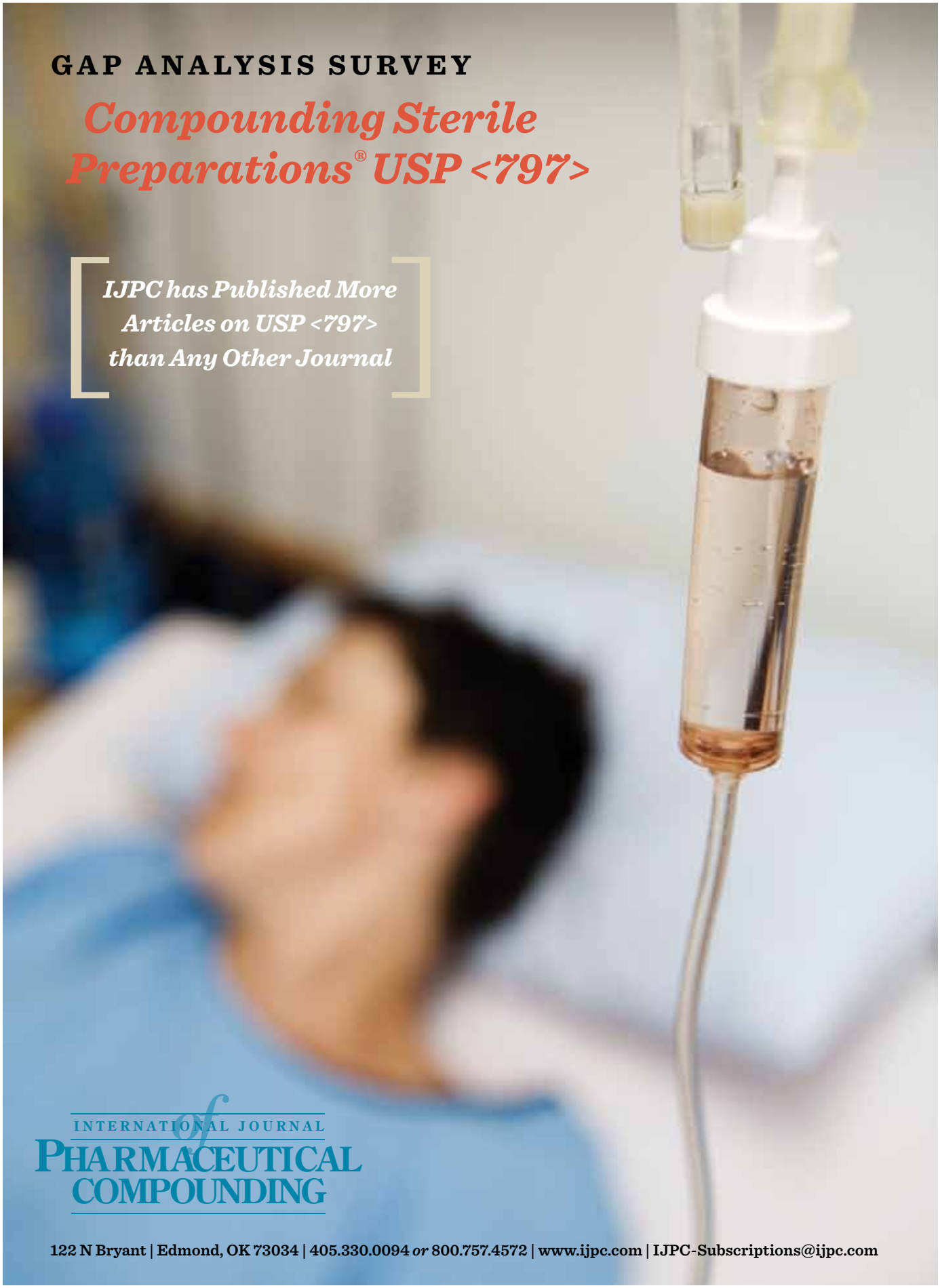

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GAP ANALYSIS SURVEY
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122 N. Bryant
Edmond, Oklahoma 73034
Loyd V. Allen, Jr., Ph.D., R.Ph.

Note: The purpose of this survey is to conduct a preliminary assessment of the pharmacy to determine general compliance with USP Chapter <797> Pharmaceutical Compounding-Sterile Preparations. This is simply a tool and Chapter <797> should be referred to for details and additional information.

OUTLINE OF CHAPTER <797>

Introduction
Organization of this chapter
Definitions
Responsibility of Compounding Personnel
CSP Microbial Contamination Risk Levels
Personnel training and evaluation in aseptic manipulation skills
Immediate-use CSPs
Single-dose and multiple-dose containers
Hazardous drugs as CSPs
Radiopharmaceuticals as CSPs
Allergen Extracts as CSPs
Verification of Compounding Accuracy and Sterility
Environmental quality and control
Suggested Standard Operating Procedures (SOPs)
Elements of quality control
Verification of Automated Compounding Devices (ACDs) for Parenteral Nutrition Compounding
Finished Preparation Release Checks and Tests
Storage and Beyond-Use Dating
Maintaining sterility, purity, and stability of dispensed and distributed CSPs
Patient or Caregiver Training
Patient monitoring and adverse events reporting
Quality Assurance Program
Abbreviations and Acronyms

INTRODUCTION

ITEM	REQUIREMENTS	YES	NO	COMMENT/SOP
Does the pharmacy compound sterile preparations?				
Does the pharmacy have detailed Standard Operating Procedures				
Has the pharmacy been inspected by the State Board for Sterile Compounding Practices?				
Has the pharmacy been inspected by the FDA?				
If so, was a "483" issued?				
Does the pharmacy understand the objective of USP Chapter <7697>?				
Does the pharmacy understand the use and application of other parts of the USP-NF, including the *General Notices and Requirements*, the monographs, and the other *General Chapters*?				
Does the pharmacy understand the five sources of potential problems described that may result in harm, including death, to patients?				
Does the pharmacy understand that the standards in this chapter apply to all individuals involved in preparing CSPs and to all places where CSPs are prepared?				
Does the pharmacy understand the ISO and U.S. FS 209E classification of particulate matter in room air?				
Does the pharmacy understand the depth and breadth of the application of the terminology "Compounded Sterile Preparations"?				

ORGANIZATION OF THIS CHAPTER

ITEM	REQUIREMENTS	YES	NO	COMMENT/SOP
Is the pharmacy aware of the content and organization of USP Chapters <797> and <795>.				
Is the pharmacy aware that all personnel involved in preparing CSPs are responsible for understanding these chapters?				

