Comment Submission Template for:
General Chapter <797> *Pharmaceutical Compounding—Sterile Preparations*

Revision proposed in *Pharmacopeial Forum* 41(6) Nov/Dec 2015
Send completed template to CompoundingSL@usp.org by January 31, 2016

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General Comments:

Dear USP Compounding Expert Committee:

The National Home Infusion Association (NHIA) respectfully submits the comments outlined in the table below regarding the revision released September 25, 2015, to the General Chapter <797> *Pharmaceutical Compounding – Sterile Preparations*. NHIA is the trade association representing organizations that provide compounded sterile products and services to patients in the home setting. NHIA would like to express appreciation to the committee for their work to update and improve upon the existing standard to ensure patients consistently receive safe, high quality sterile products. However, NHIA would like to caution the committee against creating standards that will restrict patient access to compounded medications based on results from single point in time testing. NHIA believes that compounding standards must allow providers flexibility in determining how best to address actionable test results, to ensure product quality without compromising patient care. Unlike a manufacturing environment, patient care settings must be continuously available and responsive in order to meet patient needs. To this point, NHIA suggests changes to the proposed language that would allow providers to maintain operations while taking steps to mitigate and address potential deficiencies. Again, NHIA appreciates the opportunity to comment on the proposed revision and asks for consideration from the committee related to the presented suggestions and concerns. If you have questions regarding the comments submitted by NHIA, please contact Connie Sullivan, NHIA Sr. Director of Education and Data/VP of Research, at (303) 747-3798 or connie.sullivan@nhia.org.

Specific Comments:

Section(s)	**Line Number (s)**	**Existing text:** (Provide the proposed text.)	**Suggested change:** (Provide the revised suggestion to replace the existing text.)	**Comment**	**Rationale / Scientific Evidence**
1.1	14	Injections	Products for injection or infusion		
1.1	24- 27	This chapter applies to all persons who prepare CSPs (e.g., pharmacists,	This chapter applies to all persons who prepare CSPs (e.g., pharmacists, pharmacy technicians,	• While the existing text is comprehensive, there is value in placing emphasis on settings offering elective hydration and/or vitamin	

		pharmacy technicians, physicians, veterinarians, and nurses) at all places where CSPs are prepared (e.g., hospitals and other healthcare institutions, patient treatment sites, infusion facilities, pharmacies, and physicians' or veterinarians' practice sites).	physicians, physician assistants, veterinarians, and nurses) at all places where CSPs are prepared (e.g., hospitals and other healthcare institutions, patient treatment sites-including those offering elective infusion treatments, infusion facilities, pharmacies, and physicians' or veterinarians' practice sites).	treatments that may be operating outside the traditional medical structure. • Physician assistants should be included in the example list of providers.	
1.1	49 – 56	Reconstituting or diluting a conventionally manufactured sterile product with no intervening steps strictly in accordance with the manufacturer's labeling for administration to an individual patient is not considered compounding. However, aseptic technique must be followed during preparation, and procedures must be in place to minimize the potential for contact with nonsterile surfaces and introduction of particulate matter or biological fluids. Any other reconstitution or dilution of a conventionally manufactured sterile product is considered compounding and must be performed in accordance with this chapter.	Reconstituting or diluting a conventionally manufactured sterile product with no intervening steps strictly in accordance with the FDA approved labeling for immediate administration to an individual patient is not considered compounding. However, aseptic technique must be followed during preparation, and procedures must be in place to minimize the potential for contact with nonsterile surfaces and introduction of particulate matter or biological fluids. Any other reconstitution or dilution of a conventionally manufactured sterile product is considered compounding and must be performed in accordance with this chapter.	• NHIA agrees the definition of compounding should be consistent with that of the FDA. • The requirement should be to follow "FDA approved" labeling rather than "manufacturer" labeling. • FDA labeling does not consider sterility and some package inserts state broad ranges for stability without factoring in the sterility considerations. • USP should use the same distinction made in the docking system section regarding immediate vs. future use. • USP should define "aseptic technique" as no current standard exists. • It is important to ensure the text allows for in-home preparation of certain medications according to the FDA approved labeling. The high cost and limited distribution of certain drugs makes preparation in a controlled setting imprudent. • USP should provide examples in this section of types of compounding would be exempt from the standard.	E.g. Etoposide Phosphate Monograph

