Compounded Medications

FDA GFI#256 & Office Stock

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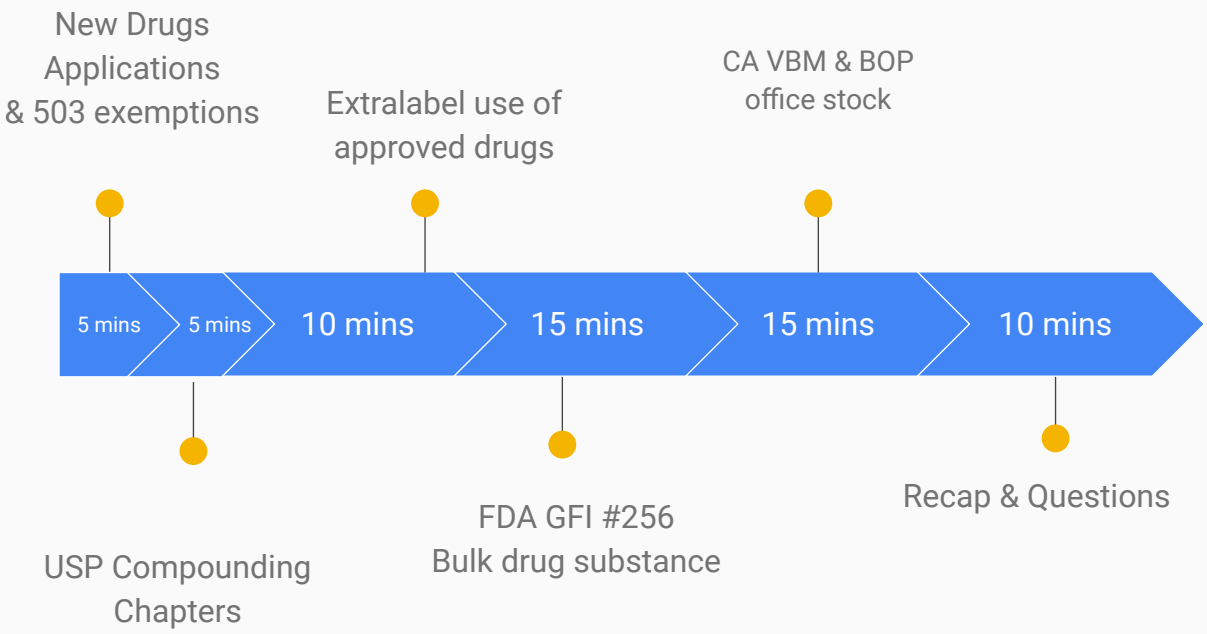
Outcome

Develop a working understanding of the compounding regulatory environment so you can

1) Acquire the products needed for use in your practice
2) Ensure patient access to compounded medications
3) Be aware of compounded option to help solve problems



New Drug Applications

NDA Section Topics

- FDCA
- FDAMA
- DQSA (Title I and II)

NDAs

FDCA

1938 Food, Drug, and Cosmetic Act

- Sulfanilamide w/ diethylene glycol 100 died. FDR signed
- FDCA enforced by FDA within US Dept Health and Human Services
- Safety data, facility inspections, recalls, advertizing, labeling, new drug approvals
- 1951 Durham-Humpthy: Rx & OTC
- 1962 Kefauver-Harris: Thalidomide Safety & Efficacy
- 1967 Medical Devices (Class I. II. III)
- 1980 Infant Formula Act
- 1983 Orphan Drug Act

Food Drug Admin Modernization Act 1997

Federal Authority to Regulate the Compounding of Human drugs, Congress report April 12, 2013

1962 Kefauver-Harris Drug Amendment

Thalidomide crisis

Pharmacies exempt from FDA registration if compound in usual course of business

FDAMA 503A exemption for pharmacies

- Compounds aren't new drugs (301)
- Don't need to be made to GMP (501)
- no directions for use (502)

Key conditions for exemption

- Valid patient specific prescription
- Approved ingredient (not withdrawn)

Maintain access while preventing manufacturing under the guise of compounding.

DQSA

2013 Drug Quality & Safety Act

- FDA: "We regulate compounding!"
- Title I Compounding Quality Act
- Title II Track and Trace

FDA Human Drug Compounding Progress Report (3 yeasr after Enactment DQSA)

503B Exemption

- Compounders register with FDA
- No RPH required
- Follow cGMP
- Label for office use only

Drug disposition: where did it come from? where did it go?

