Nonsterile Compounding and Repackaging
Learning Outcomes

• Define compounding.
• Describe steps involved in compounding process
• Describe equipment commonly used for compounding
• Identify types of preparations commonly compounded
• Explain reasons for repackaging medications
• Explain importance of record keeping for compounding & repackaging
Key Terms

• Active ingredient
• Batch record (or batch log)
• Batch repackaging
• Beyond-use
• Blister packages
• Compounding
• Compounding environment
• Compounding record
Key Terms

• Extemporaneous repackaging
• Formulation record
• Geometric dilution
• Graduates
• Inactive ingredient
• Levigation.
• Manufacturing
• Nonsterile compounding
Key Terms

- Peristaltic pumps
- Prescription compounding
- Stability
- Sterile compounding
- Trituration
- Unit-dose package
- Unit-of-use packaging
- Volumetric pumps
Prescription Compounding

• Meets unique needs of patient
  – Medication strength/dose not commercially available
• Compounding associated with specialty practice areas
  – veterinary medicine
  – dermatology
  – hormone replacement therapy
  – pain management
  – hospice
  – home care
Compound or Manufacture?

• Compounding: prepare small quantity of drug
  – based on practitioner’s prescription
  – for specific patient

• Manufacturing: prepare bulk quantities
  – without prescription or medication order
Types of Compounding

• Sterile compounding
  – strict aseptic technique
    • injections
    • ophthalmic solutions
    • irrigation solutions

• Nonsterile compounding
  – oral & topical medications
USP-NF Chapter 795

• United States Pharmacopeia-The National Formulary
• Guidelines & an enforceable set of standards
• Describes procedures/requirements for compounding
• Intent of USP is to protect both patients & pharmacists
Compounding Environment

• Adequate space
  – orderly placement & storage of equipment
• Controlled temperature/lighting
• Clean
• Sink with hot & cold running water
  – essential for hand washing & equipment cleaning
Compounding Equipment

• Equipment must be:
  – appropriate in design & size for intended purpose
  – must always be cleaned immediately after use
  – must be properly maintained & calibrated

• Must have separate & distinct areas for compounding sterile & nonsterile preparations
Stability of Preparations

• Primary packaging important
  – Examples
    • light sensitive drugs or drugs that bind to container

• Beyond-use date (BUD) on label of all medications

• Determining beyond-use dates based on
  – aqueous (water-based) or nonaqueous
  – expiration dates of ingredients used
  – storage temperature
  – references with stability data
Ingredient Selection

• USP or National Formulary (NF) chemicals preferred

• Pharmacist responsible for selection
  – chemical must meet meets purity & safety standards
  – should not use drug withdrawn from market by FDA
Compounded Preparations

• Guideline:
  – should contain between 90% & 110% of labeled active ingredient

• Guidelines specifically address these dosage forms:
  – capsules, powders, lozenges, tablets, emulsions, solutions, suspensions, suppositories, creams, topical gels, ointments, pastes
Compounding Process

• Goal of compounding process
  – “minimize error and maximize prescriber’s intent”
• Pharmacist evaluates appropriateness of order
• Only 1 preparation should be compounded at a time
  – avoid errors
  – avoid cross-contamination
Steps in Compounding

1. Calculate amount of ingredients for preparation
2. Identify equipment needed
3. Wash hands & wear proper attire
4. Clean compounding area & needed equipment
5. Collect all materials & ingredients
6. Compound prep following formulation record
7. Document name on compounding record/log
8. Label final preparation appropriately
9. Properly clean & store all equipment
Final Check

• Pharmacist is responsible for checking final prep
  – weight variation
  – proper mixing
  – odor
  – color
  – consistency
  – pH if appropriate

• Pharmacist signs & dates prescription
  – documenting/ensuring quality
Compounding Records

• USP Chapter 795 requires pharmacies to maintain
  – formulation record (master formula)
  – compounding record for each compounded preparation

• Formulation record-an individual record (like a recipe)
  – filed alphabetically
  – listing of the
    • ingredients
    • compounding equipment
Compounding Record

• Log of an actual compounded preparation
  – based on an individual prescription
  – batch may be prepared in anticipation of orders
  – includes manufacturer & lot numbers of chemicals
  – date of preparation
  – internal identification number
  – beyond-use date
  – names of individuals who prepared & verified
Records

• Compounding record for batch (batch record)
  – filed by lot number

• Compounding record for an individual prescription
  – chronological list of preparations made

• Formulation & compounding records
  – maintained as paper copies or electronically
Quality Control

• Final check on preparation
• Pharmacist must evaluate
  – finished preparation
  – compounding procedure
• Discrepancies should be noted & evaluated
• Patient Counseling
  – important with all medications
  – correct use, storage, beyond-use date, evidence of instability in compounded medication
Inactive Ingredients

needed to prepare formulation
not intended to cause pharmacologic response

- Diluents or fillers
- Binders
- Colorants
- Lubricants
- Flavorants
- Sweeteners
- Suspending agents
- Vehicles
- Emulsifying agents or surfactants
- Coating agents
- Preservatives
- Perfumes
- Acidifying agents
- Alkalizing agents
- Wetting agents
Compounding Equipment