2.0	172	supervisors of compounding personnel should observe compounding activities on a daily basis and take immediate corrective action if deficient practices are observed.	Pharmacists (or qualified designee) should routinely observe compounding activities ~~on a daily basis~~ and take immediate corrective action if deficient practices are observed.	• "Daily" may create an unintended literal interpretation that may burden providers. • Pharmacists, or a qualified individual under the direct supervision of a pharmacist, should be identified as the responsible party to provide oversight of compounding activities.	•
2.2	Box 2-1 Gloved Fingertip Sampling and Testing Procedures	Invert the plates and incubate them at a temperature and for a time period conducive to multiplication of microorganisms (e.g., 20°–35° for 5 days).	Invert the plates and incubate them at an appropriate temperature and time period conducive to multiplication of microorganisms.	• Recommendations for incubation times should reflect the compendia standards. Remove examples that provide inconsistent ranges for incubation.	
2.4	232-238	Personnel who fail visual observation of hand hygiene, garbing, and aseptic technique; gloved fingertip/thumb sampling; or media-fill tests must pass three successive reevaluations in the deficient area before they can resume compounding of sterile preparations.	Personnel who fail visual observation of hand hygiene, garbing, and aseptic technique; gloved fingertip/thumb sampling; or media-fill tests will immediately undergo re-testing in the deficient area. If a second failure occurs, the employee must pass three separate ~~successive~~ re-evaluations in the deficient area before they can resume compounding of Category 2 sterile preparations.	• USP should require failure confirmation with a second test before limiting an employee's ability to compound. • Compounding personnel failing gloved fingertip sampling tests could be required to wait as many as 15 days prior to returning to compounding due to sample incubation times, and failing a media-fill test may delay up to 42 days which may prevent patient access to critical medications. • For confirmed failures, allow for continued compounding with BUD limitations to ensure patient care is not disrupted. • Removing the term "successive" and inserting "separate" allows testing to be done in a way that minimizes the impact to the operation.	•
3.1	283	Remove all cosmetics because they shed flakes and particles	Remove all cosmetics (including false eyelashes) because they shed flakes and particles		
3.2	305-307	[NOTE—Soap must not be added to a partially empty soap dispenser. This practice of "topping off" dispensers can lead to	Delete	• Neither reference on this CDC statement is about topping off soap. The CDC guideline for hand hygiene does not recommend topping off hand hygiene dispensers. "Do not add soap to a partially empty soap	• http://www.joplink.net/prev/201005/ref/14-015.html • http://www.ncbi.nlm.nih.gov/pubmed/9350463

		bacterial contamination of soap.]		dispenser. This practice of 'topping off' dispensers can lead to bacterial contamination of soap (IA) (187,419)."	
3.3	312	Table 2	Add Mask for Category 1 CSP compounding garb and glove requirement		
3.3	312	Table 2	Remove requirement for sterile sleeves when using non-sterile gowns.	• USP standards should concentrate on the hands as the greatest source of potential contamination. If the room is clean, the clinical benefits of sterile gowns and sleeves are minimal.	
4.2	408	The buffer room must maintain a humidity below 60% at all times using an efficient heating, ventilation, and air conditioning (HVAC) system rather than through use of humidifiers and dehumidifiers, which can contain standing water that can contribute to microbial contamination.	The buffer room must maintain a humidity below 60% at all times using an exterior, integrated system in conjunction with the heating, ventilation, and air conditioning (HVAC) system rather than through use of in-room humidifiers and dehumidifiers, which can contain standing water that can contribute to microbial contamination.	• Require clarification that humidification and dehumidification equipment is required to control humidity. This equipment is not part of the HVAC unit, but is exterior to the cleanroom and integrated into the air supply. Simply running the HVAC unit longer is not an effective way to reduce humidity. • Organizations should understand that active control of humidity requires additional equipment and controls in the cleanroom. • Define the basis for the 60% target.	
4.2	447-448; 1876-1878	If a pass-through is used, it must only be opened one door at a time; both doors must never be opened at the same time. Pass-through: An enclosure with seals on interlocking doors that are positioned between two spaces for the purpose of minimizing particulate transfer while moving materials from one space to another.	If a pass-through is used, it must only be opened one door at a time; both doors must never be opened at the same time. Pass-through: An enclosure ~~with seals on interlocking doors that are~~ positioned between two spaces for the purpose of minimizing particulate transfer while moving materials from one space to another.	• The definition defines a pass-through as having interlocking doors, which is not correct. Interlocking doors are an optional feature. If required, pass-throughs without the interlocking doors would have to be replaced at great expense, as adding interlocking doors to existing pass-throughs is not currently a choice.	
4.3	576-577	Classified areas and segregated compounding areas	Segregated compounding areas and ISO 8 rooms must	• An ISO 7 or better area is prevented from having dust under current standards. LAFW, all carts, and	

