compounding
  - Goal to prevent recurrence NECC-type scandal
  - Compounding law maintains exception for physician in-office compounding that complies with USP 797
- Focus is on Sterility of the compounded materials

Source: www.cdc.gov
Importance of 797 exception for allergen extracts

- USP 797 is primarily concerned with compounding pharmacies
- Addresses Compounded Sterile Preparations (CSPs)
- Category 1 CSP:
  - By Use Date (BUD): 12 hours or less at room temperature OR 24 hours or less if refrigerated.
- Category 2 CSP:
  - BUD over 12 hours at room temperature or over 24 hours if refrigerated
- Allergen extracts clearly did not “fit” either of these categories, so we received an “exception”

USP proposed eliminating ALL exemptions, including allergy extracts

- We first became aware in late September 2015, which created real concern
- USP declined our request for meetings, encouraged us to comment in writing
- Hired expert consultant
  - Very optimistic of resolution, “want to work with us”
- USP rejected previous data from 2006 and new data as “retrospective”
  - Declined to assist in developing acceptable prospective study
  - By mid-January, was obvious “wants to work with us” means, “see things our way”
  - College, AAAAI, AAOA and AMA all worked together to help USP understand what allergen extracts are
  - That work led to the current guidelines, which DO include exemptions for allergen extracts
This is what USP expects for sterile compounding

- USP call this a Primary Engineering Control (PEC)
  - Laminar airflow workbenches (LAFWs)
  - Biological Safety Cabinet (BSCs)
  - Compounding aseptic isolators (CAIs)
  - Compounding aseptic containment isolators (CACIs)

- Allergists can mix in a Allergenic Extracts Compounding Area (AECA)

USP<797> 21. COMPOUNDING ALLERGENIC EXTRACTS

Applicable only when:

1. The compounding process involves transfer via sterile needles and syringes of conventionally manufactured sterile allergen products and appropriate conventionally manufactured sterile added substances, and

2. Manipulations are limited to penetrating stoppers on vials with sterile needles and syringes, and transferring sterile liquids in sterile syringes to sterile vials

3. **Otherwise**, compounding of allergenic extracts patient sets **must** meet the requirements for Category 1 or Category 2
   - To include requirements regarding by use date.
USP<707> 21. COMPOUNDING ALLERGENIC EXTRACTS

- Licensed allergenic extracts are mixed and diluted into prescription sets for an individual patient.
- Because patients must be maintained on a maintenance dose of prepared concentrated allergenic extracts for a period of time longer than the Beyond Use Dates (BUDs) specified for Category 1 and Category 2, longer BUDs are required for prescription sets to achieve effective therapy.
- Allergenic extracts prescription sets must follow standards at least as stringent as those in this section.

Facilities: AECA Specific Requirements

- Must have a visible perimeter (tip: indicate boundaries)
- During compounding activities, no other activity is permitted in the AECA.
- Surfaces of walls, floors, fixtures, shelving, counters, and cabinets in the AECA must be cleanable.
- Carpet is not allowed in the AECA.
- Surfaces should be resistant to damage by cleaning and sanitizing agents.
Frequently Asked Questions

- Do I need to have a laminar flow hood or equivalent?
  - No. But you must have a dedicated Allergenic Extracts Compounding Area

- Must the mixing room be dedicated to mixing only? Can I use it for something else when I am not mixing?
  - When mixing is being done there must be no other activity that would distract the mixer or cause increased traffic in the room. At other times, the room may be used for other activities.

- Does there have to be sink within the confines of the AECA?
  - No. If there is a sink it must be at least one meter from the mixing work surface

Best Immunotherapy Clinic

- What systems can I put into place to minimize errors?
- What systems can I put into place to maximize safety?
- What additional training or documentation must office personnel have?
- How do I meet all the documentation of USP797, to include documentation?
Immunotherapy Orders

- Standardized ordering format
  - Electronic
  - Paper based
- Conscious decision regarding seasonal changes in dose
- Consider cross reacting Antigens
- Consider protease containing antigens
- Constant review
  - Monitor patients pre and post injection
  - Encourage review and discussion

Immunotherapy Mixing and Safety

- Standardized labels and marking
- Expiration dates for extracts clearly marked
- Training and testing of mixing personnel
- Provide time and place for mixing
  - Right space
  - No distractions
- Proper extract storage
VIAL Standardization