DEFINITIONS

ITEM	REQUIREMENTS	YES	NO	COMMENT/SOP
Are all personnel involved in compounding CSPs aware of the meaning of the terms and their definitions listed in this section?				
Can all personnel involved in compounding CPS explain the meaning and application of the terms in this section?				
Do all personnel know the difference in single-dose and multiple-dose containers and a pharmacy bulk package?				
Do all personnel know the difference between an "Ante-Area" and a "Buffer Area"?				
Do all personnel know the difference between a CAI and a CACI?				
Do all personnel know the relationship of "first air" to the Direct Compounding Area?				
Do all personnel know the relationship of the "critical site" to the Direct Compounding Area?				
Do all personnel know the difference in the application of the terms "preparation" and "product"?				

RESPONSIBILITY OF COMPOUNDING PERSONNEL

ITEM	REQUIREMENTS	YES	NO	COMMENT/SOP
Have the involved pharmacists received formal training in the preparation of CSPs? Documented?				
Have the involved technicians received formal training in the preparation of CSPs? Documented?				
Are the hands cleaned and disinfected appropriately?				
Are all nonsterile compounding surfaces cleaned and disinfected?				
Are protective gloves, goggles, gowns, masks and hair and shoe				

covers used?				
Is a LAF or Barrier Isolator used?				
Is the LAF or Barrier Isolator appropriate for the risk level?				
Are High Risk level nonsterile ingredients stored separately and used only for CSPs?				
Are the ingredients properly identified prior to using?				
Are the ingredients properly weighed on an appropriate balance?				
Are the ingredients properly measured using appropriate equipment?				
Are the ingredients handled and manipulated appropriately for the risk level?				
Are USP-NF grade materials used, if available?				
If USP-NF grade materials are unavailable, is the highest reasonable chemical grade used?				
Do all ingredients have an expiration date?				
Are the ingredients inspected upon receipt and prior to use in a compounded preparation?				
Are water-containing CSPs that are nonsterile sterilized within 6 hours of compounding?				
Do the sterilization methods maintain labeled strength?				
Are all the measuring, mixing, sterilizing and purifying devices clean, appropriately accurate and appropriate?				
Are preparations evaluated for bioavailability considerations?				
Is the packaging selected for the CSPs appropriate to preserve sterility and strength until the BUD?				
Do the labels list the names and amounts/concentrations of all ingredients?				
Are all CSPs inspected prior to being dispensed?				

Is all the documentation verified prior to dispensing a compounded CSP?				
Are Beyond-Use Dates assigned appropriately by direct testing, literature evaluation or other documentation?				
Are all the involved steps performed in a correct sequence and quality established for CSPs?				
If deficiencies occur in labeling, packaging and quality testing and inspection, are they rapidly identified and corrected?				
Are the compounding activities separated from the quality control activities (different personnel, etc.)?				

CSP MICROBIAL CONTAMINATION RISK LEVELS

ITEM	REQUIREMENTS	YES	NO	COMMENT/SOP
Low-Risk Compounding	*Compounding entirely with ISO Class 5 or better environment *Compounding involves only sterile ingredients, products, components and devices *Compounding involves only transfer, measuring and mixing manipulations with closed or sealed packaging systems. *Involves only aseptically opening ampules, penetrating sterile stoppers on vials with sterile needles and syringes and transferring sterile liquids in sterile syringes to sterile administration	____ ____	____ ____	

	devices and packages of other sterile products.			
Low-Risk Level CSPs with 12-Hour or less BUD	*If PEC does not meet criteria in this chapter, then only low-risk level nonhazardous and radiopharmaceutical CSPs can be prepared and administration shal begin within 12 hours of preparation or as recommended in the manufacturers' package insert, whichever is less. They also must meet the following criteria:			
	1. PECs are certified and maintain ISO Class 5 conditions for exposure of critical sites and are in a segregated compounding area restricted to sterile compounding.			
	2. Segregated compounding area is of appropriate construction and location.			
	3. Personnel follow procedures described in this chapter. Sinks are separated from the immediate area of the ISO Class 5 PEC device.			
	4. Specifications in the chapter regarding cleaning, disinfecting, personnel training, competency			

	evaluation, aseptic work practices, viable and nonviable environmental air sampling in the chapter are followed.			
Medium-Risk Compounding	*Multiple units are combined or pooled to prepare a CSP that will be administered to multiple patients or to one patient on multiple occasions. *Process includes complex aseptic manipulations other than single-volume transfers. *Process requires a long time to complete. *Sterile CSPs do not contain preservatives and are administered over several days.	____ ____ ____	____ ____ ____	
High-Risk Compounding	*Nonsterile ingredients are incorporated or a nonsterile device is used prior to terminal sterilization. *Any of the following are exposed to worse than ISO Class 5 air quality: -sterile contents of manufactured products -CSPs without effective preservatives -sterile surfaces of devices and containers for the preparation, transfer,	____ ____ ____	____ ____ ____	

	sterilization and packaging of CSPs *Personnel involved in compounding are improperly garbed and gloved. *Nonsterile preparations are exposed for at least 6 hours prior to being sterilized. *Assumption that ingredients meet original or compendial specifications. *All nonsterile measuring, mixing and purifying devices are rinsed with sterile, pyrogen-free water and drained or dried prior to use. *CSPs that are steam-sterilized are filtered through a filter of not more than 1.2 μm nominal pore size. *Sterilization by filtration using a sterile 0.2 μm nominal pore size filter is accomplished within an ISO Class 5 or better air quality environment.	____ ____ ____	____ ____ ____	

Risk-Level Quality Assurance

ITEM	REQUIREMENTS	YES	NO	COMMENT/SOP
Low-Risk Compounding	*Work area is disinfected. *Air quality testing is performed. *ISO Class 5 conditions are maintained.	____ ____ ____	____ ____ ____	