		must minimize the collection of dust-collecting overhangs, such as utility pipes, or ledges, such as windowsills.	prevent the collection of dust through appropriate cleaning processes and/or facility design on difficult to access overhangs (E.g. utility pipes, or ledges, such as windowsills).	some plumbing are of greater potential as dust-collecting surfaces. Modular cleanrooms at ISO 7 or better have "ledges" at floor level which do not collect dust. The *possible* need to cover plumbing, for sinks and sprinkler water pipes is not for dust. • The standard should address the primary concern of dust accumulation in the ISO 8 and segregated compounding area, but avoid a limitation on ledges, which may or may not be of concern depending on their construction and ability to be cleaned.	
4.5	634-635	Recertification must be done at least every 6 months.	Recertification, demonstrating satisfactory performance in the specified tests, must be done at least every 6 months for both the PEC and all ISO-classified areas.		
5.3	755-756	Active air sampling of all ISO-classified areas must be conducted during typical operating conditions at least monthly.	Active air sampling of all ISO-classified areas must be conducted during typical operating conditions at least quarterly.	• Costs associated with primary screening and characterization of results on a monthly basis will place excessive financial burdens on providers.	
5.3	770-771	If a CFU count is identified below the action levels 771 in Table 4, primary screening and characterization must be performed	If any CFU is identified, but does not exceed the action levels in Table 4 then primary screening and characterization must be performed		
5.4	820-825	When surface sampling results for ISO Class 7 or 8 areas exceed the criteria in Table 5, a corrective action plan must be implemented immediately. In such a case, if compounding is continued, the BUDs for any CSPs compounded must not	When surface sampling results for ISO Class 7 or 8 areas exceed the criteria in Table 5, a corrective action plan must be implemented immediately. The action plan must identify potential sources of contamination if known, outline all corrective actions taken including a	• Limiting BUDs to Category 1 during re-testing of ISO 7 or 8 areas when action levels are exceeded may result in interruptions to operations that could compromise patient care. • Limit BUDs only if 2 successive tests exceed the action levels • An example: a 1,000 sqft centralized health system ISO 7 cleanroom is tested in ten (10) separate locations to meet surface sample requirements. In the event one	

