Broad Comparison of USP 795: Nonsterile Compounding

JANUARY 2014 VERSION VERSUS JUNE 2019 VERSION SEPTEMBER 25, 2019 BOARD OF PHARMACY MEETING

Summary

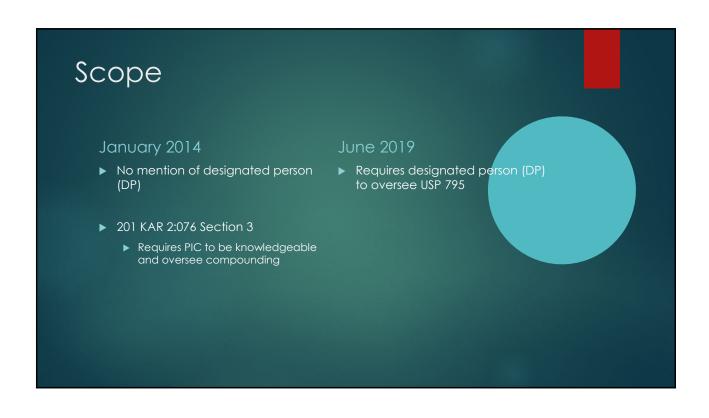
- ▶ Easier to read
- ▶ More clear about documentation requirements
- ▶ No categories of compounding (simple, moderate, complex)
- Clearer definition of compounding, does not include reconstitution, repackaging or tablet splitting
- USP 800 incorporated for nonsterile compounding with hazardous drugs
- ▶ No mention of pets, performance or food producing animals, entire chapter applies to animals and humans

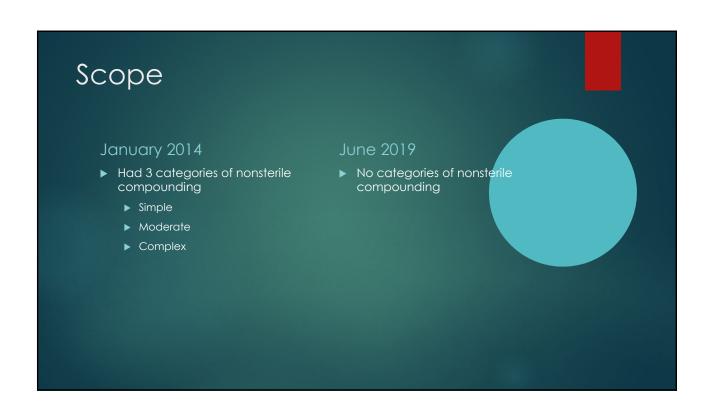
Summary

- ▶ Must have a designated person
- ▶ Training must be done initially and every 12 months
- Must wash hands and wear gloves to compound
- ▶ No carpet in designated compounding area
- ▶ Must keep sink clean
- No humidity monitoring required
- ▶ Descriptive cleaning schedule
- ▶ Evaluation to determine need for powder containment hood, etc.
- ▶ APIs must be from FDA registered facility

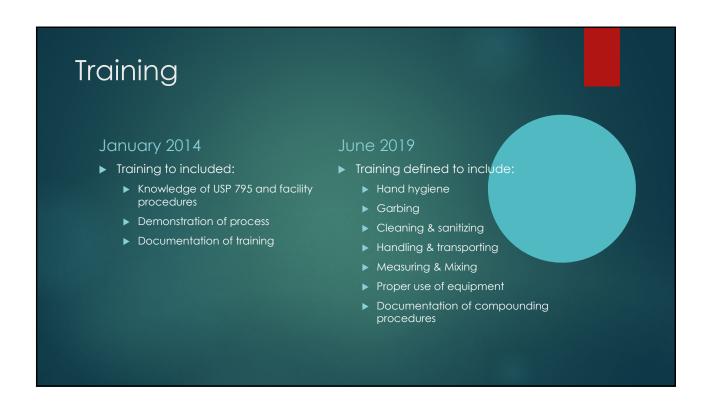
Summary

- ▶ Must have spill kit with policy and training
- ► Master Formulations very similar
- Compound Records very similar except no duplicate label required
- ▶ BUDs extended for some dosage forms but max for all dosage forms at 180 days
- ▶ SOPs more extensive
- Quality Assurance and Quality Control more robust including complaint and adverse event investigations
- ▶ Patient counseling not included





January 2014 Initially trained Recommended annually Ongoing to ensure accurate and adequate compounding June 2019 Initially trained Refresher training required every 12 months Ongoing by monitoring and observing to correct any issues at any time