	*Personnel are properly donning and wearing appropriate items of protective garments and goggles. *All orders and packages of ingredients are reviewed to assure correct identity and amounts of ingredients are used. *CSPs are visually inspected to ensure they are particulate-free, not leaking and labeling is accurate and complete.	____ ____	____ ____	
Medium-Risk Compounding	*Work area is disinfected. *Air quality testing is performed. *ISO Class 5 conditions are maintained. *Personnel are properly donning and wearing appropriate items of protective garments and goggles. *All orders and packages of ingredients are reviewed to assure correct identity and amounts of ingredients are used. *CSPs are visually inspected to ensure they are particulate-free, not leaking and labeling is accurate and complete.	____ ____ ____ ____	____ ____ ____ ____	
High-Risk Compounding	*Work area is			

	disinfected. *Air quality testing is performed. *ISO Class 5 conditions are maintained. *Personnel are properly donning and wearing appropriate items of protective garments and goggles. *All orders and packages of ingredients are reviewed to assure correct identity and amounts of ingredients are used. *CSPs are visually inspected to ensure they are particulate-free, not leaking and labeling is accurate and complete.	____ ____ ____ ____ ____	____ ____ ____ ____ ____	

Risk-Level Media-Fill

ITEM	REQUIREMENTS	YES	NO	COMMENT/SOP
Low-Risk Compounding	*Performed by each person compounding this level CSPs. *Test is completed with interruption.	____	____	
Medium-Risk Compounding	*Performed by each person compounding this level CSPs. *Test is completed with interruption. *The test is more challenging than Low-Risk.	____ ____	____ ____	
High-Risk Compounding	*Performed by each person compounding this level CSPs. *Test is completed with interruption.	____ ____	____ ____	

	*The test is most challenging.			

PERSONNEL TRAINING AND EVALUATION IN ASEPTIC MANIPULATION SKILLS

Media-Fill Challenge Testing

ITEM	REQUIREMENTS	YES	NO	COMMENT/SOP
Personnel compounding CSPs are properly trained.				
Personnel compounding CSPs participate in continuing education programs about CSPs before beginning to prepare CSPs.				
The facility has sufficient and appropriate SOPs related to aseptic manipulation and media-fill challenge testing.				
Personnel are evaluated according to SOPs on media-fill procedures.				
Personnel who need correction receive additional instruction and participate in additional verification procedures prior to returning to work in the facility.				
Media-fill tests that are used by personnel represent the most challenging situation to be encountered in the facility.				
Media-fill test media are appropriately incubated for the required number of days at the desired temperature.				
Results are evaluated and recorded properly.				
Testing is done at appropriate intervals based upon the risk level of compounding performed.				

IMMEDIATE-USE CSPs

ITEM	REQUIREMENTS	YES	NO	COMMENT/SOP
Does the facility have a legitimate reason for using the "Immediate-Use" provision (emergency or immediate patient administration of a CSP)?				
Are the following criteria met to				

qualify for the "immediate-use" exemption?				
Does the compounding involve simple transfer of not more than 3 commercially manufactured packages of sterile nonhazardous products or diagnostic radiopharmaceutical products?				
Are not more than 2 entries into any one container or package made?				
Anti-neoplastics are not compounded as immediate-use CSPs.				
The compounding procedure is continuous and does not exceed one hour.				
Aseptic technique is followed.				
If not immediately administered, the CSP is under continuous supervision until administration.				
Administration is started not later than one hour after the start of the compounding process.				
Unless administered by the individual compounding the CSP, it contains a label bearing the patient identification information, names and amounts of all ingredients, name or initials of the person preparing the CSP and the exact 1-hour BUD and time.				
If administration is not begun within the 1 hour time limit, the CSP is properly, properly and safely discarded.				

SINGLE-DOSE AND MULTIPLE-DOSE CONTAINERS

ITEM	REQUIREMENTS	YES	NO	COMMENT/SOP
Are single dose containers used?				
After opening or needle-puncturing single dose containers in worse than ISO Class 5 air, the contents are used within 1 hour. Any remaining material is appropriately discarded.				
After opening or needle-puncturing single dose containers in ISO Class				

5 or air, the contents are used within 6 hours. Any remaining material is appropriately discarded				
Are multiple dose containers used?				
After multiple dose containers are initially entered or opened, a BUD of 28 days is observed unless otherwise specified by the manufacturer.				

HAZARDOUS DRUGS AS CSPs

ITEM	REQUIREMENTS	YES	NO	COMMENT/SOP
Pharmacy has appropriate SOPs in effect for handling hazardous drugs.				
Pharmacy has a list of "hazardous drugs".				
Hazardous drugs are stored separately from other inventory.				
Storage area for hazardous drugs is under negative pressure and/or has sufficient general exhaust ventilation with not less than 12 air changes per hour.				
Chemotherapy gloves are used for receiving, distribution, stocking, inventorying, preparation for administration and disposal of hazardous drugs.				
Access to where hazardous drugs are stored or compounded is limited.				
Hazardous drugs are compounded in a BSC or CACI meeting appropriate standards.				
The BSC or CACI used for compounding hazardous drugs is contained in an ISO class 7 environment.				
If CACI is not in a buffer area, is compounding area under negative pressure and a minimum of 12 air changes per hour?				
If closed system vial transfer devices are used, are they used within a BSC or CACI?				
If compounding a low volume of hazardous drugs, are two tiers of				

containment in a non-negative pressure room used?				
Is there documentation that all personnel handling hazardous drugs are fully trained in their storage, handling and disposal?				
Are any personnel handling hazardous drugs of reproductive capability?				
If so, have they confirmed in writing that they understand the risks involved and obtained appropriated training.				
Is the disposal of all hazardous drugs done in compliance with all applicable federal and state regulations?				
Are all individuals involved in waste removal and cleaning activities in storage and preparation areas for hazardous drugs properly trained in proper procedures to protect themselves and prevent contamination?				

RADIOPHARMACEUTICALS AS CSPs

ITEM	REQUIREMENTS	YES	NO	COMMENT/SOP
Does the pharmacy compound radiopharmaceuticals?				
If "yes", are there adequate SOPs covering all the various aspects related to receipt, storage, handling, compounding, dispensing, disposal and other aspects of radiopharmaceuticals?				
If "yes" and if the pharmacy prepares radiopharmaceuticals for positron emission tomography (PET), is the pharmacy in compliant with USP <823> Radiopharmaceuticals for Positron Emission Tomography?				
Does the pharmacy meet the requirements for Low-Risk Level CSPs? (The radiopharmaceuticals are compounded from sterile				

components in closed sterile containers and with a volume of 100 mL or less for a single-dose injection and not more than 30 mL taken from a multiple-dose container)				
Is the compounding done in an ISO Class 5 Primary Engineering Control located in an ISO Class 8 or cleaner air environment?				
Is the compounding done using appropriately shielded vials and syringes?				
If technetium-99m is compounded involving multi-use vials exposed to ISO Class 5 Environment and punctured by needles with no direct contact contamination, are they used up to the time indicated by the manufacturers' recommendations?				
If applicable, are technetium-99m/molybdenum-99 generator systems stored and eluted under conditions approved by the manufacturer and applicable state and federal regulations?				
Are personnel involved in inspections appropriately protected according to ALARA?				
If low-risk level CSPs with a 12 hour or less BUD are prepared, are they prepared in a segregated compounding area as prescribed?				

