Pharmacy Mixing and Handling Standards – What you need to know

Dawn Holcombe, MBA, FACMPE, ACHE
DGH Consulting
Willis Triplett, PharmD
Comply797

Part 1 – USP Chapters – A Threat to the oncology delivery model

What <797> and <800> are and why we need to learn all about them

USP – What it is and why we should care

- USP stands for The **United States Pharmacopeial Convention.**
- Official compendium of **drug facts** for the USA.
- Formed in 1822 by prominent physicians from each state.
- Set out the identification methods, formulas, quality and purity attributes for the best drugs that physicians accepted at the time.
- The motive was to eliminate "medicine shows" and "snake oil salesmen" who traveled from town to town peddling ineffective and toxic or deadly remedies, called "Patent Medicines"

- **USP is to pharmacy as NCCN/ONS/ASCO is to oncology, but potentially enforceable**
  - Civil law suits can be based on failure to comply with USP standards. (negligence per se)

USP-Legal Standing

- USP drug data are recognized in federal law (Food Drug & Cosmetic Act or FDCA) as the scientific authority for identity, strength, quality, and purity of drug substances in the USA
- USP compendial drug data regarding scientific characteristics of drugs can be the basis for charges of adulteration by regulatory bodies (FDA and Professional Boards)
- USP is a private, voluntary, not-for-profit, scientific organization and **cannot write laws or regulations, cannot govern professional practices and has no enforcement powers**

USP's "Compounding Committee"

- Long after 1822, USP decided to create a "Compounding Committee."
- Purpose was to assemble world experts from the compounding community to compile "best practices" for the activity.
- Compounding practices are professional customs, habits, and behaviors, NOT drug facts – therefore NOT compendial.
- Professional compounding practices are governed by the state professional boards, NOT THE USP.
- State Professional Boards often lack expertise in compounding and sometimes elect to adopt USP Compounding Standards as regulations. We must work with Boards of Pharmacy to focus on more appropriate regulations as they look at medical practice compounding.

USP Standards as law and regulation

- An actual LAW ENFORCEMENT body elects to enforce it
- How could this happen?
  - New Jersey "Hazardous Drug Safe Handling Act"
  - CA – Occupational Exposure to Anti-Neoplastic Drugs (2013)
  - California Board of Pharmacy Regulations (1735 and 1751)
  - Michigan Board of Pharmacy statute
  - Washington
  - Maryland
  - New Hampshire
  - Adoption of USP Compounding Standards – Board of Pharmacy battleground state-by-state – Make it a Board of MEDICINE battleground ALSO
- Federal
  - FDA
  - OSHA
- OR – some other entity decides to hold practices accountable to what are the standards of pharmacy mixing
  - Lawyers and the public/press
  - Clinical trial networks
  - Health Systems
  - Competitors within oncology, and/or specialty pharmacies

USP <797> and <800> impact

- Pharmacy is topsy turvy – budgets turned upside down - $500 M in California alone – billions around the globe
- So if enforcement is uncertain – why not IGNORE it?
  - Payers (CMS and Private Payers can mandate standards)
  - Accreditation – Joint Commission leaning toward enforcement
  - Close out practices from collaborative research protocols
  - Tort Claims from your staff and former staff
- Protection of healthcare workers equated to everything wholesome and good.
- TRUE wholesome and good is patient access to your life-saving care – which <800> threatens.

Three Sections on USP

- USP Chapter <795> Non-Sterile Compounding
- USP Chapter <797> Sterile Compounding
- USP Chapter <800> Hazardous Drug Handling by Healthcare Workers

  * - <800> does not replace <797> - they overlap

  * - In USP's language "should" means a suggestion; "shall" or "must" means a requirement

USP "COMPOUNDING" Standards-Timelines

- USP Chapter <797> Sterile Compounding
  - 2004 1st Version adopted;
  - 2008 2nd Version adopted;
  - 2015 Proposed 3rd Version, never adopted;
  - 2018 Proposed 4th Version open for comment until November 30. May be adopted 12/1/2019.
- USP Chapter <800> Hazardous Drug Handling
  - 2014 Proposed 1st Version, never adopted;
  - 2015 Proposed 2nd Version;
  - 2016 2nd Version Adopted for 7/1/2017;
  - 2017 – Adoption postponed until 12/1/2019.

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* - In USP's language "should" means a suggestion; "shall" or "must" means a requirement

USP Chapter <797> is currently “live”

- Given the current state of oncology sterile compounding procedures, vast any audit/inspection based on <797> would be a challenge
- We practice safe medicine, but not in concordance to Pharmacy World standards
- Even the current (2008) version of <797> covers fine details of:
  - Physical facilities and fixtures;
  - Garbing/Gowning/Gloving;
  - Training and Competency;
  - Tracking, and Trending of Environmental Monitoring;
  - Cleaning and Disinfection – materials and practices;
  - Written Standard Operating Procedures that are strictly followed;
  - Faithfully executed Aseptic Technique;
  - Thoughtful and validated Beyond Use Dates;
  - Rigorous and thoroughly documented Quality Assurance Program; and
  - Many other explicit requirements.

Critically Important for the Oncology community to COMMENT on <797> Proposed Revisions

- As currently proposed for 2018, <797> is potentially becoming even more prescriptive and arbitrary, leaving less room for variations in practice and attempting to remove professional judgment.
- It imposes heavy financial costs on oncology practices without any revenue increases to offset those costs – "unfunded mandate."
- Many issues previously covered by <797> are migrating to <800>, but USP Compounding Committee is adamant that <800> is set in stone.
- Oncology Community must develop, deploy, and execute a united strategy to address USP <797> and <800>.

Should we study <797> and comply?

