STATE BOARD OF PHARMACY

DEPARTMENT OF CONSUMER AFFAIRS
SUBCOMMITTEE TO EVALUATE DRUG DISTRIBUTION WITHIN HOSPITALS
MINUTES

DATE:	March 2, 2009
LOCATION:	Crowne Plaza Hotel – Irvine 17941 Von Karman Ave. Irvine, CA 92614 (949) 863-1999
BOARD MEMBERS PRESENT:	Kenneth Schell, Pharmacist Member, President Robert Graul, Pharmacist Member
STAFF PRESENT:	Virgina Herold, Executive Officer Anne Sodergren, Assistant Executive Officer Caroline Kline, Legislation and Regulation Coordinator Kristy Schieldje, Senior Staff Council Tessa Fraga, Administrative Analyst
CONSULTANTS PRESENT:	Val Sheehan, Meeting Facilitator Carmen Fraser, Senior Associate

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The meeting was called to order at 9:30 a.m.

1. Welcome, Agenda Overview, Introductions

Val Sheehan, Meeting Facilitator, introduced herself and Senior Associate, Carmen Fraser and welcomed the group to the subcommittee meeting. Ms. Sheehan then introduced Board of Pharmacy staff and board members who were in attendance. Board President Ken Schell gave opening remarks and noted the importance of the meeting as a vehicle for professionals to review the rules, regulations and practices pertaining to the practice of pharmacy in hospital settings with the ultimate purpose of improving patient care and safety. Ms. Herold also gave opening remarks echoing Dr. Schell's comments and cautioned pharmacists with pending citation and fine appeals not to discuss their situation in detail in order to preserve the integrity of the appeals process. She urged those individuals to keep their comments more general in nature.

Ms. Sheehan reminded audience members to sign in, in order to receive more information on future meetings and to sign in if they wanted to receive continuing education credits for the meeting. Ms. Sheehan emphasized that people were not required to sign in if they preferred to remain anonymous. Ms. Sheehan then asked everyone in the audience to introduce themselves, again with the understanding that if an individual did not want to identify him/herself, then he/she was under no obligation to do so. Ms. Sheehan reviewed the agenda, meeting values, and meeting courtesies and noted that a section of the agenda towards the end of the meeting had been set aside for public comment. Ms. Sheehan added that audience members could also comment at the end of each agenda item as well. Ms. Sheehan concluded by asking for any questions. One question arose about whether or not the meeting was being recorded. Ms. Sheehan confirmed that the meeting was being recorded and announced that

minutes from the meeting would be available on the Board of Pharmacy's web site as part of the April Board Meeting materials.

2. Overview of Federal and State Regulatory Agencies Involved in Product Recalls

Alonsa Cruse, District Director for the U.S. Food and Drug Administration (FDA) gave a presentation on product recalls. Major points from Mr. Cruse's presentation included:

- The three main stages of a product recall are:
  - First Alert – FDA hears about problems through adverse event reporting. Alerts can come from patients, pharmacies, hospitals, manufacturers and even the CDC.
  - Alert the Public – FDA posts regular updates about recalls to its website and all recalls appear in the agency's weekly enforcement reports. Not every recall gets reported; it depends on the severity.
  - Effectiveness Checks – FDA reviews all of a company's corrective actions to determine when a recall is complete.

- All product recalls are classified as I, II or III relative to the degree of health hazard presented by the product being recalled. The FDA uses a Health Hazard Evaluation to determine the classification.
  - Class I – A situation in which there is a reasonable probability that the use of, or exposure to, a violative product will cause serious adverse consequences or death.
  - Class II – A situation in which use of, or exposure to, a violative product may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote.
  - Class III – A situation in which use of, or exposure to, a violative product is not likely to cause adverse health consequences.

- A recall is a voluntary action by a firm although the FDA has the authority to take to court manufacturers who do not order recalls on their own. He added that it is important for supply chain members to act immediately. The FDA can take legal action (seize a product) or issue press if a firm is not complying. As a matter of practice, it is important for firms to have a recall strategy as part of a business plan, no matter what size the organization/business is.

- The FDA or firm will eventually issue a press release for almost all Class I recalls where a product is likely to be in the hands of the consumer. The FDA can seize a product or issue a press release if the firm is not complying. FDA alerts are listed on their website: www.fda.gov/opacom/7alerts.html.