- Vials now should conform to a standardized color coding and labeling convention
- Vial standardization makes for a much more consistent work environment in the shot room

Labels

- 2 forms of patient ID
- Contents of vial
- Clearly marked expiration date
### Labels

- Concentration
  - Vial #
  - 1 is MOST concentrated
- Dilution
- Color Code

#### Consistent labeling

- Color coding of vial tops
- Per Practice Parameters:
  - Red (highest concentration), then yellow, blue, green and silver
### Suggested nomenclature for labeling dilutions from the maintenance concentrate

<table>
<thead>
<tr>
<th>Dilution</th>
<th>Vol/vol</th>
<th>label No.</th>
<th>Color</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maint. concentrate</td>
<td>1:1</td>
<td>1</td>
<td>Red</td>
</tr>
<tr>
<td>10-fold</td>
<td>1:10</td>
<td>2</td>
<td>Yellow</td>
</tr>
<tr>
<td>100-fold</td>
<td>1:100</td>
<td>3</td>
<td>Blue</td>
</tr>
<tr>
<td>1000-fold</td>
<td>1:1000</td>
<td>4</td>
<td>Green</td>
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<tr>
<td>10,000-fold</td>
<td>1:10,000</td>
<td>5</td>
<td>Silver</td>
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Ordering IT: Dosing & Standardization

Expiration Dates

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<tr>
<th>DILUTION</th>
<th>Recommended Expiration Time</th>
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<tr>
<td>Maintenance concentrate, vol/vol</td>
<td>6-12 Months*</td>
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<tr>
<td>1:10</td>
<td>6 months</td>
</tr>
<tr>
<td>1:100</td>
<td>6 months</td>
</tr>
<tr>
<td>1:1,000</td>
<td>6 weeks</td>
</tr>
<tr>
<td>1:10,000</td>
<td>Unknown</td>
</tr>
</tbody>
</table>

*The expiration date of the maintenance dose should be the expiration date of the earliest expiring constituent that is added to the mixture.
Summary

- IT is safe and effective
  - And has been for over 100 years
  - There is still much room for improvement
- Concerns about safety in the compounding of sterile products due to patient adverse events, including death following contaminated Compounded Sterile Preparations (CSP)
  - NOT an allergy extract, but materials for intrathecal injection
- USP 797 has published new guidance, effective December 1, 2019
  - Allergists must follow the requirements for compounding of allergenic extracts

Thank You

Bryan.martin@osumc.edu
USACAEL: A Quality Tradition in Military Medicine (1976-2021)

David Schwartz, MD
COL, MC, USA
Program Director NCC A/I Fellowship
Allergy & Immunology Consultant, OTSG

No Conflicts to Disclose
Objectives

• At the end of this session, participants should be able to:
  – Define the population served & the annual prescription volume processed by USACAEL
  – Understand the quality assurance steps & best practice recommendations implemented by USACAEL to decrease prescribing errors
  – Determine which practices used by USACAEL should be applied in your practice

Mission Specifics

• USACAEL (US Army Centralized Allergen Extract Lab)
  – Unique worldwide mission
  – Patient allergen extract vaccines, testing allergens and related biological products
  – Active duty military, family members & military retirees
  – Over 500 medical treatment facilities worldwide (Army, Navy, Air Force, VAMC and Public Health Service)
  – 30,000 patient prescriptions per year.
  – 100,000 vials of allergen extract shipped annually
USACAEL 2020 Totals

- Tri-Service World Wide Mission for the provision of patient Rx, skin test antigens, DTH, venoms
- Annual responsible for:
  - 28,227 prescriptions
  - 76,228 vials
  - $2.9 million
- Work in conjunction with:
  - ARMY (120 clinics)
  - AIR FORCE (~94 AF clinics)
  - NAVY/USMC (~58 clinics)
  - VAMC (41 clinics)
  - USPHS, Coast Guard and Civilian Sites

FY 2010-2020 New and Refill RX Processed and Shipped

13% decrease from 2019
USACAEL Turnaround Time

• Turnaround time significantly increased in 2020 (10-12 weeks) due to:
  – Personnel shortages
  – COVID-19 related workplace precautions

