

Ensuring Quality Pharmacy Compounding: Implications for Pharmaceutics Education

Loyd V. Allen, Jr., Ph.D.
Professor & Chair Emeritus
University of Oklahoma HSC College of Pharmacy
Editor-in-Chief
International Journal of Pharmaceutical Compounding

Contact Information

- www.ijpc.com
- Lallen@ijpc.com
- 122 N. Bryant
- Edmond, OK 73034
- USA
- 405-330-0094

Objectives

- Role of the USP in ensuring best practices in pharmacy compounding
- Current USP standards regarding compounding personnel and training
- Future initiatives of USP with regard to ensuring best practices in pharmacy compounding (emphasis on personnel and training)
- Expectations for pharmacy education with regard to ensuring best practices in pharmacy compounding

Outline

- I. Introduction
- II. US Pharmacopeia
- III. USP Chapters <795>, <797> and <1163>
- IV. Pharmacy Compounding Regulations
- V. Future initiatives
- VI. Expectations for pharmacy education

Role of the Compounding Pharmacist

- "Individualizing Drug Therapy"

I. Introduction

- History of Pharmaceutical Compounding
- Reasons for Growth
- Special Patient Populations

History of Pharmacy Compounding in the U.S.

- In the past, *Compounding Was Pharmacy*
- 1900s gave way to commercially prepared pharmaceuticals
- Many strengths/dosage forms available
- Economics changed all that
- Limited strengths/dosage forms
- “One Size Fits All” approach

Reasons for the Growth of Pharmacy Compounding

- Limited dosage forms
- Limited strengths
- Home health care
- Hospice
- Nonavailable drug products/combinations
 - Discontinued Drugs
 - Drug Shortages
- Orphan drugs
- Veterinary compounding
- New therapeutic approaches
- Special Patient Populations

SPECIAL PATIENT POPULATIONS

- Pediatrics
- Geriatrics
- Bioidentical Hormone Replacement Therapy
- Pain Management
- Dental Patients
- Environmentally & Cosmetic Sensitive
- Sports Injuries
- Veterinary Compounding
 - Small, Large, Herd, Exotic, Companion

II. U.S. PHARMACOPEIA

- Setting Official Standards for Drugs in the U.S. since 1906

Pharmacopoeias of the U.S.

- Jan 1820 First U.S. Pharmacopeial Convention
- Dec 1820 First U.S. Pharmacopeia was published
 - 272 pages containing 217 drugs/preparations

Pharmacists Pharmacopeia

- 1820 USP developed for pharmacy
- 1900's USP became more oriented towards manufacturing
- 2000's USP must meet the needs of both pharmacists and manufacturers
- January 2004: USP: Pharmacists Edition

U.S. PHARMACOPEIA ACTIVITIES (2000-2010)

- Almost 200 official monographs related to compounding
- More monographs being prepared
- 4 official chapters
 - USP <795> Pharmaceutical Compounding-Nonsterile
 - USP <797> Pharmaceutical Compounding-Sterile
 - USP <1163> Quality Assurance in Pharmaceutical Compounding
 - USP <1160> Pharmaceutical Calculations
- Stability Studies

Uniform Formulations

- Official monographs
- Documented beyond-use dates
- Patient receives same preparation all over the U.S.

III. USP Chapters <795>, <797>, and <1163>

- USP <795>
 - Pharmaceutical Compounding-Nonsterile Preparations
- USP <797>
 - Pharmaceutical Compounding-Sterile Preparations
- USP <1163>
 - Quality Assurance in Compounding

Three Categories-Nonsterile

- I. Simple
- II. Moderate
- III. Complex

Three Categories-Sterile

- I. Low-Risk
- II. Moderate-Risk
- III. High-Risk

USP Chapter <795>, Revised

- Pharmaceutical Compounding: Nonsterile Preparations

USP <795> Outline
Revised 2009

- Introduction
- Definitions
- Categories of Compounding
- Responsibilities of the Compounder
- Compounding Process
- Compounding Facilities
- Compounding Equipment
- Component Selection, Handling, and Storage

USP <795> Outline (Cont'd)

- Stability Criteria and Beyond-Use Dating
- Packaging and Drug Preparation Containers
- Compounding Documentation
- Quality Control
- Patient Counseling
- Training
- Compounding for Animal Patients

USP Chapter <797>

- Pharmaceutical Compounding- Sterile Preparations

**USP <797> Content
Revised June 2008**

- 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

USP <797> Content

- 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)

USP <797> Content

- Elements of Quality Control
- Verification of Automated Compounding Devices 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

USP <797> Content

- Patient or Caregiver Training
- Patient Monitoring and Adverse Events Reporting
- Quality Assurance Program
- Appendices

