On Friday, February 13, 2015, the Food and Drug Administration released four guidance documents that further explain the regulatory framework the agency intends to use in enforcing the Drug Quality and Security Act. These guidance documents, along with the draft Memorandum of Understanding between the FDA and state agencies for the oversight of interstate distribution of compounded preparations, are draft documents. The pharmacy profession as well as other stakeholders has 90 days to review and submit comments and questions for the guidance documents and 120 days to comment on the draft MOU.

IACP has prepared this summary for you that contains information on the four guidance documents as well as the Memorandum of Understanding.

While IACP will be preparing and filing formal comments on behalf of the members of the Academy, we strongly encourage you to read the draft guidance documents and consider how their contents may affect your patients and practice. You can share your concerns and comments via e-mail with IACP [iacpinfo@iacprx.org] or you can submit those directly to the FDA by following the instructions on the first page of each guidance document.

Watch for additional information through IACP’s Capitol Connections newsletter, our email and FAX Member Alerts, our social media postings via Twitter and FaceBook. Be sure to visit the Breaking News section of our website at www.iacprx.org on a regular basis.

For Entities Considering Whether to Register As Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act


Released: 13 February 2015
Comment Deadline: 90 days – 13 May 2015

Key Takeaways

- All drugs compounded by a §503B outsourcing facility are subject to FDA inspection and oversight. That includes sterile or non-sterile compounds as well as any patient-specific prescriptions which are dispensed by the outsourcing facility.
- All drugs compounded within a §503B outsourcing facility must be CGMP compliant, follow the labeling requirements established by the FDA, and have an AERS (Adverse Event Reporting System) process in place. That includes medications for office-use, distribution, or patient specific prescription dispensing.
- An outsourcing facility must compound some sterile preparations. The amount is not specified by the FDA.
- Nothing prohibits the compounding and distribution of non-sterile preparations by a §503B outsourcing facility; however, an entity that compounds and distributes only non-sterile medications for distribution would not qualify as an outsourcing facility.
- Compounders that prepare only veterinary preparations, regardless of whether they are sterile or non-sterile, may not register as an outsourcing facility.
- Repackaging of biological as well as other drugs is permitted within an §503B outsourcing facility so long as the facility complies with additional requirements and guidance documents.
Adverse Event Reporting for Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act


Released: 13 February 2015
Comment Deadline: 90 days – 13 May 2015

Key Takeaways

- §503B outsourcing facilities must report all serious unexpected adverse events to the FDA. The agency encourages reporting of all serious AEs that might be considered expected even though that’s not required.
- The §503B outsourcing must file an AE report within 15 days with the name of the drug and the suspected adverse event.
- When investigating an AE, the §503B outsourcing facility must attempt to obtain: the name/information associated with an identifiable patient(s); the name/information of the individual(s) who reported the suspected AE; the name of the drug including dosage form, strength, lot number, and other details; and, a description with supporting documentation of the AE. That information must be filed with the FDA within 15 days.
- All ingredients and labeling information associated with the compound must be included in the AE filing. Additionally, the §503B outsourcing facility must obtain and report any concomitant medications taken by or medical conditions of the identifiable patient.
- AE Reporting will eventually be electronic but for now, §503B outsourcing facilities must use FDA Form 3500A.
- All records of AEs must be available for inspection and retained by the §503B outsourcing facility for no less than 10 years.

Repackaging of Certain Human Drugs by Pharmacies and Outsourcing Facilities


Released: 13 February 2015
Comment Deadline: 90 days – 13 May 2015

Key Takeaways

- FDA does not consider repackaging to be “compounding” and the exemptions provide for in §503A and §503B do not apply.
- Repackaging may be permitted by the FDA if, among other things:
  - It occurs in a pharmacy, a Federal facility or a §503B outsourcing facility.
  - Is done under the direct supervision of a pharmacist.
  - Is only repackaged and dispensed upon receipt of a prescription for an individual patient or an order in the patient’s chart within a healthcare facility.
  - “Anticipatory” repackaging is permitted up to a 14 day supply.
- For §503A compounders, repackaged sterile drugs shall have a maximum BUD of the following:
  - ≤ 30 hours if stored at USP controlled room temperature
  - ≤ 9 days if stored in a refrigerator; or
  - ≤ 45 days if stored in a solid frozen state between -25° C and -10° C
- For §503A compounders, repackaged non-sterile drugs shall have a maximum BUD that is no longer than the expiration date on the original drug being repackaged. All repackaging of non-sterile drugs must be done in compliance with USP <795>.
- For §503B outsourcing facilities, repackaging is permitted with additional requirements for CGMP facility compliance, adverse event reporting, labeling, and BUD verification.
- Repackaging of any drug on the “do not compound” list for safety and efficacy reasons is prohibited.
Mixing, Diluting, or Repackaging Biological Products Outside the Scope of an Approved Biologics License Application