- The Oncology community should study and thoroughly understand <797>.
- Although its concepts of “best practices” are purely theoretical, its overarching thrust is safer patient care and better outcomes.
- The suggested practices in <797> are complex and expensive and cannot all be implemented at once.
- We should probably assess which parts to implement and adopt, then set priorities regarding which we will do in what order.

What's at Stake if USP Standards are imposed on the Oncology community in December, 2019?

- Access by patients to antineoplastic treatments, especially in underserved geographic areas.
  - The costs imposed by true compliance with <797> and <800> are unaffordable except by some large health systems;
  - Many large health systems have already invested heavily in compliance – many have completed their readiness or are well underway.
- Survival of smaller/alternative delivery avenues.
  - Private independent medical oncology practices
  - Critical Access Hospitals

Since USP has NO Enforcement Powers, Is this Threat Real?

- Where might enforcement/compliance pressure come from?
  - State Boards of Health
  - State Occupational Safety/Health/Workforce Agencies
  - State Boards of Medicine
  - State Boards of Pharmacy
  - State Legislatures
  - U.S. OSHA
  - U.S. FDA
  - CMS
  - Private Payers
  - Joint Commission and other accreditors
  - Consumer Lobbies (Pew, Public Citizen, etc.)
  - Personal Injury/Class Action Law Firms

Cynicism by USP Administrative Leaders regarding the "Compounding Standards"

- USP has misled the healthcare public, using its esteemed compendial status by actively misconstruing the "best practice" suggestions written by its Compounding Committee as "Official" and therefore, COMPENDIAL. They are NOT!
- The compounding standards (<795>, <797>, <800>, et al) are not compendial because they address *professional practices*, not the *scientific drug characteristics* that are the underpinning of identity, strength, quality, and purity
- USP has abetted in peddling the myth to state pharmacy authorities that the compounding standards are the "law of the land" and implied to the pharmacy boards a duty to incorporate them into state rules

USP Compounding Standards

- The lucky truth is that USP compounding standards are not enforced by FDA although many prominent pharmacy speakers either imply or blatantly claim that they are
- The UNLUCKY truth is that if a **state** professional authority incorporates a USP Chapter into its rules/regulations *by reference* it CAN BE ENFORCED and PENALTIES ASSESSED!

USP Compounding Standards

- It is vital for our patients' health to overwrite fallacies and disinformation with truth, in the minds of:
  - Our PATIENTS
  - Our EMPLOYEES
  - The PUBLIC
  - LEGISLATORS
- The time is NOW
  - The clock is ticking toward December 1, 2019
  - USP's plan is for revisions of <795>, <797>, and <800> to "become Official" on that day

We must gain control of the dialogue on sterile compounding and HD handling

- Surely no state MEDICAL board would choose to enforce USP Compounding Chapters – would they?
- Federation of State Medical Boards (FSMB) Ethics Committee issued a position statement for comments suggesting that
  - all state medical boards adopt <800> its entirety; and
  - medical boards should "deputize" pharmacy boards to supply experienced and knowledgeable inspectors
- FSMB backed down and took this position paper off its website, but *only* after a hail of withering criticism from associations of medical subspecialties

November 2017 - New Hampshire BoP Ordered Physicians to Cease Infusing Remicade by 1/1/18

- NH Law allows broad rule-making authority for BoP to govern sterile compounding wherever it takes place
- BoP Inspector arrived, presented credentials, conducted inspection and reported findings to BoP
- BoP voted to issued Cease Order and impose FINES on physician practices
- It took a “showdown” and legislation to reverse the fine, lift the cease order and keep hundreds of Remicade patients having access to their long-term treatments and keep their medical conditions stable
- BoP recently announced intention to inspect for ASEPTIC TECHNIQUE medical practices personnel (nurses)
- BOP is working now to replace USP <797> with its own regulations, in a thoughtful and coordinated manner, but they will not cede responsibility and oversight over sterile compounding and processes.

Part 2 – ⟨797⟩ PHARMACEUTICAL COMPOUNDING — STERILE PREPARATIONS

What <797> is:
Best practice considerations for compounding STERILE PREPARATIONS

Importance of ⟨797⟩

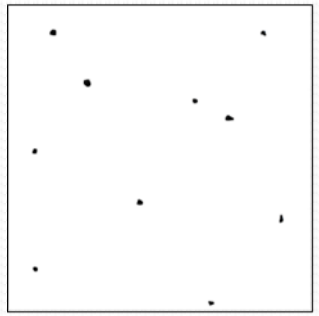
- The compounding of sterile doses is a critical risk factor for our patients – bad aseptic practices threaten their health and lives
- Patients with competent immune defenses can usually overcome small microbial contaminations, however:
  - Oncology patients are often immunosuppressed
  - Injections, infusions, irrigations and other common routes bypass the gut
  - Some parenteral routes place drugs in exotic body spaces (e.g. CSF, hepatic artery, urinary bladder, etc.). This will become more commonly seen.
- Drug preparations given by any non-oral route *ought to be sterile*.