ALLERGEN EXTRACTS AS CSPs

ITEM	REQUIREMENTS	YES	NO	COMMENT/SOP
To be exempt from the standards, does the facility meet ALL the criteria generally stated below?				
1. Compounding involves simple transfer via sterile needles and syringes of commercial sterile allergen products with appropriate sterile added substances?				
2. Are all extracts appropriately preserved OR do they comply with				

the appropriate CSP risk level?				
3.Thorough and appropriate hand cleaning is done, as described?				
4. Hair covers, facial hair covers, gowns and face masks are used?				
5. Antiseptic hand cleansing with an alcohol-based surgical hand scrub with persistent activity is used?				
6. Powder-free sterile gloves that are compatible with sterile 70% alcohol are used?				
7. Gloves are intermittently disinfected with sterile 70% IPA before and during compounding?				
8. Ampule necks and vial stoppers are appropriately disinfected?				
9. Aseptic compounding manipulations are done to minimize direct contact contamination?				
10. Labels appropriately lists the required information?				
11. Single-dose allergen extract CSPs are not stored for subsequent additional use?				
Personnel are appropriately trained and aware of greater potential risks of microbial and foreign material contamination with working with allergen extracts.				

VERIFICATION OF COMPOUNDING ACCURACY AND STERILITY

Sterilization Methods

Sterilization of High-Risk Level CSPs by Filtration

Sterilization of High-Risk Level CSPs by Steam

Sterilization of High-Risk Level CSPs by Dry Heat

Depyrogenation by Dry Heat

ITEM	REQUIREMENTS	YES	NO	COMMENT/SOP
Introduction				
The procedures and methods used for CSPs correspond to correctly designed and verifed written documentation.				
Verification of the procedures and methods includes planned testing, monitoring and documentation to demonstrate adherence to				

environmental quality requirements, personnel practices, and procedures required to achieve and maintain sterility, accuracy and purity of the finished CSP.				
Finished CSPs are visually expected for physical integrity and expected appearance, including final volume.				
The identity, concentration, amounts and purities of ingredients used in CSP is confirmed.				
Any ingredient whose identity, integrity, etc. cannot be confirmed is immediately discarded.				
Personnel are trained in changes in moisture content and testing that may be considered.				
Samples of CSPs may be assayed according to an established procedure, although not required.				
Sterilization Methods				
Personnel supervising compounding have determined that the sterilization methods used both sterilize and maintain the strength, purity, quality and packaging integrity of the CSPs.				
The individual components and the finished CSPs are considered in selecting the sterilization method(s) to be used.				
Sterilization of High-Risk Level CSPs by Filtration				
Filters used are of appropriate material for each CSP, considering chemical and physical inertness, pore size, compatibility, temperature and pressure.				
Filters are compatible for each CSP, including filter material and housing, and will not sorb or otherwise interact with the CSP.				
Filters are of appropriate size for each CSP.				
Prefilters are used for preparations with high particulate load.				
Filtration process is completed				

rapidly and without filter replacement.				
Bubble point test for integrity is used as appropriate.				
Any unusual solvent that may cause damage to the filter is investigated for appropriateness.				
Sterilization of High-Risk Level CSPs by Steam				
The autoclave is verified according to SOPs using biological indicators, as appropriate.				
Pressure and temperature is recorded with each autoclave cycle.				
The autoclave is packed appropriately to allow for steam to circulate to all areas of the autoclave.				
Sterilization of High-Risk Level CSPs by Dry Heat				
The dry heat oven is verified according to SOPs.				
Temperature is recorded with each cycle.				
The dry heat oven is packed appropriately with room between materials to allow for good circulation of air.				
Appropriate biological indicators are used for verifying proper operation of the oven.				
Depyrogenation by Dry Heat				
The oven is verified according to SOPs.				
Temperature is recorded with each cycle.				
Glass and metal devices are properly packaged and depyrogenated.				
Sterile, depyrogenated items are properly stored.				
Endotoxin challenge vials are used to confirm the proper operation of the oven.				
Items for autoclaving are appropriately packaged.				
Autoclave conditions are validated				

for specific CSPs.				

ENVIRONMENTAL QUALITY AND CONTROL
Exposure of Critical Sites
ISO Class 5 Air Sources, Buffer Areas, and Ante-Areas
Facility Design and Environmental Controls
Placement of Primary Engineering Controls
Viable and Nonviable Environmental Air Sampling (ES) Testing
- **Environmental Nonviable Particle Testing Program**
  - **Engineering Control Performance Verification**
  - **Total Particle Counts**
- **Pressure Differential Monitoring**
- **Environmental Viable Airborne Particle Testing Program**
  - **Sampling Plan**
  - **Growth Medium**
  - **Viable Air Sampling**
  - **Air Sampling Devices**
  - **Air Sampling Frequency and Process**
  - **Incubation Period**
  - **Action Levels, Documentation, and Data Evaluation**

Additional Personnel Requirements
Cleaning and Disinfecting the Compounding Area
Personnel Cleansing and Garbing
Personnel Training and Competency Evaluation of Garbing, Aseptic Work Practices, and Cleaning/Disinfection Procedures
- **Competency Evaluation of Garbing and Aseptic Work Practice**
  - **Aseptic Work Practice Assessment and Evaluation via Personnel**
  - **Glove Fingertip Sampling**
  - **Garbing and Gloving Competency Evaluation**
  - **Gloved Fingertip Sampling**
  - **Incubation Period**
  - **Aseptic Manipulation Competency Evaluation**
- **Surface Cleaning and Disinfection Sampling and Assessment**
  - **Cleaning and Disinfecting Competency Evaluation**
  - **Surface Collection Methods**

