COMPOUNDING PHARMACIES & ASCS

Regulatory Update

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DISCUSSION POINTS

- Compounding industry trends
- Backordered medication trends
- Federal regulatory statutes
- State regulatory statutes
- Working with a compounding pharmacy

COMPOUNDING INDUSTRY TRENDS

- The compounding industry continues to grow as physicians and compounding pharmacies identify unique compounds
- Today, 1 in 10 prescriptions has the potential to be compounded
- The typical compounding pharmacy is relatively small and services a small geographic area – there are a growing number of larger sterile compounders
- There is intensifying federal and state pressure on the industry post the Frank's Pharmacy and NECC issues
- Smaller compounding pharmacies do not always have sufficient regulatory counsel to stay up on these regulations

BACKORDERED MEDICATION TRENDS

- The "patent cliff" means that more and more medications are coming off of patent
- Pharmaceutical companies are spending less time on promoting these drugs and significantly reducing their production
- Generic houses are having difficulty ramping up with some of these drugs
- Many generic houses are not interested in making these drugs because there is not sufficient margin to manufacture these durgs

TENETS OF COMPOUNDING

- We cannot copy a commercial medication - this is an FDA violation
- There must be medical justification for the compound
  - Example: Removal of a preservative that causes an allergy
  - We can't product a product for price savings that isn't on backorder
- We can adjust the compound by removing an ingredient, putting together a unique formulation or,
- Providing backordered medications only during the period of time that the compounds are on backorder
  - Requires checking with the FDA
  - Requires checking with the U.S. distributors

LEVELS OF COMPOUNDING

- Low Risk
  - A sterile to sterile transfer
  - Example: One ingredient into a sterile IV bag
- Medium Risk
  - Multiple sterile to sterile transfers
  - Example - TPN
- High Risk
  - Non-sterile APIs to sterile medication
  - Higher risk – IM/IV/eyes/intrathecal administration

USP 797 BUDS FOR HIGH RISK COMPOUNDS

- USP definition
- 24 hours at room temperature (25 to 28 degrees C)
- 3 days refrigerated (2 to 8 degrees C)
- 45 days frozen (-25 to -10 degrees C)
- PCAB requires that if there is no outside testing for the BUD, then you must autoclave the product or perform sterility and endotoxin testing on the product (new 2013) – this is extremely expensive and cost prohibitive for single drugs and every single compound

PHARMACY VS. MANUFACTURING

- Pharmacy
  - Oversight by each individual state board of pharmacy
  - Non-resident licenses are required in each state
  - If mail order is occurring into another state – the pharmacy must follow most strict state regulations
- Manufacturer
  - Must follow FDA GMP – Good Manufacturing Practices
  - Can sell in bulk
  - Doesn't need to meet individual state pharmacy board regulations

FEDERAL REGULATIONS

- The FDA has the ability to provide oversight whenever and wherever drugs are aggregated
- The FDA has the right to conduct inspections of facilities with this authority
- Post NECC, the FDA put tremendous pressure on individual state boards of pharmacy to shore up their regulations and oversight
- There is new legislation (S.959) in Congress that will create a third class of compounder (manufacturer) and also has specific language for traditional compounders:
  - 10% limit on monthly office use
  - Within 14 days must have patient specific names
  - Maximum 14 day BUD (beyond use date)

IACP

- The International Association of Compounding Pharmacy
- Our compounding association
- Puts on educational forums, support the industry and lobby to get legislation that makes sense at both the state and federal levels
- Working with Congress on some of the difficult provisions of the FDA legislation
- Questionnaire developed to assess compounding pharmacies

STATE BOARDS OF PHARMACY

- California is the most stringent state in terms of oversight and regulation of sterile compounding – sterile compounders are required to have both a retail and sterile license – regulations written in conjunction with compounding pharmacists – annual inspections –
- There are states that have essentially no regulations for sterile compounders
- Many states are in flux with their regulations (e.g. Texas and Ohio now require a a telephone "inspection" for out of state pharmacies) and California is putting in funding to do onsite inspections

KEY STATE ISSUES

- Patient specific prescriptions
  - California requires all ASCs receive patient specific scripts or the ASC is accepting "furnished products
  - Ohio requires that all compounded meds are filled pursuant to a patient specific script
- Office use restrictions
  - California has no specific requirement for office use – inspectors maximize it at about 20% of total volume
  - Ohio does not allow more than 5% of total volume of office use per the current FDA regulations
  - Other states have varying regulations
- Varying levels of USP requirements
  - USP was designed for manufacturers – not for sterile compounders
  - There is technically no guarantee of sterility
  - The objective is to validate one's process
  - External testing for "batches" varies extensively