- If an organization is held accountable to pull the product, the organization must follow directions on the recall notice. Each recall is handled uniquely. If there is confusion, entities can check the FDA web site or contact their local FDA district office with questions.

Daniel Seid, Chief, Drug Safety Unit, Food and Drug Branch at the California Department of Public Health (CDPH) gave a brief presentation on his agency's role in product recalls. Major points from Mr. Seid's presentation included:

- The CA Food and Drug Branch is the enforcement arm of the CDPH. The Food and Drug Branch is similar to the FDA, but its jurisdiction is limited to California. They have the authority to investigate issues that affect the efficacy, quality or safety of a drug product in CA to determine the risk to the public.

- The Food and Drug Branch licenses manufacturers in the state and has statutory and regulatory authority over those entities. If a product is contaminated, it is considered adulterated and comes under jurisdiction of the Food and Drug Branch. Suspicion of an adulterated product is enough for the Food and Drug Branch to enter facilities and conduct investigations. They have embargo authority and can immediately tie up a product that

is just suspected of being adulterated. The Food and Drug Branch can investigate and file cases. Anyone found to be holding, selling, manufacturing, distributing or giving away adulterated or falsely advertised product can be subject to civil, administrative and criminal action.

- A question arose about how regulatory agencies were addressing the "gray market" or the sale of goods through means other than what was intended or approved by the original maker. Mr. Cruse emphasized that the closed system in the US, where a drug goes from manufacturer to wholesaler or pharmacy to patient should minimize the introduction of counterfeit product. Mr. Cruse added that drugs purchased outside the closed system (e.g., from internet pharmacies) can be called the same name, but the quality of the drug or its ingredients may be very different. Federal and state laws provide that drugs be purchased from an approved source or licensed facility. Any concerns regarding counterfeit drugs should be directed to the FDA (or under California law, to the California State Board of Pharmacy).

- Ms. Herold concurred with Mr. Cruse's comments and added that if a wholesaler is not licensed with the Board of Pharmacy, the company is operating illegally. Legitimate businesses will not sell to such firms, and any entity buying from an unlicensed source is not only violating the law, but dealing with suspect products. Ms. Herold emphasized the importance of instituting a drug tracking program such as "e-pedigree" to minimize the circulation of counterfeit drugs.

- Dr. Schell posed a question about the level of due diligence for pharmacists when they are obtaining a product or what pharmacists can do to ensure the pedigree of a product that they are receiving. The consensus was that purchasing from approved sources, providing appropriate management oversight, and possibly in large settings, assaying products are important steps to take. In addition, hospital staff must pay close attention to adverse events and report them through the MedWatch system.

- A comment was made that recall notices often do not have clear instructions about what to do with a recalled product. Mr. Cruse agreed to work with his staff to more carefully examine how closely firms are following the model recall notices. Mr. Cruse and his staff will follow up with entities as needed. He confirmed that having clear directions about whether to return, hold or destroy a product is imperative.

- A comment was made that the combination of drug shortage and the recall have created a public health crisis. The audience member noted that developing a set of best practices related to recalls may take stages or drafts before an ideal is reached. In the interim, examining templates that help hospital-based pharmacists more effectively comply with a recall will be helpful. She added that all the entities – suppliers, wholesalers, hospitals, etc. need to be involved. A lot of time and energy were lost due to confusion, and everyone would prefer to avoid a similar situation in the future. A good first step would be to develop an agreement around due diligence.

3. Examination of Hospital/Health System-based Drug Recall Processes – Case Study: Heparin

Loriann DeMartini, Chief Pharmaceutical Consultant, California Department of Public Health (CDPH), Center for Healthcare Quality (licensing and certification), gave an overview of what occurred in California during the recent heparin drug recall. Her presentation covered the FDA recall process, state and federal regulatory requirements, a chronology of recall-related events, and information uncovered by the CDPH during the recall. Main points from Dr. DeMartini's presentation included:

- Based on what was learned during the recent heparin recall, California has an incredible opportunity to lead the nation in addressing the gaps in the efficient and effective execution of drug recalls in hospitals.

- The Center for Healthcare Quality's responsibility is to enforce all state and federal laws and regulations pertaining to the provision of health care in licensed institutions. Hospitals are only one of 30 entities that they license and certify. Licensing relates to the California code of regulations, and certification relates to

federal regulations. Hospitals need to be in compliance with all applicable codes regardless of whether or not they are accredited by the Joint Commission.