Action Levels, Documentation, and Data Evaluation

ITEM	REQUIREMENTS	YES	NO	COMMENT/SOP
Exposure of Critical Sites				
Compounding procedures are organized to minimize critical site exposure.				
Critical sites are disinfected appropriately.				
ISO Class 5 Air Sources, Buffer Areas, and Ante-Areas				
The ISO Class 5 environment is				

properly located, operated, maintained, monitored and verified according to all the relevant SOPs.				
The ante-areas and buffer areas are properly located relative to each other.				
Devices and objects that are not essential to compounding in the buffer areas are either placed outside or are positioned in such a manner that they will not adversely impact the ISO Class 5 environment. Air quality is measured to verify that there is no adverse effect.				
Facility Design and Environmental Controls				
The buffer area is appropriately segregated from surrounding spaces to minimize the introduction of contaminants into the room.				
The compounding environment is clean, well-maintained and organized.				
SOPs for maintaining and working in the clean air environment are prepared, updated, maintained and implemented.				
Positive pressure is designed into the work environment.				
The required number of air exchanges per hour is met and determined by the number of personnel and activity level of operations in the room.				
Buffer areas or clean room areas are at least ISO Class 7.				
Ante-areas are at least ISO Class 8.				
Appropriate temperature and humidity is maintained in all the work areas.	*nonsterile compounding *ante room *buffer area *aseptic compounding area	____ ____ ____	____ ____ ____	
Measuring, weighing, mixing and other nonsterile manipulations are done in at least ISO Class 8				

environment.				
Only tasks involving a clean air environment are performed in the clean air portion of the room.				
Only appropriate furniture and equipment are in the aseptic compounding environment.				
Items moved into the buffer room are cleaned and disinfected prior to entry.				
Equipment used in the buffer room is not removed, except for calibration, servicing or other appropriate activity.				
Surfaces are smooth, impervious, free from cracks and crevices and are nonshedding	*ceilings *walls *floors *fixtures *shelving *counters *cabinets	____ ____ ____ ____ ____ ____	____ ____ ____ ____ ____ ____	
Junctures of ceilings to walls and floors to walls are coved.				
If panels are used in ceilings or walls, they are coated with a polymer to render them impervious and hydrophobic.				
Floors are single sheet vinyl or sealed.				
Dust-collecting overhangs are absent.				
Light fixtures are smooth, mounted flush and sealed.				
Other ceiling/wall penetrations are sealed.				
Buffer area contains no sinks or floor drains.				
Work surfaces and storage shelving are smooth and impervious, free from cracks and crevices, nonshedding, cleanable and sanitizable.				
Carts are of stainless steel wire or sheet metal construction with cleanable casters.				
HEPA-filtered air is introduced at				

the ceiling and returns are located low on the wall.				
Placement of Primary Engineering Controls (PECs)				
PECs (LAFWs, BSCs, CAIs and CACIs) are located within an ISO Class 7 buffer area unless an exception is met according to the chapter.				
If an exception is desired, documentation from the manufacturer that the CAI/CACI will meet the required standards in the area in which it is to be located must be on file.				
Viable and Nonviable Environmental Air Sampling (ES) Testing				
Environmental sampling is done under any of the following conditions:	*Commissioning and certification of new facilities and equipment. *after the facility or any equipment is serviced. *regular scheduled re-certification of facilities and equipment. *as a response to any identified problems with preparations or personnel techniques. *as a response to any issues with CSPs, observed work practices or patient-related infections as appropriate.			
Total particle counts are done no less than every 6 months and whenever the PEC is relocated or any part of the physical structure of the buffer area or the ante-area has been modified.				
Monitoring of the pressure				

differential or airflow between the buffer area and the ante-area and between the ante-area and the general environment outside the compounding area is done and recorded at least every work shift to confirm it meets the standard.				
SOPs are in place and followed governing an environmental viable airborne particle testing program.				
The sampling plan includes locations within each ISO Class 5 environment and in the ISO Class 7 and 8 areas as well as in the segregated compounding areas at greatest risk of contamination.				
The sampling plan includes sample location, method of collection, frequency of sampling, volume of air sampled, and the time of day as related to compounding activities. It also includes action levels.				
An appropriate growth medium is documented and used and is supplemented with additives as required.				
Individuals involved in air sampling are properly trained and experienced.				
Volumetric collection methods are used in the controlled air environments.				
Manufacturers recommended procedures are followed when using commercial air sampling devices.				
Air sampling is done at least every 6 months.				
Proper incubation periods are used for the growth media depending upon the type of media used and types of microbes being tested.				
Appropriate “Action Levels” have been determined based on sampling location and trending over time.				
SOPs are in place and followed related to activities required when				

Action Levels are met or exceeded.				
Additional Personnel Requirements				
No food, drinks or materials exposed in patient-care and treatment areas are permitted where components and ingredients of CSPs are present.				
Blood-derived materials or other designated biological material manipulations are clearly separated from routine CSP preparation activities.				
Packaged components and supplies are uncartoned and wiped down with a non-residue generating disinfectant in an ante-area of ISO Class 8, if possible, before transporting into buffer areas.				
There is a demarcation between the ante-area and the buffer area.				
After entry into the buffer area, provision is made for personnel to perform antiseptic hand cleansing using an alcohol-based surgical hand scrub with persistent activity followed by donning of sterile gloves.				
Cleaning and Disinfecting the Compounding Area				
An appropriate disinfectant solution is selected and is appropriately used according to the manufacturer's recommendations.				
The work area is cleaned, sanitized and organized at the beginning of each work shift.				
Disinfection of the immediate work area is repeated using sterile 70% IPA at the beginning of each work shift, before each batch preparation is started, every 30 minutes during continuous compounding periods of individual CSPs, when there are spills, and when surface contamination is known or suspected.				

For cleaning, all materials are removed from the surfaces and the area appropriately sanitized.				
All contact surfaces, including counter tops and supply carts are cleaned at the beginning of each shift..				
At least monthly, storage shelving in the clean area is emptied of all supplies and then cleaned and sanitized, using approved agents.				
Floors in the buffer or clean area are cleaned by mopping once daily, by appropriately trained personnel, proceeding from the buffer or clean area to the anteroom area.				
Monthly, the walls and ceilings are cleaned and disinfected.				
Only approved cleaning agents are used and are rotated appropriately.				
All cleaning tools, wipers, mops, sponges, are nonshedding and dedicated to the buffer or clean area.				
Trash is collected in suitable plastic bags and removed with minimal agitation.				
Precleaning of heavily soiled areas is done as needed.				
No shipping or other cartoning material is taken into the buffer or clean area.				
In the anteroom area, storage shelving is emptied of all supplies and cleaned and sanitized preferably monthly.				
These cleaning procedures apply to all risk level operations.				
IPA sterile swabs do not contact any surface prior to disinfecting the sterile entry points of containers, etc. The alcohol is allowed to dry prior to entering the container.				
Personnel Cleansing and Garbing				
Compounding personnel with any skin disorder tending to shed particles at higher than normal rates				