⟨797⟩ - Sterility Threats = Touch and Particles

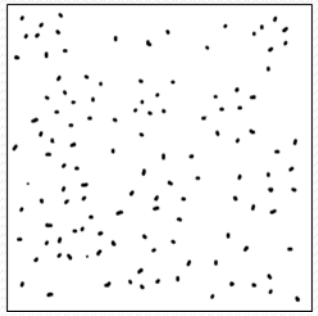
- The keys to preventing microbial contamination of sterile drugs are:
  - Human Touch (most important by FAR)
    - Sterile surfaces must only touch sterile surfaces
    - Only sterile gloves should be worn and they should be sanitized with sterile alcohol
    - If any surface is perceived to be touched by the operator the item must be discarded
    - Human touch contamination is far more dangerous than airborne particles
  - Airborne Particles (important but much less important than touch)
    - The air surrounding the sterile surfaces in drug mixing must be nearly particle free
    - The "hood" must provide an ISO Class 5 work area (Direct Compounding Area or DCA)
    - The ("buffer") room surrounding the "hood" must be very low in particles (ISO Class 7)
    - The room through which the buffer room is entered must be low in particles (ISO Class 7 if the buffer room is negative pressure; Class 8 if buffer room is positive pressure)

⟨797⟩ - ISO Class ratings are LOGARTHMIC

- Both <797> and <800> have requirements for Qualified Air.
- Qualified Air – ISO classifications – log scales



ISO-5



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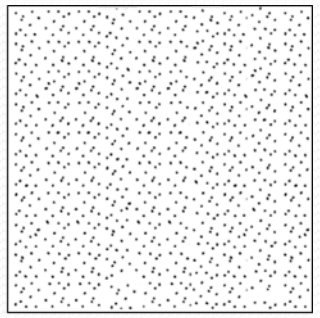


ISO-7

⟨797⟩ - Keeping Particles Out

- Humans are the primary source of particles in the qualified air spaces
- Humans shed approximately 1 million particles per hour
- The reason why pharmacy sterile products wear gowns is to prevent the particles they're shedding from reaching the air and the floors
- Paper sheds almost as fast as people
- Opening a cardboard box creates a "particle explosion"
- Every item that enters a cleanroom must be sanitized *just before transfer* – this doesn't mean a squirt of alcohol – it requires **wiping** with sterile, non-shedding wipe(s)
- Floors should be thoroughly cleaned and disinfected at least daily

⟨797⟩ is a rigorous examination of aseptic compounding practices, including:

- Attempts to set definitions of terms for a universal nomenclature
- Attempts to define its own scope (applies to whom? when?)
- Attempts to articulate responsibilities of roles
- Recommendations for training staff and demonstrating competency
- Addresses design and features of compounding areas and monitoring environmental quality and control of operational facilities
- Discusses how accuracy and sterility of compounds should be verified
- Lays out traditional sterilization methods

⟨797⟩ is a rigorous examination of aseptic compounding practices, including (continued):

- Cleaning and disinfection of the compounding areas
- Personnel cleansing and donning of garb
- Suggested Standard Operating Procedures (SOPs)
- "Elements of Quality Control" and the need for a formal, effective Quality Assurance Program (QA)
- Checks and tests for the release of finished preparations
- Storage and assignment of Beyond-Use Dating (BUDs)
- Maintenance of Sterility and Stability of finished sterile preparations
- Adverse Event monitoring, tracking, and reporting

⟨797⟩ - Compliance Norms

- Pharmacy World lacks full compliance with <797>, but is much more structured and rigorous in approach than Oncology World
- We have observed several oncology practices and most fail compliance with <797> within the first few minutes off the audit
- "We Re-spect what they In-spect." Without outside eyes, will oncology sterile compounding processes improve?
- Has <797> non-compliance ever mattered in oncology? Yes. An outbreak of bloodstream infections has been directly tied to poor compounding practices in a medical oncology practice.
- FDA? Whistle blowers? Many Directions……don't forget the lawyers

⟨797⟩ - Setting Priorities - Environment

- Maintaining the compounding environment:
  - Examples of adequate design features include seamless and rounded floor to wall junctions as well as readily accessible corners.
  - Floors, walls, and ceilings should be constructed of smooth, hard surfaces that can be easily cleaned and which will stand up to harsh disinfectants
  - Ceilings and associated HEPA filter banks should be designed to protect sterile materials from contamination.
  - Cleanrooms should not contain unnecessary equipment, fixtures, or materials and personnel traffic should be minimized
  - Sinks and drains in aseptic processing areas should be avoided (biofilm)
  - Paper, cardboard, and packing materials should never be present in aseptic processing areas

⟨797⟩ - Setting Priorities - Training

- Staff Training:
  - Most oncology practices lack formal training for sterile compounding operators; training is generally on-the-job, modeled on "W1-D1-T1"
  - Formal training should include at least:
    - Handwashing process
    - Gowning/Garbing/Gloving
    - Glove sanitization methods and frequency
    - Cleaning and disinfection (including sporicidal agent)
    - Aseptic manipulations (critical site, blocking first air, unidirectional air flow, etc.)
    - Measurement and pharmaceutical calculations
    - BUD determination
    - Checking and release inspection
    - Sterilization techniques (if applicable)

⟨797⟩ - Setting Priorities - Competency

- Staff Competency Demonstrations:
  - Most oncology practices do not require competency demonstrations by their sterile compounding operators
  - Formal competency demonstrations should include at least:
    - Gowning without contamination (proven by lack of microbial growth)
    - Growth Media volume transfers, incubated without growth
      - The media transfers should mimic the most challenging and difficult compounding task the operator performs
      - The media transfers should be performed under operational (dynamic) conditions
    - Glove Fingertip Sampling – This tests the operator's ability to don sterile gloves without contaminating them. <797> suggests three uncontaminated glove donning demonstrations prior to mixing for patients

⟨797⟩ - Setting Priorities – C & D

- Cleaning and Disinfection
  - Most oncology practices do not have explicit, detailed processes for cleaning of the "hood" and the room in which it's situated
  - Fewer still have solid protocols for appropriate disinfection, which should include application of appropriate sporicidal agent
  - Effectiveness of cleaning and disinfection should be demonstrated with bioburden monitoring
- Outside Certification
  - Most oncology practices pay outside vendors to measure airflows, pressure differentials, total particle counts and perform viable air sampling within the "hoods" to confirm that HEPA filters are working effectively
  - However, most do not track and trend the data or analyze it appropriately

⟨797⟩ - Setting Priorities – SOPs

- Do you have a Procedure Manual for sterile compounding ops?
- If so, is it dusty? Or is it a "Living Document?"
- Outside inspectors (state or FDA) will observe processes in use watching closely for variances from WRITTEN procedures.
- Whenever a process is changed:
  - the Quality Governance Body should sign off on the change
  - the governing SOP should be edited and publicized to all staff
  - all affected staff should be retrained for the change
- At FDA the joke is, "Healthcare professionals write SOP manual on Post-it Notes."