- The FDA has the responsibility for securing the drug system as codified in 21 Code of Federal Regulations (CFR). Their recall policy is "to remove a product that is in violation of laws administered by the FDA." [21CFR 7:40] The FDA also ensures that the recalled product is removed from the system.

- The FDA conducts a Health Hazard Evaluation (HHE) to determine the classification of a recall. The HHE has six components:

    1. Whether any disease/injuries have already occurred.
    2. Whether any existing conditions could contribute to a clinical situation that could expose humans to a health hazard.
    3. Assessment of the hazard to various segments of the population.
    4. Assessment of the degree of seriousness of the health hazard.
    5. Assessment of the likelihood of the occurrence.
    6. Assessment of the consequences of the hazard.

- Based on results of the HHE, the FDA classifies each recall as I, II or III. In the absence of product seizures, all recalls are voluntary and they usually are effective. Elements of a recall strategy include the depth of the recall, public warning and effectiveness checks.

- Recalling firms are responsible for promptly informing each of their affected direct accounts that further distribution is prohibited. A consignee who receives a recall notification, such as a hospital, must immediately act upon and carry out instructions set forth in recall notice.

- Relevant state and federal regulatory requirements include:

    1. It is unlawful for any person to manufacture, sell, deliver, hold, or offer for sale any drug or device that is adulterated. [HSC 111295]. A recalled medication is an adulterated drug [HSC 111285]
    2. It is unlawful for any person to receive in commerce any drug or device that is adulterated or to deliver or proffer for delivery any drug or device. [HSC 111305]
    3. No contaminated or deteriorated drugs shall be available for use. [CCR Title22 § 70263(q)(9)]
    4. The P&T committee shall develop written policies and procedures for establishment of safe and effective use of medications [CCR Title 22 § 70263(c)(1)].
    5. Entities must take all reasonable steps to conform to all applicable federal, state and local laws and regulations including those relating to…safety measures. [CCR Title 22 §70701(a)(5)]
    6. Outdated, mislabeled, or otherwise unusable drugs must not be available for patient use. [42CFR § 482.25(b)(3)]
    7. Drugs maintained on the nursing unit shall be inspected at least monthly by a pharmacist. [CCR Title 22 § 70263(q)(10)]
    8. In order to provide patient safety, drugs must be controlled and distributed in accordance with applicable standards of practice, consistent with Federal and State law [42 CFR § 482.25(b)]
        - Guidelines state: "Medications dispensed by the hospitals are retrieved when recalled." Survey procedures; "Does the hospital retrieve and remove medications available for patient use when the hospital has been informed of a drug recall? Does the recall include notification of patients that have been impacted and those that would order, dispense or administer the medication?"
    9. The recipient of a recall notification "should immediately carry out the instructions set forth by the recalling firm." [21 CFR § 7.49(d)]

- Dr. DeMartini summarized the events of the heparin recall notification and added that the heparin recall was unusual because the Board of Pharmacy and the CDPH were very involved. Both entities became involved because heparin continued to be found in hospital facilities even after five recalls. Dr. DeMartini added that California wasn't the only state that had difficulties removing the recalled drug. She stressed the importance of learning from what happened from this event in order to prevent future occurrences.

- The Board of Pharmacy conducted an initial inspection and found that 40% of California hospitals had heparin products available even after receiving recall notices. The Board ultimately found heparin in 94 of 533 hospitals. Based on information provided by the Board of Pharmacy, the CDPH then conducted 87 of its own inspections.

- The results were that nearly 20% of hospitals were identified with recalled medications available for patient use. The total potential patient exposure from recall to removal of medication(s) numbered in the thousands.

- Dr. DeMartini stated that the findings revealed systemic deficits in hospital recall processes and drug distribution systems. She stated that the failures came down to a few issues: communication, education, and getting other disciplines involved. She reiterated that this was an important opportunity for improvement and prevention of a recurrence.

- A comment was raised about the discrepancy in the recall process between what wholesalers considered immediate as opposed to hospitals. For example, once a drug is sent back, there is an expectation that a drug won't be sent out again by a wholesaler. Ms. Herold commented that there needs to be a better partnership among entities in the drug supply chain to avoid this type of scenario in the future.

- One audience member commented that having more specific language about the definition of immediate (e.g., "within 24 hours") would be helpful. The consensus was that "immediate" needs to be taken seriously and adhered to as much as possible.