• Time currently is back to previous standards
  – 1-2 weeks for refill prescriptions
  – 2-3 weeks for new prescriptions

• In-house turnaround time is posted and updated on homepage

Color Coded Vial Tops
(10-fold dilutions)

<table>
<thead>
<tr>
<th>Maintenance Concentration (1:1 V/V)</th>
<th>Color</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:10 V/V</td>
<td>Red</td>
</tr>
<tr>
<td>1:100 V/V</td>
<td>Yellow</td>
</tr>
<tr>
<td>1:1000 V/V</td>
<td>Blue</td>
</tr>
<tr>
<td>1:10,000 V/V</td>
<td>Green</td>
</tr>
<tr>
<td></td>
<td>Silver</td>
</tr>
</tbody>
</table>

Assure vial color coding matches label v/v concentration and vial solution color (red vial is labeled strongest concentration (1:1 v/v) and solution will be darkest in color….
**Standard Compounding Practices**

- 10 fold dilutions from full strength (red) vial
- Labeling per v/v concentration, vial number or highest antigen concentration
- Manufacturer and Genus/species consistency
- Stock antigen concentration consistency
- Antigen lot number documentation (ELMS)

**Standard Vial Label**

**Practice Parameters:**
- 2 Identifiers
- Expiration Date
- Contents
- Conc (v:v)
- Color-coding (opt)
- Numbering (opt)

**USP 797- Include:**
- Patient Name
- Beyond Use Date
- Storage Temperature

**USACAEL Labels**
- Name, Rx#, Birth date
- Expiration Date
- Contents (eg: T,W,G)
- Conc (v:v & W/V, BAU, AU)
- Color coding
- Vial Numbering
- Storage Temperature (2-8 degrees C)
ELMS Vial Label

U.S. ARMY ALLERGEN EXTRACT LABORATORY

RX01884898  Red, #1
MOUSE, MICKEY
1/1/1950
T,G,W
1:50 w/v
10,000 BAU/ml
Exp: 13-Feb-16  1:1 (Maint) w/v

USACAECL: Standardized Procedure and Quality Review Checkpoints

1 QA Rx Review on Receipt (RX Form, Authorization, Treatment record, Labels generated for formulation)
2 Supervisory Processing Review
3 Rx Formulation Reviews (pre mix, co worker check after draw and after dilution color check)
4 Final Packing and Shipping Review
USACAEL - Quality Assurance Checkpoints

- Rx Order Received - Admin staff review of patient Rx treatment info, vial label generation for mixing
- Order Reviewed - Supervisory check of labels and Rx
- Order Pre-Mix Check - Mixing Technician Rx review before drawing up antigens for formulation
- Order Pre-Mix Check - Co-worker reviews the amounts, concentration and antigens drawn up for formulation
- Order QA Dilution Check - Co-worker does a solution color check for each dilution vial
- **Shipping QA final check - Medical Technician (last check before it leaves USACAEL

To Err is Human.....Error Tracking for Root Causes and Solutions

- USACAEL Error Tracking Log in the packing area
- Compounding Errors documented by Packing Area Technician - "no staff member name" event error reporting
- Types of errors reviewed for possible causes and preventive measures to be taken
- Instrumental in implementing Quality Assurance Checkpoints over the years

PACKING ROOM IN-HOUSE ERROR TRACKING SHEET
WHAT TO LOOK FOR:
1. Mislabeled vials (ie. Concentration is incorrect, full strength vial is lighter in color)
2. Wrong patient name, RX# or formulation contents on vial labels
3. Color coding is incorrect (blue vial label on red vial, blue or green switched etc)
4. Patient paperwork is with the wrong set of vials

Column1  Column2  Column3  Column4  Column5  Column6  Column7  Column8  Column9  Column10  Column11
DATE  Brief Description of Error  # VIALS
USACAEEL’s Extract Lab Management System (ELMS)

ELMS- A Quality Improvement Initiative

- HIPAA compliant web-based ordering of patient prescriptions and diagnostic testing materials
  - Generate electronic SF 559 (Aeroallergen) and DD 2482 (Venom) forms
  - User tracking of order status (received, processed, shipped)
  - Patient shot tracker and clinic record documentation
  - Dosing and cross reactivity alerts
  - In-house QA documentation of prescription processing and formulation procedures
Prescriber Alerts: Cross Reactivity, Protease and Dosing

Your prescription has been compared to recommendations in the most recent Allergen Immunotherapy Practice Parameters. The following considerations are presented for your review before finalizing this prescription.