⟨797⟩ - Setting Priorities – QA

- The most important words in <797> come just before the Appendices:

  A provider of CSPs shall have in place a formal QA program intended to provide a mechanism for monitoring, evaluating, correcting, and improving the activities and processes described in this chapter. Emphasis in the QA program is placed on maintaining and improving the quality of systems and the provision of patient care. In addition, the QA program ensures that any plan aimed at correcting identified problems also includes appropriate follow-up to make certain that effective corrective actions were performed.

⟨797⟩ - What do we do?

- Learn what <797> says so you're ready to make your case
- Join your peers in ensuring state regulators do not enforce <797>
  - Make frequent contact with medical authority (members & admins)
  - Lobby state legislators and executives face-to-face in groups
  - Energize your state medical association/society
- While fighting back to ensure that we don't want it imposed upon us, keep in mind that following parts of it would be best for our patients
  - Gaining compliance with <797> will be a process, not an event
  - Routinely reevaluate the aseptic technique in use by staff
  - Formalize and improve your training
  - Take ownership of the quality – Form a "Quality Oversight Body" to actively examine and improve aseptic compounding quality

Part 3 – <800> HAZARDOUS DRUGS—HANDLING IN HEALTHCARE SETTINGS

What it is:

Bank-breaking, unscientific, overreaching rules for how you must ensure no humans are exposed to the drugs you buy, unpack, store, mix, administer and discard

Purpose for <800> and categorization of HD

- The stated purpose of USP <800> is eliminate or minimize exposure to healthcare workers whose duties require handling "hazardous drugs."
- Although the USP Compounding Committee states the scope of the chapter to be all hazardous drugs its central lynchpin is oncology workers mixing antineoplastics
- USP not only appointed itself to speak for all hazardous drugs, it also anointed the "NIOSH List of Hazardous Drugs" as the list healthcare "must" look to
- The NIOSH List first appeared as an appendix to the 2004 NIOSH Alert, *"Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care Settings"* (The Alert was written by Edward Burroughs, Thomas Connor, Melissa McDiarmid, Kenneth Mead, Luci Power, and Laurence Reed. Among the contributors was Martha Polovich.)

NIOSH HD Groupings

- The NIOSH List is divided into three tables/groups:
  - Table 1. Group 1: Antineoplastic drugs, including those with the manufacturer's safe-handling guidance (MSHG)
  - Table 2. Group 2: Non-antineoplastic drugs that meet one or more of the NIOSH criteria for a hazardous drug, including those with the manufacturer's safe-handling guidance (MSHG)
  - Table 3. Group 3: Non-antineoplastic drugs that primarily have adverse reproductive effects

<800> - Drug Handling by "Table/Group"

- Drugs on the NIOSH list that ***must*** follow the requirements in this chapter include:
  - Any HD API
  - Any antineoplastic requiring HD manipulation
- Drugs on the NIOSH list that do ***not*** have to follow ***all*** the containment requirements of this chapter if an assessment of risk is performed and implemented include:
  - Final dosage forms of compounded HD preparations and conventionally manufactured HD products, including antineoplastic dosage forms that do not require any further manipulation other than counting or repackaging (unless required by the manufacturer)
  - For dosage forms of other HDs on the NIOSH list, the entity may perform an assessment of risk to determine alternative containment strategies and/work practices

<800> Much Broader Than <797>

- <800>:
  - "…applies to all healthcare personnel who handle HD preparations and all entities that store, prepare, transport, or administer HDs."
  - (e.g., pharmacies, hospitals, and other healthcare institutions, patient treatment clinics, physicians' practice facilities, or veterinarians' offices.)
  - "…pharmacists, pharmacy technicians, nurses, physicians, PAs, home healthcare workers, veterinarians and veterinary technicians."
  - Scope includes:
    - Receipt, Handling, Storage, Disposal, Humans Physically Present in the facility
    - **Everyone** in the vicinity (nurses, receptionists, billing staff, executives, patients, waiting room, couriers, cleaning crew, and even staff who **receive** and **unpack** drugs)
    - Not just sterile, but non-sterile drug forms such as topicals and orals

<800> A Crushing Unfunded Mandate

Main Impact Areas:

- Physical Facilities and Equipment (& electrical energy)
  - requires single-pass air (summer air – chill it, adjust humidity – one pass - expel it)
  - requires negative-pressure PECs vented to the outside
  - negative-pressure SEC, hard walls, door, 12 or 30 ACPH (12 for C-SCA, 30 for Ante+Buffer)
- SOPs + HD Quality Assurance Program + "Designated Person"
- Training - required for all staff members
- Huge overhead increases from doubling the required disposable supplies – gowns, garb, gloves, etc. HD overhead items must be HD-ready thus cost more
- Surveillance
  - HDs in the Office Environment
  - Medical Conditions of your Personnel (including future)

Typical Current State in Chemotherapy Compounding Areas

- Wooden counters, drawers, shelves (wood->particles and cannot disinfect)
- Contains paper, cardboard, carpet, drapes, holes in walls, etc.
- The C-PEC is a usually BSC resting on a wooden counter
- Contains compressor-style refrigerator(s) (usually dust bunnies if you check)
- Open to unrestricted foot traffic
- Walls, flooring, ceilings are of inappropriate surface for cleaning/disinfection and not maintained by protocol
- Compounding performed by seasoned R.N. – main focus is on clinical aspects of the drug-patient combination – NOT on sterility/stability of CSP (Is an RN mixing drugs like a racehorse pulling a plow?)