		exceed the BUDs for Category 1 CSPs until the surfaces are retested and the results fall below action levels in Table 5.	triple-cleaning process, and re-testing of the affected areas. If results of the repeated test remain above the criteria in Table 5, then the BUDs for CSPs made may not exceed Category 1 until subsequent mitigation and testing is completed by a qualified third party entity and ~~the surfaces are retested and the~~ results fall below action levels in Table 5.	surface sample test, say by a weigh station, exceeds action levels, the proposed text requires that all production from the cleanroom be affected, including those at the work bench 30 ft away, regardless of the cause. This includes false positives, operator error, localized causes of contamination, and other variables where such a requirement would unduly affect access to care without consideration for assessments and action plans developed by the compounder.	
6.2	856-858	All cleaning tools (e.g., wipes, sponges, and mop heads) must be sterile and low-lint, preferably composed of synthetic microfibers and dedicated for use in buffer or ante areas or segregated compounding areas. All cleaning tools must be cleaned and re-sterilized after each use. They must be discarded after an appropriate amount of time, to be determined based on the condition of the materials.	~~All~~ Disposable cleaning tools (e.g., wipes, sponges, and mop heads) must be sterile and low-lint, and preferably composed of synthetic microfibers and dedicated for use in buffer or ante areas or segregated compounding areas. ~~All~~ Non-disposable cleaning tools must be low-lint, preferably composed of synthetic microfibers and dedicated for use in buffer or ante areas or segregated compounding areas, and cleaned and disinfected after each use. ~~They~~ Cleaning tools must be discarded after an appropriate amount of time, to be determined based on the condition of the materials.	• The combination of antimicrobial cleaning solutions (including bleach, quaternary solutions), along with non-reusable cleaning tools offers sufficient protection from introducing contamination. • “Disinfection” rather than “sterility” is a more appropriate standard for non-disposable cleaning tools.	•
6.5	893- 895	Before compounding supplies are introduced into buffer areas, they must be wiped with a suitable disinfectant (e.g., sterile 70% IPA) that	Before compounding supplies are introduced into buffer areas, they must be sprayed or wiped with a suitable disinfectant (e.g., sterile 70% IPA) that	Not all supplies can be wiped, and the next sentence indicates both spraying and wiping are allowed.	

		is delivered from a spray bottle or other suitable delivery method.	is delivered from a spray bottle or other suitable delivery method.		
6.5	895 - 897	After the disinfectant is sprayed or wiped on the surface to be disinfected, the disinfectant must be allowed to dry, during which time the item cannot be used.	After the disinfectant is sprayed or wiped on the surface to be disinfected, the disinfectant must be allowed to dry, during which time the item cannot be disturbed.		
12.3	1540	The maximum BUD for Terminally Sterilized CSPs where sterility testing is performed is 28 days RT, 42 days RF, 45 days without a preservative and 42 days RT, 42 days RF, 45 days FZ with a preservative.	Remove BUD limitations for terminally sterilized CSPs.	• The limitations on BUDs for terminally sterilized products appear arbitrary. If the sterility of a product has been validated, what is the justification for the limits?	
12.3	1457-1461	If a sterility test is performed and there is an urgent need to dispense the CSP before sterility test results become available, a CSP can be dispensed to a patient before the end of the sterility testing period if: The prescriber specifically requests dispensing before completion of the sterility test, and the request is documented.	If a sterility test is performed and there is an urgent need to dispense the CSP before sterility test results become available, a CSP can be dispensed to a patient before the end of the sterility testing period if: ~~The prescriber specifically requests dispensing before completion of the sterility test, and the request is documented.~~ A procedure is maintained for notifying the patient and prescriber of a potentially contaminated product.	• Dictating prescribing requirements exceeds the authority of USP. • The existing text attempts to transfer responsibility to contaminated product from the compounder to the prescriber.	
12.4	1506-1507	The in-use time is the time before which a conventionally manufactured product or a CSP must be used after it has been opened or needle-punctured.	The in-use time is the time before which a conventionally manufactured product or a CSP must be used or administered after it has been opened or needle-punctured.	• While the Chapter states the scope of USP <797> ends at the start of administration, there is potential for confusion from the “in-use” terminology. Request adding the term “administered” to differentiate “in-use” time from administration.	

12.4	1518, 1520	Compounded single-dose container	Compounded single-dose container (e.g. bag, syringe, elastomeric)		
General				Response to exceeding action levels for viable air sampling needs to be consistent with those taken for exceeding action levels for surface sampling.	
General				All USP Chapters referenced in <797> should be made available in the USP Compounding Compendium	
General				USP should allow a minimum of 12 months for implementation of the revised standard to allow providers needing to make facility upgrades sufficient time to do so.	

(Add additional lines to the table as necessary.)