- Electronic or class A torsion balance
- Powder papers or weigh boats
- Brass weight sets with class A torsion balances
- Graduates
- Mortars & pestles
- Ointment slab (pill tile) & spatulas
  - trituration
  - levigation
  - geometric dilution
• Electronic mortar & pestle
• Hot plates
• Refrigerator with freezer
• Stirring rods
• Stir plates with magnetic stir bars
• Strainers
• Molds for suppository, troche
• Blenders
• Capsule filling equipment
• Mixers
Compounded Preparations

• Commonly compounded preparations
  – ointments
  – creams
  – solutions
  – suspensions
  – suppositories
  – lozenges/troches
  – capsules
Ointments & Creams

• Active ingredient in commercially prepared base
  – petrolatum-based products
  – emollient creams
  – vanishing creams

• Choice of base depends on condition being treated

• Examples of medications in creams & ointments
  – corticosteroids
Solutions & Suspensions

• One or more drug ingredients
• Mixed in homogenous or single phase
• No visible undissolved particles

• Solutions
  – solid drug that dissolves in liquid

• Suspensions
  – two phases:
    • insoluble solid particles (active ingredient)
    • liquid
Suspensions

• Insoluble particles settle to bottom
• Suspending agents
  – added to allow insoluble particles to re-suspend
• Suspensions
  – levigate insoluble powder to smooth paste
  – appropriate wetting agent
• Flavoring & sweetening agents
Suppositories

• Suppositories may contain
  – analgesics
  – hormones
  – anti-nausea agents
  – laxatives
  – vaginal anti-infectives

• Once inserted, suppository melts or dissolves
  – suppositories must remain solid at room temperature & melt at body temperature
Lozenges/Troches

• Also known as pastilles
• Small, medicated squares can be soft or hard
• Intended to dissolve slowly between cheek & gum
• Medication(s) absorbed through oral mucosa
• Useful for pediatric & geriatric patients
Capsules

- Capsule-filling machine
- Powders mixed in mortar, zippered plastic bag, or specialized blender
- Lids or capsule tops are removed
- Capsules drop even with plate
- Powder is distributed into capsules
- Lids or tops are replaced
- Numerous capsule sizes & colors available
Other Compounds

• Powders are very fine, dry active & inactive ingredients
• Granules are powders moistened & passed through screen
• Emulsions are mixture of 2 immiscible liquids
• Gels are semi-solid systems consisting of suspensions
• Tablets are made by compression
Repackaging

- Pharmacies repackage medications from bulk containers into patient-specific containers
  - unit-of-use
  - single-unit
  - unit-dose
Extemporaneous Versus Batch

- Extemporaneous repackaging
  - quantities to be used within short period of time
  - done on an “as needed” basis
  - based on anticipated immediate need
  - also known as “just-in-time” packaging

- Batch repackaging
  - periodic repackaging of large quantities of medications
  - unit-dose or single-unit packages
  - extended stability
Packaging

• Prepare in advance = pre-packaging
• Saves
  – time
  – materials
  – money
Repackaging Materials

• Must protect drug from
  – harmful external elements
    • light
    • heat
    • moisture
    • air
    • microbial contaminants

• USP defines containers & closures
  – based on degree to which contents protected
Repackaging Equipment

• Oral Solid Systems
  – blister packages
  – pouch packages
• Manual Systems
• Automated Systems
• Oral Liquid Systems
• Semi-automated Systems
• Volumetric pumps
• Peristaltic pumps
Beyond-Use Dating & Labeling

• Labeling-responsibility of dispenser
  – storage conditions
  – beyond-use date
  – USP offers standards for determining an appropriate expiration date in absence of published stability data
USP Guidance:

• “For nonsterile solid and liquid dosage forms that are packaged in single-unit and unit-dose containers, the beyond use date shall be one year from the date packaged or the expiration date on the manufacturer’s container, whichever is earlier.”
ASHP Guidance

• Current federal labeling requirements
  – Described in ASHP Technical Assistance Bulletin on Single Unit and Unit Dose Packages of Drugs

• Generic name & brand name

• Dosage form, strength, amount delivered in package, notes

• Expiration date

• Control number or lot number

• Bar code
Record Keeping

• Standards of practice & government regulations
  – maintaining accurate, complete records
  – focal point for quality assurance program
  – maximize technician’s role in repackaging

• repackaging record systems
  – computerized
  – individual state laws & regulations will dictate:
    • what needs to be kept, whether records may be maintained as paper or electronic records, how long records must be maintained
Quality Control

• Ensures high-quality repackaged medications
• Quality control
  – written procedures
  – formal training for operators of equipment
  – maintenance of equipment
  – checkpoints during process
  – end product testing
  – strict adherence to good manufacturing practices (GMP)
GMP

• Refers to guidelines of production
• Manufacturing/repackaging processes clearly defined
• Instructions/procedures are written in clear language
• Documentation of personnel training
• Records: show procedures were followed
• Storage & distribution of final product minimizes negative effects to quality
• System for recalling any batch of product
GMP

• Written Procedures
• Personnel Training and Competency
• Maintenance of Equipment
• End-Product Testing
Checkpoints May Include:

1. Double-checking drug & dosage
2. Double-checking fill volumes
3. Double-checking calculations
4. Double-checking information on label