- Another comment was made that it can be challenging to communicate with administrators, CFOs, etc. about the importance of using staff to comply with a recall. The group agreed that communicating effectively with different entities can be challenging and that it may mean quantifying the cost of failure to comply with a recall as the cost of negative press, the price of a lawsuit or even the value of one human life.

- One audience member asked about the regulation requiring notification to all patients and what is expected to be in compliance with that regulation. Dr. DeMartini said that the expectation of the CDPH is that each hospital knows where medications are so they can be removed and that they are notifying patients who may have received recalled medications. If a hospital is not tracking what brand of medication is going to each patient, then that hospital needs to notify all patients.

- One participant asked if the recalled heparin that was found during the investigations was outside the usual drug storage areas. Dr. DeMartini reminded participants that drugs, no matter where they are in a hospital, are the responsibility of the pharmacist. Dr. DeMartini elaborated that wherever they touched heparin was where a pharmacist could touch it (it wasn't in lab coats or lockers).

4. Discussion of Best Practices Related to Drug Recall Processes in Hospitals/Health Systems

Ms. Sheehan asked participants to form ten small groups and discuss the following questions:

- What's working well in relation to drug recall in CA hospitals/health systems?

- What's not working as well in relation to drug recall in CA hospitals/health systems?
  i. How could these be improved?
  ii. Are there any other state or national practices, policies or laws that are needed in CA to help improve the drug recall process?

Each group shared two to three best practices and two to three suggestions for improvement.

Group	Best Practices	Suggestions for Improvement
1	▪ Maintain all stock in cabinets in order to easily and quickly do an electronic lockout in the event of a recall. ▪ Implement an Adverse Drug Reaction (ADR) system that allows you to go back and track what occurred in relation to a recalled drug. This would allow a hospital to capture the data in order to better communicate with patients. ▪ Create a duties list or detailed list with all the steps needed during a recall so that any staff member can effectively carry out the steps.	▪ Have a more effective notification system that should come from one source listing what the issue is, what should be done, what steps should be taken, etc. Having one notice from one source with all the relevant information would minimize confusion. ▪ Institute bar coding to better track drugs.
2		▪ Messages are not always clear. Improve and simplify messages regarding recalls. ▪ One department has to take responsibility for something that is the responsibility of the whole hospital. If the emphasis was placed on the CEO or president instead of the PIC, a lot more action might have been taken. ▪ Hospitals need to prioritize bar coding technology.
3	▪ Limit the number of people pulling the product during a recall for better accountability and control. ▪ Set up an organized storage facility for drugs – just one place to go. ▪ Establish a dedicated and trained "recall team" who knows all the policies, procedures and pertinent regulations.	▪ Electronic tracing or notification (e.g., secure email) of recall would be helpful.
4	▪ Minimize the number of and maximize the quality and authority of the individuals carrying out the immediate and monthly inspections. Someone who's authorized to do what's necessary is ideal. ▪ Establish a method to close the loop and perform an audit. For example, recall notices were faxed	▪ Institute RFID or bar codes and advocate to have standardized methodology in the way the information is sequenced. This should apply to the entire lifecycle of the product. ▪ Require that drugs be stored in a specific location and institute consequences when

	-	drugs are stored out of the area.
5	▪ Continue to collaborate and communicate effectively with wholesaler.	▪ Establish a centralized method to interpret and disseminate information about recalls.
6		▪ Have a better system to identify outpatient clinics that are on the facility's license. This would help clarify what a PIC is responsible for. ▪ Improve coordination of recall notices, especially for ubiquitous products. ▪ Expand policies to increase responsibility of other department heads during a recall.
7	(Felt that they didn't have a good demonstrated best practice.)	▪ Have a centralized system or body in a hospital that would disseminate recall information through email. This would hopefully create better accountability and better response time. ▪ Increase authority of PIC to better control where and how drugs are stored.
8		▪ Recall notices should state whether this is a Class I, II or III recall. Also, notices should have clear instructions about what actions to take. ▪ Establish radio frequency identifiers (RFID) as a way to track drugs (a non line-of-sight read). This would be one way to carry e-pedigree. E-pedigree would be a way to better execute a recall.
9	▪ Electronic receipt of recall.	▪ To avoid confusion, create recall notices with more uniform language or have notice come from one source. ▪ Establish an authorized storage area. If something is not in an authorized storage area, then it is stored unlawfully. ▪ Increase accountability. All health care providers that are touching the drug are accountable. ▪ Outside medications from vendors or contractors should not be allowed in the hospital.