Released: 13 February 2015
Comment Deadline: 90 days – 13 May 2015

Key Takeaways
- This guidance addresses the mixing, diluting, and repackaging of certain types of biological products when that is not consistent with the FDA approved labeling.
- Other sections of the law apply for repackaging of biologicals, not just this guidance document.
- The FDA will not take enforcement action if the biological is mixed, diluted or repackaged upon receipt of a valid prescription for an identified, individual patient or a written order in a patient’s chart in a healthcare setting.
- A pharmacy may repackage a biological in advance of receiving a prescription – but may only dispense based upon receipt of either the individual patient prescription or the written order in the patient’s chart.
- Repackaging of biological in single-dose vials must be done in accordance with the FDA approved product labeling. For example, Avastin® may be repackaged into smaller units if other sections of the labeling including diluents and storage conditions are met.
- For §503A compounders: repackaged biological will have a 4-hour or less BUD or up to a 24-hour BUD if a microbial challenge study has been completed in accordance with specified requirements.
- For §503B outsourcing facilities, the BUD rules also apply; however, they may establish a maximum 5-day BUD after successful completion of container and other studies.

Draft Memorandum of Understanding (MOU) Between A State and the US Food and Drug Administration Addressing Certain Distributions of Compounded Human Drug Products


Released: 13 February 2015
Comment Deadline: 120 days – 13 June 2015

Key Takeaways
- FDA has defined “distribution” to include office use as well as dispensing to an agent of a patient or to an individual patient themselves.
- Nothing within the MOU negates the FDA requirement that a compounder must obtain a prescription for an individually identified patient.
- There are no exceptions for “border pharmacies.”
- FDA will not be enforcing the MOU until the public comment period has finished, the document has been edited/changed if the agency decides to do so, and then providing 180 days for the states to decide whether to enter into the MOU. The amount of days that a State should be given will also be open for comment.

- If a State does NOT enter into an MOU, the amount of compounded medications distributed interstate shall not exceed 5% of the total prescription orders dispensed or distributed by the pharmacy.

- If a State enters into an MOU with FDA, the State bears two duties: (1) the duty to investigate complaints relating to compounded human drug product distributed outside the State; and (2) the duty to determine whether the pharmacist, pharmacy, or physician is distributing inordinate amounts of compounded medication interstate.
State’s Duty to Investigate Complaints Relating to Compounded Human Drug Products Distributed Outside the State

If a State enters into an MOU with FDA, the State where the pharmacist, pharmacy, or physician is located must investigate complaints received regarding compounded medications distributed outside the State.

- Complaints that the State must investigate include adverse drug experiences or product quality issues that could lead to public health risks.
  - An adverse drug experience can include an adverse event occurring in the course of the use of a drug product in professional practice; an adverse event occurring from drug overdose, whether accidental or intentional; an adverse event occurring from drug abuse; an adverse event occurring from drug withdrawal; and any failure of expected pharmacological action.
  - A product quality issue can include any incident that causes the drug product or its labeling to be mistaken for, or applied to, another article; any bacteriological contaminations; any significant chemical, physical, or other change or deterioration in the distributed drug product; or any failure of one of more distributed batches of the drug product to meet the applicable specifications. Contamination including mold, fungal, bacterial or particulate contamination is a product quality issue.

- The State investigation must include a determination of whether there is a potential public health risk or safety concern associated with the compounded medication and confirmation that any risk or safety concern is adequately contained.
- If a complaint is found to be valid, the State must take action to require the pharmacy to determine the root of the problem and correct the issue.
- The State must notify FDA within 72 hours of receiving any complaint.
- The State must keep records for at least 3 years.

State’s Duty to Determine Whether The Pharmacist, Pharmacy, or Physician is Distributing Inordinate Amounts of Compounded Medication Interstate

If a State enters into an MOU with FDA, that State must review compounding records during inspections to determine whether the pharmacy, pharmacist, or physician is distributing inordinate amounts of compounded medications interstate.

- “Inordinate Amount” = If the number of units of compounded human drug products distributed interstate in a calendar month is equal to or greater than 30% of the number of units of compounded and non-compounded drug products distributed or dispensed both interstate and interstate.
  - The only exception to this rule – prescriptions that have been dispensed to an out-of-state patient at the facility in which the drug was compounded, and the patient or the patient’s agent carries that across state lines, are not counted in the calculation.

- If the State determines that the pharmacy, pharmacist, or physician has in fact distributed inordinate amounts of compounded drugs interstate, the State must notify FDA within 7 days.
- The State must also take action against the pharmacy, pharmacist, or physician which may include a warning letter, enforcement action, suspension or revocation of a license, or other action consistent with State law.
- FDA may also take action against the pharmacy, pharmacist, or physician.