are excluded from working in the ISO Class 5 and ISO Class 7				
All visible jewelry and piercings are removed prior to entering the ISO Class 5 clean room.				
No cosmetics are used by personnel when compounding CSPs.				
All personal outer garments are removed prior to entering the ISO Class 5 clean room.				
No artificial nails or extenders are worn by personnel compounding CSPs. Natural nails are kept neat and trimmed.				
Personnel don the appropriate garb in the following order: Shoes/shoe covers, head and facial hair covers, face masks. Next a hand cleansing procedure is done. Then, a nonshedding gown is donned, followed by antiseptic hand cleansing with a waterless alcohol-based surgical hand scrub with persistent activity and drying followed by donning sterile gloves.				
SOPs are followed covering activities if compounding personnel exit and re-enter the ISO Class 5 area.				
Personnel Training and Competency Evaluation of Garbing, Aseptic Work Practices, and Cleaning/Disinfection Procedures				
Compounding personnel are appropriately and conscientiously trained and evaluated prior to compounding CSPs.				
All compounding personnel are evaluated using media-fill testing at least annually for low- and medium-risk compounding and semiannually for high-risk compounding.				
Personnel that fail any tests are re-trained and re-evaluated and must pass prior to compounding CSPs.				

Glove fingertip sampling is used to evaluate compounding personnel.				
Personnel must pass the glove fingertip sampling test at least three times prior to being allowed to compound CSPs.				
The facility has determined the Action Level appropriate for their specific situation for fingertip sampling testing.				
Surface sample testing is accomplished according to facility SOPs.				
Surface sampling is done by either contact plates or swabs according to a verified procedure.				
Plates are appropriately incubated and interpreted.				
Action levels, if exceeded, immediately result in an investigation and corrective action.				
Action Levels, Documentation, and Data Evaluation				
Action levels are determined for each type of testing.				
If any action level is exceeded, an investigation is initiated that should result in corrective action.				
Corrective action measures are taken as required and documented.				

SUGGESTED STANDARD OPERATING PROCEDURES (SOPs)

The facility has appropriately determined, written, approved and implemented SOPs.				
Note: The following SOPs are abbreviated from USP <797> and are not intended to be all-inclusive.				
1. Buffer area access is limited only to qualified personnel with specific responsibilities or assigned tasks.				
2. Supplies are removed from cartons and decontaminated prior to placing them on a clean and properly disinfected cart or other conveyance for movement into the buffer area.				

3. Frequently-used supplies may be properly decontaminated and stored on shelving in the ante-area.				
4. Carts used for transporting supplies from storage cannot be rolled beyond the line of demarcation in the ante-area; carts used in the buffer area cannot be moved outward beyond the demarcation line unless cleaned and disinfected prior to re-entry.				
5. Supplies for scheduled operations are disinfected and brought into the buffer area, preferably on one or more movable carts.				
6. Nonessential objects, especially those that shed particles, are not brought into the buffer area.				
7. Essential paper-related products shall be wiped down appropriately prior to being brought into the buffer area.				
8. Traffic-flow entering and exiting the buffer area is minimized.				
9. Personnel entering the buffer area shall first remove all personal outer garments, cosmetics and all hand, wrist, and other visible jewelry or piercings.				
10. Personnel entering the ante-area shall don appropriate attire as described in "Personnel Cleansing and Garbing and Personnel Training and Competency Evaluation of Garbing, Aseptic Work Practices and Cleaning/Disinfection Procedures.				
11. Personnel shall thoroughly wash hands and forearms to the elbow with soap and water for at least 30 seconds; then dry with disposable nonshedding towels or air dryer.				
12. Personnel entering buffer area shall perform antiseptic hand cleansing prior to donning sterile gloves using a waterless alcohol-				

based surgical hand scrub with persistent activity.				
13a. No chewing gum, drinks, candy or food items shall be brought into the buffer area or ante-area.				
13b. No materials exposed in patient care and treatment areas shall ever be introduced into areas where components and ingredients for CSPs are present.				
14. At the beginning of each compounding session and when spills occur, the involved surfaces will be cleaned with USP Purified Water followed by disinfection with a nonresidue-generating agent using a nonlinting wipers.				
15. Primary engineering controls are operated continuously during compounding activities. When turned off, only one person shall enter the buffer area for turning on the blower where it should run for at least 30 minutes, and for disinfecting the work surfaces.				
16. Traffic is minimized and controlled in the area of compounding activities.				
17. Supplies to be used are collected, decontaminated prior to introducing into the aseptic work area.				
18. Supplies are arranged in the work area to reduce clutter and provide for maximum efficiency and order in the work flow.				
19. Items are arranged in the work area to minimized any flow disruption of the HEPA-filtered air. The exposed critical site is protected from flow interruptions at all times.				
20. Touch contamination is minimized at all times. Gloves are disinfected frequently during the compounding process.				
21. All stoppers and necks of ampuls are disinfected by wiping with				

sterile 70% IPA.				
22. The contents of the CSP are thoroughly mixed and then inspected for the presence of particulates, evidence of incompatibility or other defects.				
24. Used syringes, bottles, vials and other supplies are removed with a minimum of exit and re-entry into the work area to minimize the risk of introducing contaminations. These supplies also maintain their arrangement for ease of quality checking.				

ELEMENTS OF QUALITY CONTROL

Ingredients and Devices

Sterile Ingredients and Devices

Nonsterile Ingredients and Devices

Equipment

ITEM	REQUIREMENTS	YES	NO	COMMENT/SOP
For all individuals involved in aseptic technique, there is a written description of specific training required and obtained.				
For all individuals involved in aseptic technique, there is a written performance evaluation program .				
Ingredients and Devices				
Documentation is available to show that ingredients used in CSPs are of the correct identity and appropriate quality.				
A written procedure is in place and followed that all commercial products, containers and devices used in CSPs are thoroughly inspected before use.				
All nonsterile components (including containers and ingredients) are accompanied by certificates of analysis and are inspected prior to use.				
Bulk and unformulated drug substances and excipients are stored in tightly closed containers under				

appropriate temperature, humidity and lighting conditions.				
Date of receipt is clearly and indelibly marked on each package of ingredients.				
If an "expiration date" is not listed on the ingredient, it is used within 1 year of receipt unless testing indicates it still retains its purity and quality.				
All bulk and unformulated drug substances are visually inspected upon receipt.				
Equipment				
Written documentation is available on the calibration, annual maintenance, monitoring for proper function of each piece of equipment used in compounding CSPs.				
SOPs are followed on the routine calibration, maintenance and use of each piece of equipment and are kept on file for the lifetime of the equipment.				
SOPs are followed on the training required for the proper operation, use and care of each piece of equipment.				
Personnel are trained in determining whether or not each piece of equipment is functioning properly.				