		▪ At the site level, involve nurses, physicians, dialysis techs, therapists, administrators in discussion about accountability. Pharmacists need more authority if held accountable. ▪ Bring together management, California Hospital Association, Medical Board, Nursing Board. Others should be willing to accept citations and fines.
10		▪ Encourage wholesalers to take more responsibility in terms of communicating recalled lot numbers. ▪ Increase accountability and collaboration among members of the health care team. There is a lack of consequences for other health care professionals.

5. Brainstorming Session: Future Topics for the Subcommittee to Improve the Drug Delivery Systems

Ms. Sheehan asked participants to form small groups to brainstorm topics for future meetings. Before the brainstorming session began, Ms. Sheehan asked Ms. Herold to address the group regarding parameters for the discussion. Ms. Herold shared that the goal of these meetings is to examine possible changes in pharmacy law or in practice settings that the Board of Pharmacy can influence or assist with in providing better care to patients. She added that some topics may be not as useful to include. For example, the California Department of Public Health has communicated that changing Title 22 is not a high priority at this time, so any discussion regarding changing Title 22 would not be useful. Ms. Herold encouraged the group to explore what they need for effective patient care. She urged them to consider questions such as, what is impeding your ability to provide quality care to patients? What's keeping you as a pharmacist from exercising control over drug distribution in hospitals? She added that in the coming year, the Board of Pharmacy will pursue some means to authorize satellite pharmacies. The law currently does not recognize satellite pharmacies, yet many hospitals have them. She added that this session was their opportunity to come forward with ideas.

Dr. DeMartini added that while today's discussion is focused on the heparin recall, the bigger issue is about the drug distribution system and whether or not it supports effective patient care in the hospital setting. She encouraged participants to consider whether or not other aspects of the drug distribution system prevent the pharmacist from being an effective patient advocate. She encouraged participants to think beyond an effective recall.

A comment was made by an audience member that the things that get people's attention around quality and safety are those things that are fiscal or regulatory mandates. She added that it would be in the best interest of pharmacists to bring other boards together to discuss shared accountability. A key stakeholder is the California Hospital Association although no representative was at the meeting.

Another audience member wanted to know about the likelihood of creating interpretive guidelines for Title 22. Dr. DeMartini confirmed that they are prohibited from creating interpretive guidelines. She added that furnishing specific language from Title 22 that clarifies certain sections would also not be helpful because each facility is unique and one size does not fit all.

After brainstorming and sharing potential ideas and topics, the group voted on the most desired topics. The following is a list of all the suggestions ranked by the number of votes that each one received (similar topics were consolidated to minimize redundancy).

Topic	Number of Votes
Pharmacy Technicians – licensing, training program, "intern" hours, practical experience	25
Registered Pharmacist/Patient Ratio by "x" Date – by level of service	18
Pharmacy Director Role – including reporting to CEO, give pharmacist authority and accountability	17
Automation – rules and regulations, scope of use	15
Separating Rules and Regulations Between Hospitals, Retail Pharmacies and Correctional Facilities	12
Effective Patient Care – legal requirements of number of RPhs staffing, alternatives to recalled drugs (who makes decision), refocus on patient care including process vs. taking care, mandate percentage of time in clinical role, minimum pharmaceutical care standards [added from discussion following the voting]	11
Healthcare Information Technology – guidance, QA, distribution, impact of automation (ADL, BPOC)	10
E-pedigree – gray market (ethics/contamination of source), market manipulation, monopoly	9
Pharmaceutical Care Standards – board certification	8
Provision of Pharmaceutical Care – quality and safety of drug distribution and clinical services, role of satellite pharmacies	8
Electronic Record Retention – purity of the order, controlled substance records (1 year on-site)	7
Authority vs. Accountability - recognition by other disciplines (e.g., nursing, respiratory, medical)	7
Hospital vs. Retail Health Safety Codes	6
PIC's Responsibilities for Outpatient Hospital-based Clinics	5
Compounding – manufacturing?	3
Summit with Other Boards and Organizations (e.g., CHA, ONA (?) ?	3
Infusion Center Licensing	2
Hospital Administration Involvement – increase awareness/importance of issue	2
Professional Guidelines	1
Clinical Pharmacy Services – required clinical services	1
Licensing of a Hospital Administrator	1
Limit Number of Orders Reviewed by Registered Pharmacist Per Shift or Per Hour	1
Organize Communication Process – identify roles in recall process, standardize recall process	1
Unit Inspections – content of inspection, inspecting individuals	0
Authority of Pharmacy	0
Conflicting/Unclear Language Between Title 22 and Board of Pharmacy Regulations	0
Requirement of Chief Pharmacy Officer vs. PIC Definitions – PIC accountability for more than one physical location	0
Clarification Regarding Laws and Applicability to Different Pharmacy Practice Sites (inpatient, retail, manufacturer, SNF)	0
Compensation for Certifications	0
Increase Wholesaler Requirements for Recall Notifications	0
Medical Storage Areas – licensing and regulation, penalties not to pharmacists, but to hospital administrators	0