Training

January 2014

- ► Training to include:
 - Reading and be familiar with USP 795 and other relevant publications
 - Read and interpret SDS
 - Read and be familiar with procedures

June 2019

- ▶ Training to include:
 - Read and understand USP 795 and other relevant literature
 - Understand and interpret SDS and COA, if needed
 - Read and understand pertinent procedures

Training

January 2014

- Compounder demonstrates procedures
- ► Compounder observes and guides employee throughout process
- Employee repeats procedure without assistance from, but under the direct supervision or, compounder
- Employee demonstrates a verbal and functional knowledge, then can compound without direct supervision

- Personnel guided throughout process
- Personnel demonstrates competency under direct supervision
- Personnel may compound without direct supervision after demonstrating competency

Training January 2014 ► Does not address if only one compounder Left only one compounder in facility, person must document: Left only one compounder in facility, person must document in facility, person must document in facility, person must document in facility, person m



Personnel Preparation

January 2014

► Compounding personnel maintain good hygiene

June 2019

- Compounding personnel MUST remove:
 - Outer garments
 - ► Hand & wrist jewelry and piercings if interfere with garbing
 - ► Ear buds & head phones
- DP may make allowances if state of control is maintained

Hand Hygiene

January 2014

- ▶ Shall have access to:
 - ▶ A sink
 - Soap or detergent
 - ▶ Single use towels or
 - ▶ Air dryer

- Before entering compounding area, personnel MUST:
 - Wash hands and forearms up to elbows for at least 30 seconds with soap and water
 - Dry with single use/disposable towels or wipers
 - Allow hands to dry before donning gloves

Hand Hygiene January 2014 Hand hygiene is not specifically addressed June 2019 During compounding, personnel: SHOULD wipe or change gloves between compounding with different components Must change gloves if ripped, torn, punctured, etc.



Buildings and Facilities: Compounding Space

January 2014

- ▶ Shall have adequate space
- Compounding environment is suitable
- Separate areas for sterile and nonsterile compounding
- Compounding done in clean and sanitized area dedicated to compounding

June 2019

- Space specifically designated for compounding
 - ➤ SOP to describe method of designation (i.e. visible perimeter)
 - Other activities cannot be occurring in this space at the same time as compounding
- No carpet

Buildings and Facilities: Storage Area

January 2014

 Appropriate temperature and humidity monitoring

- Must monitor temperatures
 - Manually daily
 - ► Continuously electronically
- Documentation must be retrievable
- Must calibrate temperature monitoring devices every 12 months
- Components must be stored in appropriate conditions
 - ▶ Temperature, humidity, lighting

Buildings and Facilities: Water Source

January 2014

 Must have sink with hot and cold water easily accessible to compounding area

June 2019

- Must have sink with hot and cold water easily accessible to compounding area
- Sink must be emptied of all items not related to compounding when washing equipment
- Must clean sink when visibly soiled before using to clean equipment for compounding

Cleaning and Sanitizing

January 2014

 Compounding is done in appropriately cleaned and sanitized area

- Work surfaces
 - ▶ At beginning and end of each shift
 - ▶ When spills, contamination occurs
 - Between compounding with different components
- ▶ Floors
 - ▶ Dail
 - ► After spills, contamination
- ▶ Walls
 - ▶ Every 3 months
 - ▶ After spills, contamination

Cleaning and Sanitizing

January 2014

 Compounding is done in appropriately cleaned and sanitized area

June 2019

- Ceilings
 - When visibly soiled and if known contamination happened
- Storage Shelving
 - ▶ Every 3 months
 - ▶ After spills, contamination
- If not compounding daily, must clean before starting to compound
- No specific agents discussed

Equipment and Components: Equipment

January 2014

Use of Containment Ventilated Enclosures (CVE), Biological Safety Cabinets (BSC), single use containment glove bags not specifically addressed

lune 2019

- Must evaluate to determine need for using:
 - CVE must be CETA certified every 12 months
 - ▶ BSC must be CETA certified every 12 months
 - Single use containment glove bag

Equipment and Components: Equipment Cleaning

January 2014

Equipment must be cleaned after use

June 2019

- CVE, BSC must be cleaned:
 - ▶ Beginning and end of shift
 - ► Spills, contamination
 - ► Horizontal work surface
 - Between compounding with different components
- ▶ Other Equipment must be cleaned:
 - Before use and according to manufacturer
 - If nothing from manufacturer, between compounding with different components