VERIFICATION OF AUTOMATED COMPOUNDING DEVICES (ACDs) FOR PARENTERAL NUTRITION COMPOUNDING

Accuracy

Precision

ITEM	REQUIREMENTS	YES	NO	COMMENT/SOP
Accuracy				
Are automated compounding devices used?				
The automated compounding device is tested?	*volume *weight	____	____	
A detailed SOP is used for testing the automated compounding device.				
A detailed SOP is used to detail procedures to follow if the				

automated compounding device is out of specifications.				
Specific gravities of ingredients are used in the automated compounding device. If specific gravities are used, a detailed procedure is available on determining specific gravity in the event an ingredient does not have it listed in its package information.				
Tolerances are well defined for the automated compounding device.				
Final volume is checked and compared to theoretical volume.				
Periodically, chemical testing is done for quality assurance.				
Precision				
Daily records are maintained on performance characteristics of the automated compounding device.				
The daily records are regularly evaluated to confirm the performance of the automated compounding device.				
Ingredients with narrow therapeutic indices (KCl, etc.) are monitored especially closely.				

FINISHED PREPARATION RELEASE CHECKS AND TESTS

Inspection of Solution Dosage Forms and Review of Compounding Procedures

Physical Inspection

Compounding Accuracy Checks

Sterility Testing

Bacterial Endotoxin (Pyrogen) Testing

Identity and Strength Verification of Ingredients

ITEM	REQUIREMENTS	YES	NO	COMMENT/SOP
Inspection of Solution Dosage Forms and Review of Compounding Procedures				
All CSPs are visually checked for presence of particulate matter.				
Prescription orders, written procedures, preparation records and expended materials used to make CSPs at all contamination risk levels are inspected for accuracy of				

correct identities and amounts of ingredients, aseptic mixing and sterilization, packaging, labeling and expected physical appearance before administration or dispensing.				
Physical Inspection				
All CSPs are inspected immediately after compounding and prior to dispensing (if stored) using a lighted white/black background for particulates and foreign matter.				
CSPs are inspected for container-closure integrity and for any other apparent visually apparent defect.				
CSPs with defects are immediately discarded or marked and separated from acceptable preparations.				
CSPs not distributed promptly after preparation shall be inspected just prior to distribution/dispensing to ensure that defects, such as precipitation, cloudiness, and leakage, have not developed between time of preparation/release and time of distribution.				
Compounding Accuracy Checks				
SOPs for double-checking compounding accuracy of all CSPs are in effect and closely followed.				
All containers and supplies (syringes, etc.) used in the preparation of CSPs are quarantined together with the final preparations until the final preparation check is completed.				
Every step in the preparation of CSPs is visually confirmed, preferably by a second compounding individual.				
Compounding checks include specific gravity calculations and determinations, if appropriate.				
Sterility Testing				
Batches consisting of more than 25 identical individual single-dose packages or multiple dose vials for				

administration to multiple patients, or are exposed longer than 12 hours at 2 to 8° and longer than 6 hours at warmer than 8° before sterilization are tested to ensure sterility prior to dispensing or administration.				
The membrane-filtration method (or a suitable alternative) for sterility testing is used.				
If non-sterility occurs, the batch is immediately quarantined.				
If non-sterility occurs, SOPs describe a prompt, rapid and systematic investigation to identify sources of contamination and correct problems in the methods or processes.				
Bacterial Endotoxin (Pyrogen) Testing				
Batches consisting of more than 25 identical individual single-dose packages or multiple dose vials for administration to multiple patients, or are exposed longer than 12 hours at 2 to 8° and longer than 6 hours at warmer than 8° before sterilization are tested to ensure they do not contain excessive endotoxins.				
If monograph information is not available on endotoxin limits, USP Chapter <85> Bacterial Endotoxins Test will be utilized to establish limits.				
Identity and Strength Verification of Ingredients				
SOPs are followed for verifying the correct identity and quality of CSPs before they are dispensed or administered.	*labels bear correct names and amounts or concentrations of ingredients, the total volume, beyond-use date, appropriate route of administration, storage conditions and other information for safe use.	____	____	

	*The original written order is compared to the written compounding record for the CSP. *Correct fill volumes and correct quantities of filled units are obtained. *If not obtained, the CSPs must be assayed by methods that are specific for the active ingredients.	____ ____	____ ____	

STORAGE AND BEYOND-USE DATING
Determining Beyond-Use Dates
Proprietary Bag and Vial Systems
Monitoring Controlled Storage Areas

ITEM	REQUIREMENTS	YES	NO	COMMENT/SOP
SOPs are in place and followed in the assignment of beyond-use dates.				
Beyond-use dates are assigned based on USP Chapters <797> and/or <795>.				
Compounded CSPs are stored as labeled, to ensure stability.				
Compounded CSPs stored for longer than 4 hours at temperatures warmer than the warmest labeled limit, but not exceeding 40° C, are discarded, unless documentation or direct assay data confirm their stability.				
Determining Beyond-Use Dates				
When manufactured products are used for CSPs, manufacturer-generated data is used, in addition to USP <797> and <795>.				
If multiple dose vials (MDV's) are used, after they are penetrated, they are refrigerated when not in use.				
MDV's are discarded after 28 days after opening or according to the manufacturers instructions.				
Documentation is available for				

specific preparations that do not use the USP <797> and <795> default dates.				
Proprietary Bag and Vial Systems				
Manufacturers recommendations are followed when proprietary bag and vial systems are used.				
Monitoring Controlled Storage Areas				
All drug storage areas are monitored at least once daily according to SOPs and documented.	*Room temperature *Refrigerators *Freezers	____ ____	____ ____	
All ovens and incubators are monitored according to SOPs and documented.	*Ovens *Incubators	____	____	
Controlled Room Temperature with a mean kinetic temperature of 25° C, Controlled cold temperature with mean kinetic temperature of 8° C, cold temperature (2-8° C) and freezing temperature (-25° to -10° C) are followed as well as media-specific temperature ranges for microbial culture media.				