A comment was made acknowledging the Board of Pharmacy's history of and leadership role in promptly addressing clinical pharmacy services in California. The participant added that going forward, she wanted to

preserve that focus on the pharmacist's role in clinical care. Another participant added that there was a need to be cognizant of pharmacist/patient ratios in order to be able to provide high quality patient care. Ms. Sheehan concluded the session by thanking everyone for their time and input to the Board of Pharmacy for their further consideration.

6. Additional Public Comment

Ms. Sheehan asked if there were any public comments before the meeting was officially adjourned. A participant raised the issue of collaboration and what it means in the context of these meetings. He added that one way to look at collaboration would be to emphasize the role of regulation and enforcement to keep patients safe while another model of collaboration would focus more on open dialogue and developing a common purpose between regulators and pharmacists in order to make patient care safer. Creating a mutual understanding of what's trying to be accomplished is ultimately what's important. Another comment underscored the need to collaborate with other disciplines because decision-making around patient care involves more than just the pharmacist. The person added that continued enforcement with just pharmacists may not necessarily bring about the desired change that everyone would like to see.

7. Closing, Evaluation, Adjournment

Ms. Sheehan closed the meeting and thanked the speakers and the Board of Pharmacy for hosting the meeting. Dr. Schell added his appreciation on the behalf of the Board of Pharmacy for everyone's time and commitment to improving patient care and safety.

The meeting was adjourned at 3:00pm

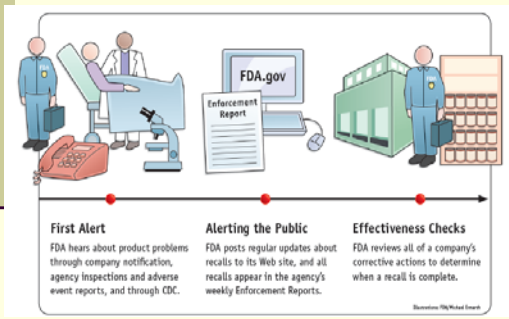
Introduction to FDA Recalls

Alonza Cruse District Director
Los Angeles District Office
Alonza.cruse@fda.hhs.gov

FDA-Los Angeles District Recall Team
Tamala Bogan
949-608-3504/949-233-4120
Larry Howell
949-608-4440/949-302-8784

FDA 101: Product Recalls

From First Alert to Effectiveness Checks



Definitions 21CFR7.3

- Recall
- Product
- Correction
- Market Withdrawal
- Stock Recovery
- Classification

Recall

- A firm's removal or correction of a marketed product(s) that the Food and Drug Administration considers to be in violation of the laws it administers and against which the agency would initiate legal action, e.g., seizure.

Product

- An article subject to the jurisdiction of the Food and Drug Administration, including any food…intended for human or animal use…

Correction

- Repair, modification, adjustment, relabeling, destruction, or inspection (including patient monitoring) of a product without its physical removal to some other location.

Market withdrawal

- A firm's removal or correction of a distributed product which involves a minor violation that would not be subject to legal action by the FDA or which involves no violation (normal stock rotation, routine equipment adjustments, etc.)

Stock recovery

- A firm's removal or correction of a product that has not been marketed or that has not left the direct control of the firm, i.e. the product is located on premises owned by, or under the control of, the firm and no portion of the lot has been released for sale or use.

Name This Action

Stock Recovery - Market Withdrawal - Recall

- Product implicated in an outbreak of E. coli O157: H7. **Recall**
- Product does not declare a net weight, but is still in the firm's warehouse. **Stock Recovery**
- Label does not list mfg city and has been shipped to retail stores. **Market Withdrawal**
- Positive Shigella sample, with no reported illnesses. **Recall**

Classification

- Numerical designation, i.e., I, II, or III, assigned by the Food and Drug Administration to a particular product recall to indicate the relative degree of health hazard presented by the product being recalled.