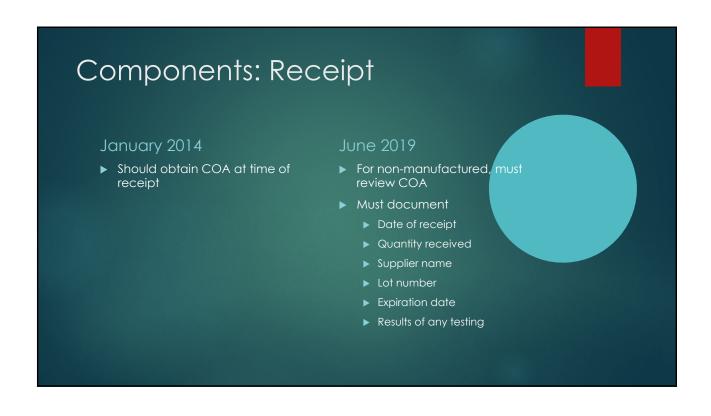
Components: Selection

January 2014

- Active Pharmaceutical Ingredients (APIs) and all components
 - ► Recommended USP/NF source
 - ► First attempt to obtain from an FDA registered facility

- Active Pharmaceutical Ingredients (APIs)
 - Must comply with USP/NF monograph, if there is one
 - Must have a Certificate of Analysis (COA)
 - Must be from FDA registered facility

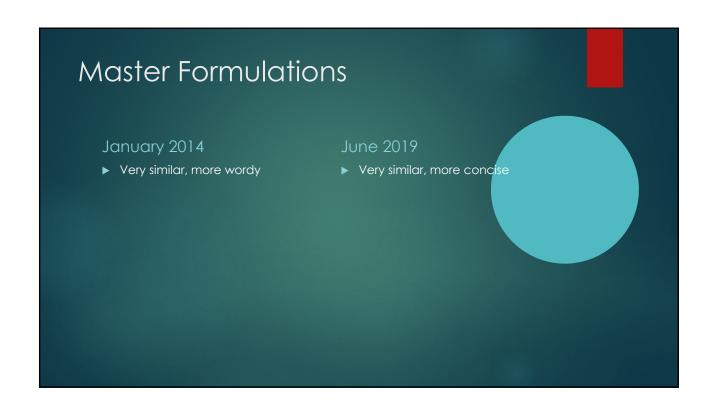
Components: Selection January 2014 Active Pharmaceutical Ingredients (APIs) and all components Recommended USP/NF source First attempt to obtain from an FDA registered facility COA consulted June 2019 All components other than APIs Should have a COA Should be from an FDA registered facility



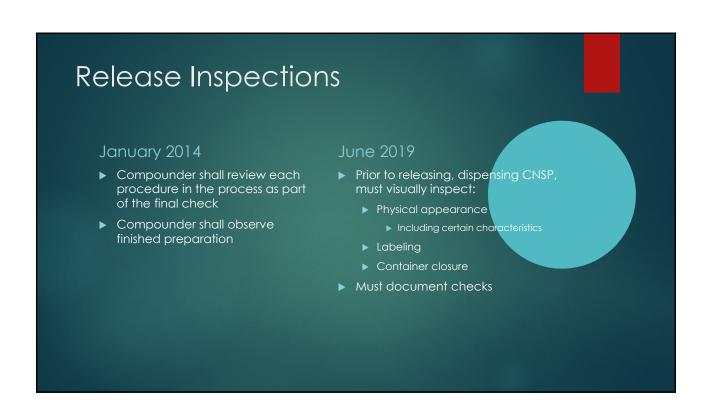
Components: Receipt January 2014 • Allows transfer of components to other containers June 2019 • Once component is removed from original container, SHOULD be discard • For example, excess from weighing