IV. Pharmacy Compounding Regulations

- Pharmacy State Boards
- Food & Drug Administration
- Drug Enforcement Agency
- OSHA-EPA

State Boards of Pharmacy

- Regulating the practice of pharmacy
- Some states are very active
- Other states are not very active
- National Association of Boards of Pharmacy

FDA ACTIVITIES

- → 1938 Compounding regulated by states
- 1938 FDA Created for manufacturers
- 1938 → FDA regulated manufacturers
- 1938 → State Boards regulated compounding
- Mid 1990s FDA began investigating a number of pharmacies that were compounding large quantities of selected drug products.
- Manufacturing under the guise of compounding
- FDA is trying to bring compounding under their jurisdiction by their definition of "New Drugs"

Food and Drug Administration Activities

- FDA considered compounded preparations as "New Drugs" and subject to the New Drug Provisions
 - IND
 - NDA
 - Safety
 - Efficacy
- Enforcement Activities

New Drug Issue

- Compounding DOES NOT create "New Drugs" as defined by the FDA.
- Square pegs don't fit into round holes!
- Let's look at the following....

“New Drug”

- 1) Any drug (except a new animal drug or an animal feed bearing or containing a new animal drug) the composition of which is such that such drug **is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the condition prescribed, recommended, or suggested in the labeling thereof.**

“Labeling”

- ...includes all written, printed, or graphic matter accompanying an article at any time while such article is in interstate commerce or held for sale after shipment or delivery in interstate commerce.

“Labeling”

- ...means any display or written, printed, or graphic matter on the immediate container of any article, or any such matter affixed to any consumer commodity or affixed to or appearing upon a package containing any consumer commodity.
- CFR 21 Ch 1 (4-1-08 Edition); 1.3 Definitions

Labeling

- Compounding is a part of the professional practice of pharmacy.
- The practice of pharmacy is governed by the state boards of pharmacy.
- The state boards of pharmacy have authority over labels for dispensing prescriptions, including compounded prescriptions, in their states.

V. Future Initiatives

- Expand Accreditation (PCAB)
- Monograph Development (USP)
- Introduce Certification
- Expanded Quality Assurance Activities
- Expand Educational Offerings

Quality Issues

- Standards for Quality
- Standard Operating Procedures
- Testing (Analytical, Microbiological)
- Beyond Use Dating

Standards for Quality

- cGMPs
- cGCPs
- CPGs
- USP
- FDA

STANDARD OPERATING PROCEDURES

- Written procedures should exist for all compounding, quality control, packaging and labeling processes.
- Master Formula Records should be written to provide adequate instruction and documentation of the compounding operation.

Testing

- Physical observation
- Potency, Analytical
- Sterility
- Endotoxin
- Other

ANALYTICAL METHODS**

Weight*	• Melting Point*
Volume*	• UV/Vis/IR Spectroscopy
Macro/Micro*	• HPLC
pH*	• GC
Osmolality*	• Sterility*
Refractive Index*	• Endotoxin*
Specific Gravity*	

VI. Compounded Dosage Forms

Traditional Compounded Dosage Forms

Oral Solids (Capsules, Tablets)
 Oral Liquids (Solutions, Susp, Emulsions)
 Topicals (Creams, Ointments, Gels)
 Suppositories, Inserts
 Injectables
 Troches/Lozenges
 Nuclear Pharmaceuticals
 Intravenous Admixtures
 Many, many others....

Newer Dosage Forms

- Rapid-Dissolving Tablets
- Gummy Gels
- Oral Pastes (VET)
- Lollipops
- MiniLollipops
- Popsicles
- Minitroches
- Sublingual drops
- Transdermal PLO Gels
- Rapid-Penetrating Topical Solutions
- Intrathecal Pain Management
- Sponge Disks
- Implantable Beads
- Iontophoresis/Phonophoresis

Newest Dosage Forms

- Liposomes for Nail Delivery
- Films
 - Skin
 - Topical
- Pluronic Gels
 - Chest cavity
 - Esophageal
- Nasal Spray-Gels
- Gel-Creams

VII Expectations for Pharmacy Education

Educational Needs

- Dosage Forms/Formulation
- Physical Pharmacy
- Drug Stability
- Analytical Methods
- Microbiological Methods
- Calculations
- Experiential Rotations
- Compounding Laboratories

Extent of Pharmacy Compounding

- NCPA 76% of Membership
- Hospitals Almost 100% compound
- Chains About 10% of stores compound
- Total % Rxs Estimated about 10% of all
- % RPh Estimated about 25% do some compounding in their practice

Summary

- Patient care often involves specialized medications
- Specialized medications require compounding
- Compounding pharmacists are some of the most involved clinical pharmacists in practice today (worldwide)
- Pharmacists should be the best trained to do this...but are we?



Thank
You