<800> Conforming Physical Rooms

- For compliant ***rooms***, we can choose between two strategies:

ISO-7 Clean Room Complex (Ante + Buffer-Both ISO-7)

Versus

Containment Segregated Compounding Area (C-SCA – no air qualification)

- Choice depends on the BUD times we can afford to operate with:
  - If we can live with 12 Hour BUDs, we can use C-SCA approach (more affordable)
  - If we must give full BUDs, we must use a qualified air Anteroom* plus ISO-7 Buffer Room

(*If anteroom connects to HD buffer room it must be ISO-7. If it leads to a Non-HD buffer, it can be ISO-8)

<800> C-SCA Alternative

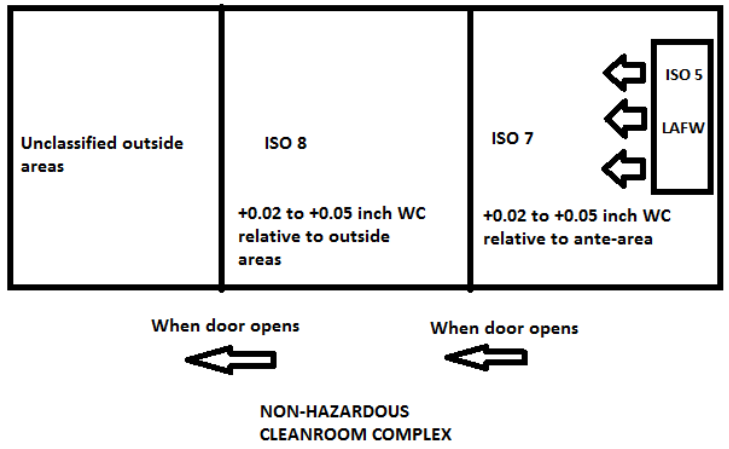
- C-SCA is a "Containment Segregated Compounding Area"
  - Less costly to build and operate than Ante + Buffer configuration
  - Acceptable for CSPs with BUDs ≤ 12 hours
  - C-SCA requires:
    - C-PEC ("Hood") vented to the outside
    - The air of the C-SCA must also vent to the outside
    - Solid walls and door must enclose the C-PEC
    - Negative pressure vs. adjacent spaces maintained in the range -0.01 to -0.03 inch WC
    - Minimum of 12 ACPH
    - No compounding of Medium- or High-Risk CSPs (Medium Risk means complex multistep compounding; High Risk means starting with non-sterile drug powders and then sterilizing them during or after compounding)

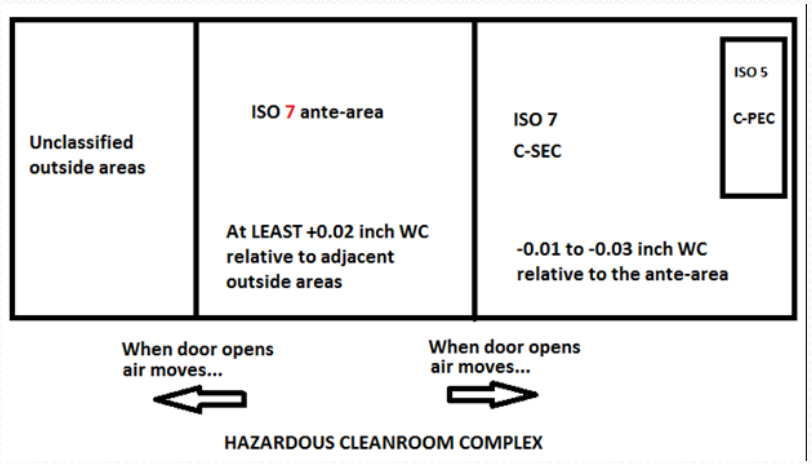
<800> - “Deactivation & Decontamination”

- For any aseptic compounding room, all surfaces (walls, ceilings, floors, equipment) must be smooth, hard, impermeable, and free of any cracks or crevices
- This is to (1) deny any places for particles to collect and (2) make for easy cleaning and disinfection
- For HD aseptic compounding rooms, the floors, walls, and ceilings must be:
  - Cleaned
  - Disinfected
  - Possible HDs DEACTIVATED
  - Possible HDs DECONTAMINATED

<800> - Construction Costs

- Many hospitals have paid > $1,000,000 for <800> compliance
- The room design and construction typically $80,000 to $250,000
- HVAC costs
  - Air Handler - at least 30 Air Changes per Hour (ACPH) for an Ante + Buffer setup (every 2 min) 60 ACPH resource is a good idea – might need spare capacity to hit minimum of 30
  - Air BALANCING is key and must be monitored regularly to ensure airflow directions are right





<800> - Exhausted Outside

- Both the Biological Safety Cabinet (BSC or “hood”) and the room it is in MUST be exhausted to the outdoors
- In existing multistory buildings (especially hospitals) it is very difficult to locate a pathway (called a “chase”) for the ducts to reach directly to the outdoors
- State Building Codes and Local Ordinances often specify how much above the tallest roofline the exhaust duct has to reach (often as much as 10 feet)
- Although scientifically absurd, codes and ordinances often specify a minimum distance between the exhaust that expels air with potential trace HD and the air intakes for other internal spaces
- Although <800> did not specify this, BSC user manuals and HVAC experts will always insist on a perpetually running fan to prevent backflow of exhaust