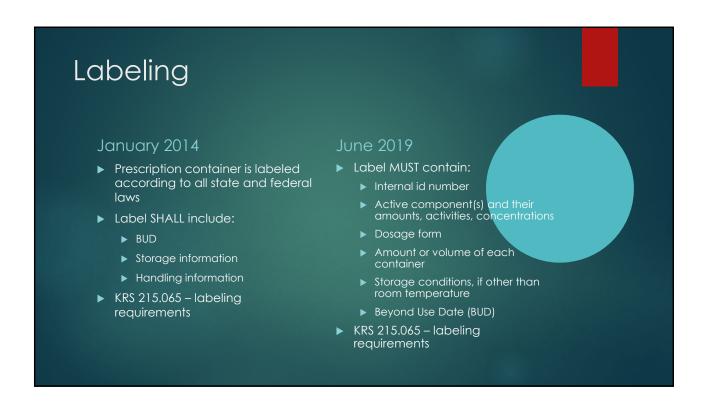
Components: Spill and Disposal January 2014 Spills not specifically addressed June 2019 Must maintain chemical hazard and disposal information (SDS) and update every 12 months Must have a spill kit accessible to compounding area Must train personnel in use of spill kit Refresher training every 12 months







January 2014 No definition of labeling and label June 2019 Labeling – all labels and other written, printed, graphic matter on immediate container or, on or in, any package wrapper in which CNSP is enclosed Label – the part of the labeling on the immediate container



Labeling

January 2014

► Labeling SHOULD indicate that this is a compounded preparation

June 2019

- ▶ Labeling SHOULD contain:
 - Route of administration
 - ▶ Indication prep is compounded
 - Any special handling instructions
 - Any warning statements
 - Name, address, contact info of compounding facility if CNSP leaves facility

Beyond Use Dates (BUDs): Water Activity (Aw) June 2019

- ▶ June 2019 version takes into account water activity (Aw) as described in USP 1112, Application of Water Activity Determination to Nonsterile Pharmaceutical Products
 - ► This is the Aw of manufactured products
- Aw aids in determining CNSP susceptibility to microbial contamination and degradation due to hydrolysis
- ► CNSPs with Aw > 0.6 SHOULD have antimicrobial agent or be refrigerated

Beyond Use Dates (BUDs)

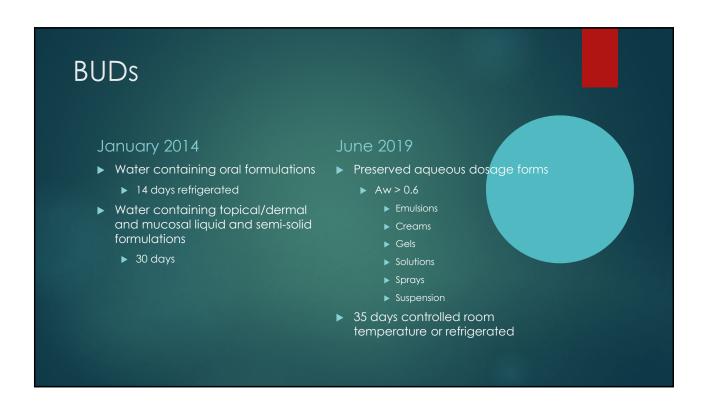
January 2014

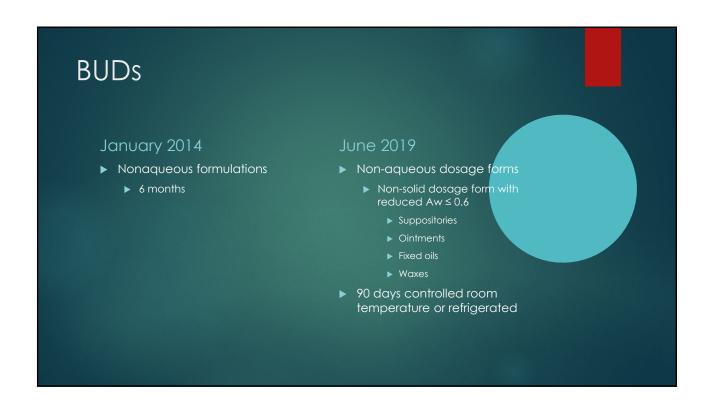
- Beyond Use Date (BUD) the date after which a compounded preparation should not be used
- Determined from the date the preparation is compounded