United States Pharmacopeia (USP)

USP Section Topics

- AVMA News Jan 2024
- USP Chapters
- <797> Sterile
- <795> Non-Sterile
- <800> Hazardous

AVMA News


AVMA | News

USP revised compounding standards go into effect

By Coco Lederhouse

January 04, 2024

- Compounding: FAQ for veterinarians
- Compounding
- AVMA Compounding Policy

Compound, when needed, based on the Veterinarian relationship with the client

USP Chapters

USP Overview

- Required Chapters: readable, with clear acceptance criteria
- Informative Chapters:, guidance, forward looking, no acceptance criteria
- Validation vs Compliance mentality

Chapter Numbers

- Less than <1000> required, readable, with clear acceptance criteria
- <1xxx> informational, guidance, forward looking, no acceptance criteria
- Not intended to be required by regulatory agencies

United States Pharmacopeia

<797> Sterile Compounding

USP <797> Sterile Compounding

- Policies and Training
- Facility design
- Equipment validation
- Ingredient quality
- Cleaning methods and frequencies
- Microbial monitoring
- Beyond Use Dating

United States Pharmacopeia

<795> Non-Sterile Compounding

USP <795>

- Same structure as <797>
- Dating based emphasis on water content
- Focus on preventing cross-contamination

United States Pharmacopeia

<800> Hazardous Compounding

USP <800> Hazardous Compounding

- Protects worker from exposure
- Handling, packaging, and transport
- Cleaning and decontamination
- Vague concept of “deactivation”

Can USP be enforced on veterinarians?

Maybe?

Vet Extralabel Use

Extralabel Use Section Topics

- AMDUCA ‘94 Scope
- Definitions
- Conditions
- Requirements

Extra Label Use

Scope and Purpose

Animal Medical Drug Use Clarification Act

- FDA AMDUCA Info page
- AVMA FAQ about EDLU
- CFR Title 21/Ch 1/SubCh E/ Part 530

Scope and purpose

- Applies to any approved drug (vet or human)
- On lawful order of vet
- For extralabel use in animals
- When health is threatened or suffering/death from failure to treat

Definitions

Extra Label Drug Use (ELDU)

- FDA AMDUCA Info page
- AVMA FAQ about EDLU
- CFR Title 21/Ch 1/SubCh E/ Part 530

Definitions

- Extralabel: actual use not in accordance with approved labeling
- Use in species not listed in labeling
- Doses, freq, or routes not listed
- Valid patient relationship

Conditions

- FDA AMDUCA Info page
- AVMA FAQ about EDLU
- CFR Title 21/Ch 1/SubCh E/ Part 530

Permitted if non-food producing and…

- No approved vet or human drug appropriate
- Done by pharmacist or vet
- Procedures ensure effective product
- State laws are followed

Extra Label Use

Requirements

- FDA AMDUCA Info page
- AVMA FAQ about EDLU
- CFR Title 21/Ch 1/SubCh E/ Part 530

Key Points

- Doesn't permit advertising
- Keep records (ingred, Dz, doses)
- Dispense label (vet, drug, directions)
- Use FDA drugs (vet or human)
- Food producing animals… careful

FDA 2022
Guidance for Industry #256

GFI #256 Section Topics

- FDA Guidance Intent
- Bulk Drug Substances
- Clinical Difference
- Office Stock BDS Lists

GFI #256

FDA Guidance Intent

FDA Guidance #256
"Compounding Animan Drugs from Bulk Drug Substances"

- By or under supervision of a Vet or state licensed pharmacy
- Does not apply to extralabel drug use
- Applied to Bulk Drug Substances

"Provide current thinking"

- Not rules or rights or binding on FDA
- Won't question document determinations
- Balance risks against need to treat
- Significant concerns : food producing, copies, office stock

GFI #256

Bulk Drug Substances

Key Points

- Compounds of BDS not approved
- Not intend take enforcement action
  - Meets state laws
  - USP-NF quality
  - Prescription order
  - Not a copy of marketed drug
  - Prescription labelled

Key Points

- Keep records
  (ingred, disease, doses)
- Dispense label (vet, drug, directions)
- Use FDA approved drugs
- Food producing animals… read the rules