<800> - SOPs, QA, Designated Person

- As with <797>, observed operational behaviors must reflect SOPs
- As with <797>, an effective Quality Assurance program must exist for monitoring and improving the processes that pertain to HD handling
- <800> has a requirement that a “Designated Person” be in assigned the responsibility for every person, place or process that might affect HD handling and exposure
- Features include:
  - Qualified and trained in all aspects of HD handling
  - Oversees legal and regulatory compliance of the entity
  - Must understand risk prevention and the risks of non-compliance
  - Must oversee monitoring, testing, sampling and act appropriately on these results

<800> - Staff Training

- Personnel who handle HD must be trained based on their job functions
- Training must occur before employee independently handles HDs
- Effectiveness of training must be demonstrated for each employee
- Competency reassessed every 12 months
- Each employee trained for every new HD and every new or altered SOP
- Not enough to train your staff, you must demonstrate that you did
- Must demonstrate that training was effective
- Not enough to train initially, we must demonstrate that training has been reiterated regularly and staff know what they need to know to protect themselves and others from HD exposure

<800> - Overhead - Garbing

- The garb/gloves – 2 layers
  - Layer next to human to prevent particles from shedding to the clean environment
  - Outer Layer – to prevent human from exposure to HDs being handled – repellant materials
- The HD facing garb and gloves must present a seamless, uninterrupted, impermeable barrier preventing human contact with HDs, such as:
  - Tyvek coated gowns that tie in back
  - Goggles or faceplates or both
  - Gloves that have been tested to prevent HD permeation (Standard ASTM 6973) that are worn over the first set of gloves
  - Double shoe covers
  - All garb/gloves/booties disposed of as potentially trace contaminated

<800> - Overhead - CSTDs

- Closed System Transfer Devices (CSTD)
  - Should be used in **compounding** HDs
  - MUST be used in **administering** HDs
- Purpose – to CONTAIN the HD within the infusion fluids and prevent HD escape to contaminate the healthcare operator
- CSTD examples include:
  - PhaSeal (BD)
  - Equashield Closed System (includes syringes and connections)
  - ChemoClave (ICU Medical)
  - OnGuard (B.Braun)

<800> - Overhead – Site Maintenance

- Cleaning, Disinfection, Deactivation, and Decontamination fluids are expensive and sterilized versions are ten-fold more. Cleaning personnel must be extensively trained
- HD containers, liners, pickup, destruction, tracking
- Certification of hoods and rooms ($4,000 to 8,000 per visit)
  - HEPA leak testing
  - Total particle counting
  - Viable particle sampling (active sampling, impelled onto agar plates)
    - Microbiological laboratory incubation costs
    - Recertify on failure
  - Smoke pattern demonstration (video recording)
- HD Surface Contamination Surveillance Testing (“Wipe Studies”)
  - Cost #1 is doing them in the first place
  - Cost #2 is remediating and doing them again if you find traces

<800> - Hazard Communication

- There has been an OSHA (federal) regulation [29 CFR 1910.1200(g)] in place since 1994 that requires an effective program of Hazard Communication to all staff.
  - When new personnel hire on each must be presented with a list of all hazardous substances they might contact in the workplace.
  - How do you know it is a hazardous substance? It will have an Safety Data Sheet (SDS)
  - The regulation requires that the employer make the SDS (formerly MSDS) readily available to each employee (MSDS.com – a subscription service)
  - Most oncology practices seem aware of the federal regulatory requirement
  - OSHA does not appear to make routine inspections of physician offices or pharmacies, but do respond to "whistle-blower" complaints
  - OSHA has levied substantial fines against healthcare provider organizations in response to such complaints
  - This requirement is a shared responsibility of Human Resources and Operational Leadership

<800> & Drug Administration

- HDs must be administered using protective devices and techniques (needle-less, closed systems)
- Appropriate PPE must be worn when administering HDs
- Used PPE must be disposed of in a waste container approved for trace-contaminated HD
- Equipment and packaging materials disposed likewise
- CSTDs must be used to administer antineoplastic HDs whenever the dosage form allows
- Eye protection when working at or above eye level

<800> - Medical Surveillance

- <800> says
  - our workers who handle HD should be enrolled in a medical surveillance program
  - we should involve assessment and documentation of symptom complaints, physical findings and lab values to "determine whether there is deviation from the expected norms.
  - We should perform an "Initial Baseline Assessment" of workers' health status and medical history before they begin their duties
  - Methods used to assess exposure history should include a review of:
    - Records of HDs handled, with quantities and dosage forms
    - Estimated number of HDs handled per week
    - Estimates of hours spent handling HDs per week and/or per month
    - Performance of a physical assessment and laboratory studies linked to target organs of commonly used HDs, such as a baseline complete blood count. Biological monitoring to determine blood or urine levels of specific HDs is not currently recommended in surveillance protocols, but may have a role in the follow-up of acute spills with a specific agent.

Motherhood and Apple Pie – which side represents Science and Truth?

- USP <800> folks and their allies have wrapped themselves up in "doing what's right."
  - What's right is designing and building new cleanrooms, certifying those new cleanrooms and the "hoods" inside them, selling you truckloads of single-use disposable supplies you never knew you needed, and selling you books and on-site training to teach you how to follow <800>
  - Why it's right is "making the workplace safe," against supposed cancers when the scientific evidence is extremely weak
- Our side needs to answer that "doing what's right" is making sure that patients have easy access to their cancer treatments in smaller, rural communities

Pharmacy Standards What can WE do?