Your prescription contains the following group(s) of cross-reactive extracts:

<table>
<thead>
<tr>
<th>Group</th>
<th>Extracts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>[MITES, FARINAeus] [MITES, PTERONY]</td>
</tr>
</tbody>
</table>

Have you factored in these cross-reactivity in selecting your antigens and dosing? If you no longer wish to see cross-reactivity messages, click here.

The most recent Immunotherapy Practice Parameters contains probable effective dose ranges for standardized and non-standardized allergen extracts. Your prescription contains one or more of the following:

- Doses for standardized extracts that are outside the probable effective dose range.
- Doses for non-standardized extracts that are below or at least 4x greater than these ranges.

### Cat Dosing Alert

Have you verified that the doses of your included extracts will ensure optimal dosing?

- Standardized schedules - by physician or clinic
- ELMS Prescription Generation (optional)
Thank You to the USACAEL staff!

A Special thank you to Ms. Sue Kosisky, chief of USACAEL, for her assistance in preparing this presentation

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  - Eric Riddock (Lead)
  - Olijawola Abegunrin
  - Nikki Anspach
  - Donald Cowles
  - Hanna Fantu
  - Michael Frank
  - Cassandra Gamble
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  - Ignacio Ponce-Toledo
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➢ **Administrative Staff**
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➢ **Supply Administration**
  - Rosa Soliz

• Thank you for your time and attention.
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The Allergenic Extracts Compounding Area (AECA)

Sarah Spriet DO, FACAAI
Bethesda, MD

Objectives

At the end of this session, participants should be able to:

• List the facility requirements for extract mixing per USP 797
• Specify the recommended measures to clean and disinfect the AECA
• Identify the appropriate garb and recommended methods to ensure aseptic technique
What does your mixing area look like?

What’s required?

• ISO Class 5 Primary Engineering Control (PEC)
  OR
• Allergenic Extract Compounding Area (AECA)

• Most practices will use an AECA
Allergenic Extracts Compounding Area

- Dedicated space away from unsealed windows, traffic flow
- Not adjacent to restroom, breakroom or storage areas, and at least 1 meter away from sinks
- Visible perimeter
- Restricted to authorized personnel when actively mixing
- Surfaces must be clean, intact and resistant to damage
- Well-lit and temperature controlled
Cleaning & Disinfecting AECA

• All direct compounding surfaces: **daily** and when surface is **contaminated**

• Apply sterile **70% isopropanol (IPA)** to the horizontal work surface between each prescription set

• **Vial stoppers** on packages of manufactured sterile ingredients must be wiped with sterile 70% IPA and allowed to dry before use

Cleaning & Disinfecting AECA

• All direct compounding surfaces: **daily** and when surface is **contaminated**

• Walls and doors within the perimeter: **monthly** and when surface is contaminated

• Ceilings within the perimeter: when visibly soiled, contaminated
Personnel Hygiene & Garbing

Hand Hygiene

Washing:
- Remove visible debris from under fingernails under warm running water using disposable nail cleaner
- Wash hands & forearms to the elbows with soap and water for at least 30s
- Dry completely with low-lint disposable towels

Sanitizing:
- Apply alcohol-based hand rub to dry skin following manufacturer’s instructions
- Apply product to one hand then rub hands together, covering all surfaces
- Allow hands to dry thoroughly before donning sterile gloves
Compounding Garb

Minimum requirements:
• Low-lint garment with sleeves that fit snugly at the wrists and enclosed at the neck
• Disposable head covers for hair/ears*
• Face mask
• Sterile powder-free gloves
• Must apply sterile 70% IPA onto all surfaces of the gloves and allow to dry thoroughly

Quality Assurance

Gloved fingertip and thumb samplings
• Evaluate compounder’s hand hygiene and garbing competency

Media-fill test
• Assess whether the aseptic procedures are adequate to prevent contamination during allergen extract compounding
Questions?