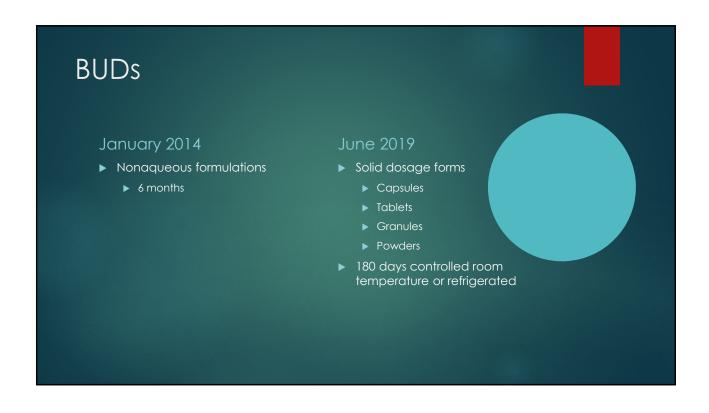
June 2019

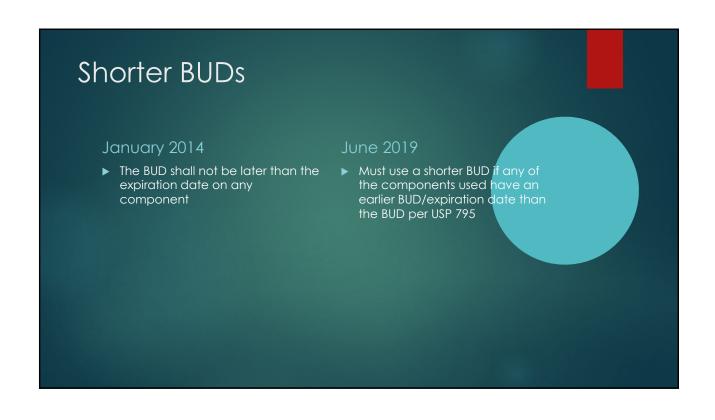
- Beyond Use Date (BUD) the number of days after which a CNSP is prepared and beyond which it cannot be used
- ► The day of compounding is Day 1

Beyond Use Dates (BUDs) January 2014 Mater containing oral formulations 14 days refrigerated Mater containing topical/dermal and mucosal liquid and semi-solid formulations 30 days June 2019 Non-preserved aqueous dosage forms Mw > 0.6 Emulsions Creams Gels Solutions Sprays Suspension 14 days refrigerated

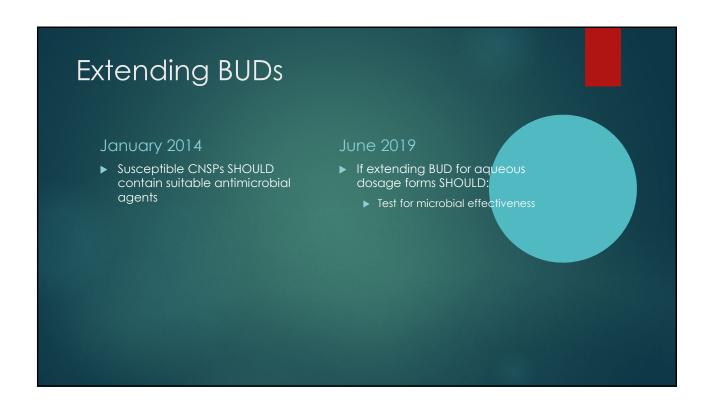








Extending BUDs January 2014 May use stability information to extend BUDs June 2019 If there is a USP/NF monograph May use BUD of monograph CNSPs with stability information Maximum of 180 days Stability study using stability indicating assays for: API CNSP Container closure May be published or unpublished



Standard Operating Procedures (SOPs)

January 2014

- ► SHOULD have written SOPs covering all significant procedures performed in compounding area
- Only minimal required SOPs

June 2019

- Must have SOPs on all aspects of compounding operation
- Personnel conducting or overseeing compounding must be trained in SOPs
- Personnel responsible for ensuring SOPs followed

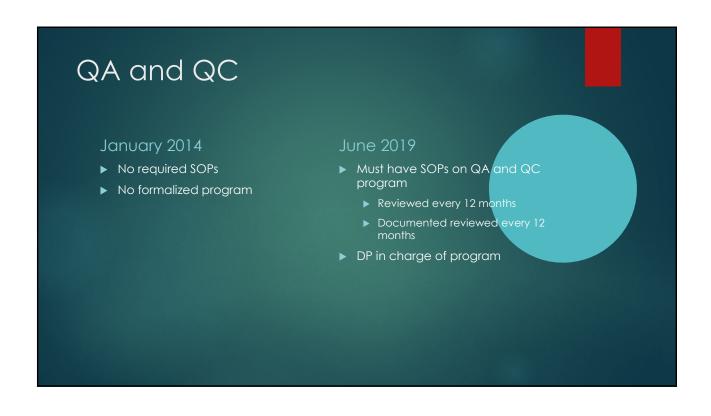
Quality Assurance and Quality Control

January 2014

- Quality Control
 - ▶ Checking documentation
 - ► Checking compounding process

- ► Quality Assurance (QA)
 - System of procedures, activities and oversight that ensures the compounding process consistently meets quality standards
- Quality Control (QC)
 - Sampling, testing and documentation of results that, taken together, ensure that specifications have been met before releasing the CNSP