- Read them (USP, CA BOP)
  - (purchase the USP Compounding Compendium $150)
  - http://www.usp.org/compounding/general-chapter-797
  - http://www.usp.org/compounding/general-chapter-hazardous-drugs-handling-healthcare
  - http://www.pharmacy.ca.gov/
- Understand the jargon, learn the acronyms
- Monitor state legislation – meet proactively with Legislators
- Call them Out – the emperor has no clothes!
- Attack their science (until they produce some)
- Collaborate across professions and stakeholders
- Activate the "green" groups over the energy & co2 load

- BUT STILL PREPARE YOUR TEAM AND YOUR PRACTICE – STRATEGIZE FOR BEST AND WORST CASE SCENARIOS

Reality of Pharmacy Standards

- Delays do not make AB1202 or <800> go away. <797> is real now (despite pending revisions), as are lawyers on the prowl
- Review and Prepare now - Can plan implementation steps
  - Gaps
  - Processes and training
  - Any renovations need to have flexibility built in
  - Plan external ventilation and other more onerous <800> type requirements but hold until required
- Find good resources – limited supply
  - Consulting - Standards, SOPs, training, monitoring, implementation
  - Construction (clean room, oncology, and CA knowledgable)
- Advocate for logic and <797> and <800> transformation

Tips

- Separate your non hazardous and hazardous mixing, as well as storage
  - Three rooms where one is often now used. Subdividing is possible.
- No cardboard, wood, shedding fibers, cleanable ceilings walls and floors
- No makeup, fake nails, outside clothing
- No walkins or travel into/out of the space without appropriate PPE handling
- SOPs and enforcement and tracking
- Training and competency
- Look around every corner – anticipate
- Start early, no matter what the deadlines are
- Get good help (Consider staff mix and roles!!!!!)

Proposed <797> out for comments

- http://www.usp.org/compounding/general-chapter-797
- Read. Consider. Stay Tuned. Comments Due By Nov. 30, 2018.
- Major Issues
  - Lack of evidence for opinion based standards
  - Requires all disposable gowns, rather than reusable with sterile sleeves
  - Disposable non scented soaps
  - Incongruity on pass through window use, practicality for medical practice
  - Tacky mats, prohibited or allowed? Evidence?
  - Sinks should be placed in ante rooms
  - Carts passing through clean sides of anterooms and CSCs must be wiped and cleaned each time

Who else are major players, and how can we take action?

Federal OSHA

- What role might OSHA play?
  - None in <797>, but ominous regarding <800>;
  - OSHA has tried to stay “arms-length” from medical practices, but has unquestioned ability to inspect;
  - Hazardous Communication Plan (29 CFR 1910.1200)
    - Federal regulation since 1994, revised in 2012;
    - Enforcement in medicine has been purely complain based;
    - Requires every business entity handling hazardous chemicals to
      - Inform every employee of all hazardous chemical in use in the workplace;
      - Train every employee in the handling of hazardous chemicals;
      - Maintain access of every employee to Safety Data Sheets for every hazardous drug in use.

U.S. FDA

- The lucky truth is that USP compounding standards are not enforced by FDA although many prominent pharmacy speakers either imply or claim that they are
- However, FDA does enforce Current Good Manufacturing Practices (cGMP), which requires processes to prevent “cross-contamination or mix-ups” of “potent or hazardous” drugs
- FDA has inspected one medical oncology practice concerning its sterile compounding processes after an outbreak of fungal infections in its patient population.

CMS and Private Insurance Payers

- CMS and private payers have Conditions of Participation which typically state that contracted practitioners will follow “well accepted standards of practice.”
- Although this terminology is not well defined, USP Compounding Standards could be construed by payers to fit their interpretation.
- This could result in withholding of payment if the payers conclude that we are not in compliance.
- Payers are ill-equipped to sort out good practices from bad practices but often defer to accreditations or certifications to do so.

Joint Commission and other accreditors

- The Joint Commission (TJC) appears to be supportive of deployment of USP Compounding Standards.
- TJC is evolving standards to require compliance with USP Standards by 12/1/2018.
- Hospitals cannot afford to lose TJC accreditation, as it jeopardizes payment by CMS and other payers.

Political Action Lobbies

- Consumer Lobbies (Pew, Public Citizen, etc.)
- Massive public media/social media/legislative lobbying presence to overestimate the danger of compounding to the public health.
- Pew always leads with the statistics from the fungal meningitis outbreak and any subsequent unsubstantiated headlines to instill fear that sterile compounding delivery is unsafe.
- Pew never mentions that the denominator is in the BILLIONS of doses of sterile compounds.

Tort Claims

- Perhaps the largest threat is Tort Claims by current or former employees.
- We know that malignancies are the second leading cause of death:
  - Heart disease: 635,260
  - **Cancer: 598,038**
  - Accidents (unintentional injuries): 161,374
- We know that we or our staff are likely to die from cancer
- Most of us subscribe to the axiom that antineoplastic drugs cause cancer, so how often will our former staff attribute their cancers to the fact they worked around antineoplastics?

What can WE do to maintain Patient Access?