MAINTAINING STERILITY, PURITY, AND STABILITY OF DISPENSED AND DISTRIBUTED CSPs

Packaging, Handling and Transport
Use and Storage
Readying for Administration
Redispensed CSPs
Education and Training
Packing and Transporting CSPs
    Packing CSPs for Transit
    Transit of CSPs
Storage in Locations Outside Compounding Facilities

ITEM	REQUIREMENTS	YES	NO	COMMENT/SOP
Pharmacy personnel are aware of and follow proper storage and security requirements for CSPs				
Pharmacy personnel are aware of and follow proper packaging and handling requirements for CSPs.				
Pharmacy personnel are aware of and follow proper transportation requirements for CSPs.				

SOPs are in place for proper storage, security, packaging, handling and transportation of CPSs.				
Packaging, Handling and Transport				
The performance of noncompounding personnel involved in packaging, handling and transportation of CSPs is closely monitored and evaluated.				
Detailed SOPs are in place addressing specific packaging requirements including maintaining integrity of syringes, syringe plungers and syringe tips during handling and transportation.				
Appropriate procedures are in place for specialty items that should not be shaken or exposed to excessive heat and light.				
Special requirements are in place for handling chemotoxic and other hazardous CSPs.				
Use and Storage				
Appropriate procedures are in place to ensure that CSPs will maintain their quality in the patient-care setting until administration.				
SOPs are in place for the training and monitoring of delivery and patient-care-setting personnel.				
Any outdated or unused CSPs are returned to the compounding pharmacy for disposition.				
SOPs are in place to ensure storage in patient-care-settings is appropriate to maintain the quality of the CSPs.				
Drug storage refrigerators are monitored daily to ensure temperature remain between 2 and 8° C.				
Storage areas are inspected monthly by compounding personnel.				
Drug products stored in patient-care areas are secured from unauthorized				

personnel, visitors and patients.				
Readying for Administration				
Involved personnel are competent in or can adequately teach the patient or caregiver proper hand washing, aseptic technique, site care and change of administration sets, and other special procedures as required..				
Redispensed CSPs				
The pharmacy has sole authority to determine the disposition of unopened, returned CSPs.				
The pharmacy has a detailed SOP on handling returned CSPs.				
The pharmacy does not redispense a CSP if documentation is not available on the storage and handling conditions of the CSP.				
Redispensing is supported by an appropriate BUD to allow for administration with the original BUD.				
Education and Training				
SOPs are followed concerning a formal education, training and competency assessment program encompassing packaging, handling, transport, use, storage, readying for administration , packing and transporting CSPs; including assessment and documentation of breaches, administration mishaps, side effects, allergic reactions and complications.				
Packing and Transporting CSPs				
***Packing CSPs for Transit**				
The pharmacy has an SOP governing the appropriate packing containers and insulating and stuffing material to protect CSPs from damage, leakage, contamination and degradation as well as protecting personnel transporting the CSPs.				
***Transit of CSPs**				

Pharmacy has SOPs to maintain temperatures of CSPs during transit are within the required range on the labels.				
Pharmacy properly labels outside of containers for carriers.				
Pharmacy periodically confirms carrier is meeting all the required standards for maintaining quality of CSPs.				
Storage in Locations Outside Compounding Facilities				
Pharmacy confirms labels and accessory labeling is complete and appropriate.				
Pharmacy confirms patient or recipient can properly store CSPs, including refrigeration and freezing facilities				

PATIENT OR CAREGIVER TRAINING

ITEM	REQUIREMENTS	YES	NO	COMMENT/SOP
Patients or caregivers are provided with a formal program to ensure understanding and compliance with the storage, handling and administration of CSPs.				
The patient or caregiver will be able to describe the therapy involved.	*disease or condition being treated. *goals of therapy. *expected therapeutic outcome *Potential side effects	____ ____ ____	____ ____ ____	
The patient or caregiver is trained to inspect all drug products, devices, equipment and supplies on receipt to ensure no evidence of deterioration or defects related to temperatures during transit.				
The patient or caregiver is trained to handle, store and monitor all drug products and related supplies and equipment in the home.				
The patient or caregiver is trained to visually inspect all drug products, devices and other items the patient				

or caregiver is required to use immediately prior to administration to ensure that all items are acceptable for use.				
The patient or caregiver is trained to check labels immediately prior to administration to ensure the right drug, dose, patient and time of administration;.				
The patient or caregiver is trained to clean the in-home preparation area, scrub hands and use proper aseptic technique and manipulate all containers, equipment, apparatus, devices and supplies used during administration.				
The patient or caregiver is trained in all techniques and precautions associated with CSP administration, care for catheters, changing dressing and maintaining site patency as appropriate.				
The patient or caregiver is trained in monitoring for and detecting occurrences of complications and how to respond immediately to emergency or critical situations and when and how to obtain professional emergency services or professional advice.				
The patient or caregiver is trained to handle, contain and dispose of wastes associated with CSP use.				
The patient or caregiver is provided with written materials associated with CSP administration.				

PATIENT MONITORING AND ADVERSE EVENTS REPORTING

ITEM	REQUIREMENTS	YES	NO	COMMENT/SOP
Patients receiving CSPs are clinically monitored according to state requirements.				
Patients receiving CSPs have access to personnel that can respond to their questions.				
There is an adverse event reporting	*Receipt	____	____	

program.	*Acknowledgment *Dating *Recording *Filing *Evaluating	____ ____ ____ ____	____ ____ ____ ____	
Adverse events are reviewed.	*Promptly *Thoroughly	____	____	
Adverse events are addressed:	*Correction *Prevention	____	____	
Adverse events are reported to the USP or the FDA				

QUALITY ASSURANCE (QA) PROGRAM

ITEM	**REQUIREMENTS**	**YES**	**NO**	**COMMENT/SOP**
A formal quality assurance program is in place for monitoring, evaluating, correcting and improving the activities and processes associated with CSPs..	*formalized in writing. *includes environmental testing, validation, etc. *describes specific monitoring and evaluation activities. *specifies how results are to be reported and evaluated. *identifies appropriate follow-up mechanisms when action limits or thresholds are exceeded. *delineates individuals responsible for each aspect of the quality assurance program.	____ ____ ____ ____	____ ____ ____ ____	
The quality assurance program is reassessed on an annual basis.				