GFI #256

Clinical Difference

"Copy" is same ingredient by same route

- Excludes ingredients for specie
- Strength or Concentration change
- Flavoring for compliance
- Protect those administering drug
- Not available to purchase

DOES NOT INCLUDE

- Pricing Difference
- Different salts are not different drugs
  Erythromycin Stearate = Erythro Ethylsucc
- ½ strength preferred…
  unless clinical reason

GFI #256

Office Stock from BDS

Does not intent to take enforcement for approval, directions, cGMP violation if :

- By vet or in licensed pharmacy
- Listed Not Listed Under Review
- Meets state, USP, and FD&C
- For same office use (no wholesaling)
- Report adverse events
- Properly labelled

Labeling Requirements

- Pharmacy/Vet compounder address
- Ordering office address
- Drug name and strength
- Specie(s) and indications for use
- Beyond Use Date
- “Report ADEs to FDA Form 1392a”
- “Compounded. Not FDA Approved.”
- “Not for use in food-producing animals”
- “Caution: Fed Law…use by..vet order"

California Boards

CA Boards Section Topics

- VBM Article 11
- BOP Links
- 503B dispensing
- Office stock

CA VMB Article 11

CA Vet Medicine Practice Act 2023
CCR Title 16, Div 20, Article 11 pg 123

- 2090 Definitions
- 2091 Vet Drug Compounding
- 2092 Policies & Procedures
- 2093 Expiration Dates
- 2094 Labeling
- 2095 Quality Assurance

2090 Definition Highlights

- Following mft direction not compounding
- Crush, split, open, flavor not compounding
- Office stock dispensed only to client or other vet on the premises

CA VMB Article 11

2091 Vet Drug Compounding Highlights

- Rely on standard in the profession
- Sterile only if capable, needed, no options
- Sterile ingredients from mft or APIs from FDA registered facilities (records 3-yrs)

2092 Policies & Procedures Highlights

- Policies for BUDs and labeling
- RVT training & QA program
- Formula (ingr, equip, steps, storage)
- Record in chart of compounder, supervisor, label info,

CA Boards

CA VMB Article 11

2093 Expiration Date Highlights

- Non-sterile NTE 180 days
- NTE ingredient expirations
- Sterile NTE 30 days

2094 Labeling Highlights

- 2032.2 (b) standard labeling requirements
- Date made and Expiration date
- Lot number assigned by compounder
- Initials of compounder

CA VMB Article 11

2095 Quality Assurance Highlights

- Document and assess errors
- Document and assess adverse reactions
- Client response and mitigation steps
- Board may review records

VMB Chapter 11 Summary

- Write formal policies
- Keep good documentation
- Label the product sufficiently
- Document adverse events

CA Board of Pharmacy

www.pharmacy.ca.gov

- 2024 Lawbook PDF
- License Lookup
- The Script Archive
- Ask an Inspector
- Compounding Self Assessment
- FDA Compounding 483s

503B Dispensing

Dispensing 503B Products FAQ

- Previously only sale office use
- Pattern of office buy & dispense
- 2022 Allows filling prescriptions by 503B
- Pharmacy may purchase and dispense

Office Stock

- 4052(a)(1) Reasonable quantity of compounded drug for office use
- 4119.5(b) Repackage & furnish to office
- 1735.2(a) Patient prescription required
- 1735.2(b) May compound in advance
- 1735(2)(c) Reasonable quantity for office use

"Reasonable quantity" furnished for office

- Purchase documentation lists number patients to be seen at office
- Signed for by office
- QS for in office use or 5-day dispensing
- RPH credible basis for quantity provided

Recap

Timeline

- 1938 FDCA
  creates requirement for NDA
- 1962 Kegauver
  Exempts Pharmacies NDA
- 1994 AMDUCA
  Vet Extralabel use
- 1997 FDAMA
  Human 503A Exemption
- 2013 DSQA
  503B and 503A refreshed
- 2022 CA
  Allows 503B dispensing
- 2022 FDA GFI #256
  Vet BDS & FOU Listed/Not Listed

FDA & BOP Intent

FDA

1. If compounding, use approved drugs whenever possible
2. Document what you do and if not using approved drugs, why not.
3. Only use drugs FDA you may

CA Boards

1. Write policies and document training.
2. Establish valid BUDs and labeling
3. Document activities and problems.
4. Know what you are doing. Do it well.

Drug disposition: where did it come from? where did it go?

Summary

Questions ?

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