- Cross-connect with our colleagues in order to build consensus
- Challenge Disinformation by USP Proponents/Sponsors
- Become engaged in USP Compounding Oversight
- Perform the Science
- Engage Government and Payers
- Explain the threat to our patient base - Build our “Advocacy Machine”)

Cross-connect with colleagues in order to build consensus

- Create a “neural network” of like-minded, non-competitors
- Connect regularly to share news, information, and strategies
- “Concierge Groups”
- Share insights and tips regarding inspections and regulatory interpretations
- Discuss hiring selections and best practices in managing staff

Challenge Disinformation by USP Proponents

- Whenever a speaker or colleagues refers to USP as "the REGS," correct them and point out that voluntary non-profit entities cannot write laws or promulgate regulations.
- When people cite NECC (the fungal meningitis outbreak) as evidence of the danger of sterile compounding, point out that there was nothing analogous before or after 2012 (now 6 years ago!). Point out that billions of doses have been administered since 2012 with very few headlines.
- If people claim that FDA enforces USP <797> or <800>, explain that FDA enforces cGMP, which is federal administrative law (i.e. federal regulation).

Engage in USP Compounding Oversight

- COMMENT ON <797> BEFORE 11/30/2018!
- Not a single medical oncologist sits on the USP Compounding Committee.
- Seek a significant number of seats on the Compounding Committee to provide oncology insights.

Question/Challenge the Science behind <800>

- The main reason we can't quantify the influence handling chemotherapy drugs has on cancer rates – if any – is that we have not done the epidemiology.
- We know who has handled large quantities of antineoplastics over long periods of years (even decades?) and all we need to do is compare their cancer rates to some control groups matched for age.
- Expert Oncologists should review the published evidence that antineoplastics are hazardous, evaluate the scientific validity and render a consensus opinion on relative risk.

Engage Government, Payers, and Pharma

- The national oncology leadership should make USP Chapters <797> and <800> key features in lobbying efforts at both state and federal legislatures.
- The oncology sector should engage payers and pharma to help them understand the implications and costs of USP Chapter compliance. Some sectors of care are several times more costly than others and the impact of USP compliance is likely a “game-changer.”

Energize our patients – Create our “Advocacy Machine”

- Our patients are a massive Advocacy Machine if they are informed.
- If we explain that USP compliance can threaten our ability to receive their chemotherapy treatments conveniently and close to home and if we facilitate the communication of their messages to government entities, their combined voices will be impossible to ignore.

How to Comment to USP Regarding <797>

- Post Comment on or before November 30, 2018
- To Download the Proposed Revision OR to Comment, click this link: DOWNLOAD or COMMENT on Proposed Revision of USP <797> http://www.usp.org/compounding/general-chapter-797
- When you click the purple comment button, you will prompted to provide demographic information about yourself, including name, address (city, state, zip, nations), organization, role, etc.
- You may make a *Specific* Comment tied to a Line Number of the Proposed Revision OR you may make a *General* Comment. Even if you wish to make a line-specific comment, we recommend that you also choose to make some general comments.

What should our comments be?

- USP Standards should be written like standards, not regulations. There are far too many statements of "must" and "shall" and far too few "should" statements. The language must be made less arbitrary and less prescriptive. What we do in oncology is not "one-size-fits-all."
- USP exists only as a scientific organization, and it should promote the advancement of clinical practices that are supported by scientific evidence. In the 2008 version, this pristine statement was included: "The use of technologies, techniques, materials, and procedures other than those described in this chapter is not prohibited so long as they have been proven to be equivalent or superior with statistical significance to those described herein."
  - In the Proposed Version, this language was omitted, making the Chapter reflect only the narrow experience and arbitrary views of the small number of Members of the Compounding Committee. It must be put back in!

Common Themes for Oncology comments

- Safety has not been sufficiently proven to be at risk. Improvement plans should be incremental, not one size fits all, sudden and creating financial instability to a working medical care delivery system.
- Specifics such as equipment, supplies, cleaning agents, and PPE are too constraining.
- There is a vast operational difference between standards and regulations. The standards set forth in these chapters are overly prescriptive and as such are over-reaching into the arena of operational process. Standards should be guides, and not seek to be codified as regulations or to interfere with normal operational processes of delivery of medical care.

Here is the Roster of the Compounding Expert Committee:

- Gigi S. Davidson, R.Ph., DICVP, Chair
- Connie Rae Sullivan, B.S.Pharm., Vice Chair
- Lisa Ashworth, B.S.Pharm., R.Ph.
- Gus Bassani, Pharm.D.
- Edmund J. Elder, Jr., Ph.D.
- Ryan Forrey, Pharm.D., M.S.
- Deborah Houston, Pharm.D.
- Brenda Jensen, M.A
- Patricia C. Kienle, B.S. Pharm, M.P.A.
- William A. Mixon, M.S.
- John Musil, Pharm.D.
- David Newton, Ph.D.
- Alan Parr, Pharm.D., Ph.D.
- Abby Roth, B.Sc.
- Robert Shrewsbury, Ph.D.
- James Wagner
- Brenda Yuzdepski, B.S.Pharm.

Here is the Roster of the Compounding with Hazardous Drugs Expert Panel:

- Patricia C. Kienle, B.S. Pharm, M.P.A.
- James Wagner
- Eric Kastango, B.S.Pharm., M.B.A.
- Luci A. Power, B.S.Pharm., M.S., RPh
- Thomas H. Connor, Ph.D.
- Melissa A. McDiarmid, M.D., M.P.H.
- Kenneth R. Mead, Ph.D.
- Martha Polovich, Ph.D.

What should our comments be?

- We should ask the USP, “How can it be that you are setting out arbitrary statements of ‘must do this,’ and ‘shall do that,’ yet not one single practicing medical oncologist or oncology pharmacist has a seat on your Compounding Expert Committee? How can it be that not one single physician or pharmacist specializing in oncology sat on the HD Expert Panel?”

Thank You, and Good Luck

Dawn Holcombe, MBA, FACMPE
DGH Consulting
860-305-4510
dawnho@aol.com
www.dghconsulting.net

Willis Triplett, PharmD
Comply797
317-626-6973
Willis.triplett@comply797.com