QA and QC January 2014 ► No formalized program June 2019 ► Must have a formal QA and QC program that establishes system of: ► Adherence to procedures ► Prevention & detection of errors and other quality issues ► Evaluation of complaints and adverse events ► Appropriate investigations and corrective actions



Complaint Handling and Adverse Events

January 2014

- Required to investigate and document any reported problem
- Required to take corrective action

June 2019

- ▶ DP must review all complaints
- If quality issue, must investigate and have corrective action
- Must keep readily retrievable record of all complaints, include
 - ▶ Name of complaint (or some ID)
 - Date complaint received
 - ▶ Nature of complaint
 - Response to complaint
 - ► Findings of any investigation
 - ▶ Follow-up

Complaint Handling and Adverse Events

January 2014

- Required to investigate and document any reported problem
- Required to take corrective action

- ► Adverse Event (AE)
 - ▶ DP must review all AE to determine if quality issue
 - ► SHOULD report to Med Watch or Form FDA 1932a (animals)

Documentation

January 2014

 Not as clear as to required documentation

June 2019

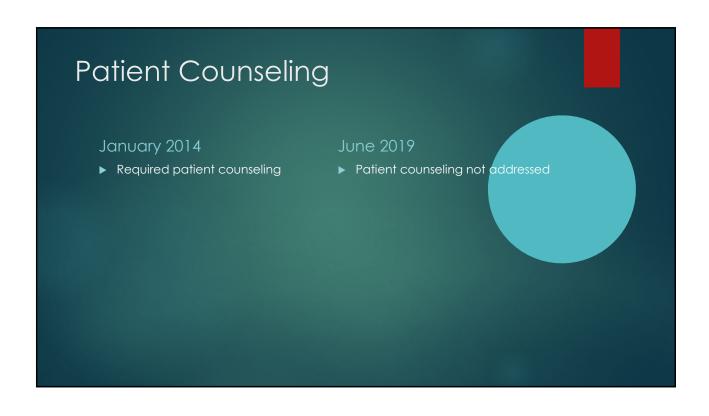
- Must have documentation of:
 - ▶ Training
 - ▶ Equipment records
 - ▶ COAs
 - Receipt of components
 - ▶ SOPs, MFs, CRs
 - Release inspection and testing
 - Complaints and AE
 - Results of investigations
 - Corrective actions

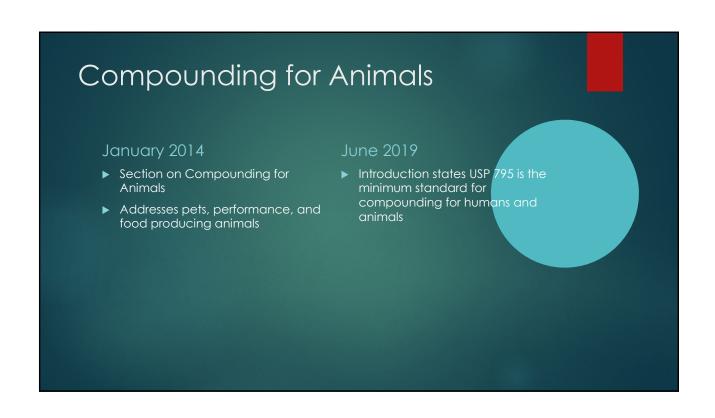
Documentation

January 2014

- ▶ No time frame for document retention
- ➤ 201 KAR 2:076 requires document retention for 5 years
 - ▶ Patient profile
 - ▶ Purchase records
 - Quality assurance records
 - Other records and reports as required by law

- Documentation relating to CNSP, must be readily retrievable for 3 years
 - ▶ MF, CR, release information
- 201 KAR 2:076 requires document retention for 5 years
 - Patient profile
 - Purchase records
 - Quality assurance records
 - Other records and reports as required by law





USP 795

- June 2019 version expected compliance Federally has been delayed to an unknown time
 - ▶ Previously was December 1, 2019
- 201 KAR 2:076 specifically references the January 1, 2014 version of USP 795
 - ▶ Waivers are allowed
 - ▶ No waivers requested as of this date