THE OHIO EXAMPLE

- See attached handout for the regulations; these should be read for each state from which you are purchasing medications (and your own state) to determine any differences
- Ohio regulations:
  - Compounders cannot copy a commercial medication
  - All compounds will be filled for an individual patient prescription
  - Office use maximum is 5% of total volume for past 12 months for compounder
  - Only 72 hours of medication can be supplied to the account
  - No specific allowance in place for ASCs receiving compounded medications
  - A maximum of 60 grams or 60 ml can be provided for non-sterile compounds
  - BUDS follow USP 797
  - All prescriptions must be sent to the patient directly or you must be approved as a stocking station by the Ohio Board of Pharmacy

CALIFORNIA EXAMPLE

- Furnishing is described as the provision of drugs that are not specific to a patient specific prescription or that are specifically for office use for a physician
- California compounders cannot supply compounded medications for "orders" to an ASC or a hospital
- California has extensive provisions on how compounds must be made in the state

THESE STATES DO NOT ALLOW NON-PATIENT SPECIFIC COMPOUNDS

- Colorado
- Georgia
- Hawaii
- Maine
- Maryland
- Massachusetts
- Michigan
- Minnesota
- Missouri
- New Mexico
- New York
- Ohio
- Pennsylvania
- Rhode Island
- Tennessee

DEA – DRUG ENFORCEMENT AGENCY

- The DEA has very specific regulations in place that govern compounded medications – both sterile and not sterile
- The DEA has allowed distributors to monitor the purchasing activity of controlled medications from pharmacies
- We have to fill out paperwork every quarter and sometimes every month if we purchase controlled medications
- Only a maximum of 5% of our total prescriptions filled can be controlled
- "Constructive Transfer" means that we cannot fill more than 5% of our total prescriptions for controlled medications for office use
- We then choose to only have these delivered to patients

PCAB

- Pharmacy Compounding Accreditation Board
- A relatively young organization (compared to JCAHO)
- Unfortunately, a number of PCAB facilities have received cease and desist orders and have continued to have sterility issues
- The California State Board of Pharmacy no longer relies on PCAB for accreditation in lieu of a sterile license (2013)
- In 2013, PCAB significantly up-leveled its sterile compounding requirements to more closely match USP requirements and to implement surprise inspections as inspections were only every 3 years

THE STERILE COMPOUNDING PROCESS

- 1. Build a USP 797 sterile room and ante-room
- 2. Verify all of the equipment on a scheduled basis
- 3. Developed details SOPs that detail every single step of the process and meet all of the regulatory body requirements
- 4. Recruit and continually train experienced pharmacists, pharmacy technicians and ancillary personnel
- 5. Develop and validate the sterile compounding process
- 6. Develop and implement a detailed QA/QI program
- 7. Consistent and regular testing and quarantining of products
- 8. Done correctly, this is a detailed and relatively expensive process

KEY STERILE COMPOUNDING ISSUES

- What is a batch?
  - USP = 25 vials
  - NECC was doing 17,000!
- What potency, endotoxin and sterility tests will be done and where?
  - There are no in house tests that are acceptable for USP 797
  - Many compounders use in house testing to save money
  - Many compounders release batches without final testing (3 days potency and endotoxin and 14 days sterility is required with current technology)
- How do we handle ASC orders in a particular state?
- How do we stay on top of backordered requirements?
- How do we manage the complex BUD process?
- How do we manage the conflicts between PCAB, our state, our non-resident states and other regulatory bodies?

THE FUTURE

- More restrictive office use regulations
- Movement to patient specific requirements across the U.S.
- A balance between full cGMP/USP 797 and pharmacy regulations
- More unique combinations for ASCs
- Shortened BUDs to match USP 797
- Improvements in managing the inventory of compounded medications
- Increased state and federal inspections of compounding pharmacies, ASCs and physicians offices where drugs are stored

KEY ASC REGULATORY ISSUES

- Receipt of compounded medications that copy commercial drugs that are not on backorder
- Receipt of large orders of compounded medications that are not patient specific
- Purchasing from pharmacies that are not compliant

ASC CONSIDERATIONS

1. What are the backordered medication requirements?
2. What unique combinations can be put into place?
3. How will we manage the office use requirements of the state?
4. How will we handle patient specific requirements?
5. How do we appropriately validate the compounding pharmacy and their requirements?
6. What is the proper pricing of compounded medications – especially from a state with more strict requirements?