Health Hazard Evaluation

- Diseases or injuries which have already occurred
- Existing conditions that can contribute to a clinical condition
- Population
- Seriousness of hazard
- Likelihood of occurrence of hazard
- Immediate and long term consequences

Classification

- **Class I** is a situation in which there is a reasonable probability that the use of, or exposure to, a violative product will cause **serious adverse health consequences or death**.

Class I Examples

- *Listeria monocytogenes, Salmonella, E. coli O157:H7 in RTE food*
- *Dietary supp. products containing aristolochic acid, a potent carcinogen and nephrotoxin*
- *Dietary supp. products containing a prescription drug that could have serious, life-threatening consequences in some people. (Liqiang Dietary Supp. containing glyburide)*

Classification

- **Class II** is a situation in which use of, or exposure to, a violative product may cause **temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote**.

Class II examples

- *Hard/sharp foreign objects 7 – 25 mm*
- *Undeclared yellow 5 & 6*
- *Unapproved/uncertified colors*
- *Cosmetic products found to be contaminated with bacteria*

Classification

- **Class III** is a situation in which use of, or exposure to, a violative product is **not likely to cause adverse health consequences**.

Class III examples

- *Mold, yeast, lactobacillus*
- *Hard/sharp foreign objects less than 7 mm*
- *Off odor/off taste from contaminant at levels not likely to pose a hazard to health*
- *Misbranded products (The label states zero mg potassium per serving; the product actually contains 370mg potassium per serving)*

What Recall Classification?

Class II

- **Chicken and beef burritos contain a very small amount of undeclared soy ingredients**
- **Egg product associated with a Salmonella outbreak**

Class I

- **Weight of Sliced-Smoked Ham is under the declared net weight.**

Class III

Recall Terminology

- Class III
  - Pathogen recently involved in recalled spinach and ground beef.
- Recall
  - A firm's voluntary removal of distributed product that is adulterated or misbranded.
- E. coli 0157: H7
  - This is a class of recall where the use of the product will not cause adverse health consequences.

Code of Federal Regulations

- 21 CFR Part 7, Subpart C: Recalls (Including Product Corrections) – Guidelines on Policy, Procedures, and Industry Responsibility
  http://www.access.gpo.gov/nara/cfr/waisidx_04/21cfr7_04.html
- Recall is a voluntary action by a firm
- Guidance on development of recall strategy (depth, public warning, effectiveness checks)
- Guidance on recall communications with consignees
- Who to contact at FDA and what information to provide

Code of Federal Regulations

- 21 CFR Part 107, Subpart E – Infant Formula Recalls (Gives FDA authority to require recalls of adulterated or misbranded infant formula that presents a risk to human health)
- 21 CFR Part 806-Medical Device Firm must report the recall to FDA and conduct the recall in the manner specified in this part (21 CFR Part 810-Procedures for FDA recall authority)
- 21 CFR Part 1271.440-Includes provisions for FDA to order retention, recall and/or destruction of Human Cell, Tissue and Cellular & Tissue-based products.

Press releases

- Issued by FDA or firm for almost all Class I recalls where the product is likely to be in the hands of the consumer
- May be issued by FDA or firm for some class II recalls
- Models for most class I recalls posted on FDA website
- Follow FDA models as closely as possible – "fill in the blanks"

Press releases (cont.)

- Do not change hazard statement – don't take out "life threatening"
- Issue press release to Associated Press
- Provide FDA with confirmation that press release was sent to AP
- FDA will issue if firm will not or if firm's is inadequate

Recent Recall Issues Involving Imports

- Melamine contaminated pet food (China)
- Ethylene glycol in toothpaste
- Heparin recall
  - Heparin sourced from pig intestine
  - Reports of anaphylactoid reactions after bolus administration
  - Hypothesis: low level contaminant
  - API manufactured in facility in China

Los Angeles Districts Recalls for FY08

	Class I	Class II	Class III	Safety Alert
CBER	0	17	5	
CDER	3	4	0	
CDRH	3	73	10	2
CFSAN	16	8	5	
CVM	1	1	0	
TOTAL	23	103	20	2

Determining the scope of a recall

- When did the problem start/end
- Can additional lots/products be affected other than the lot/product analyzed and found adulterated
- How many sizes/labels for the product
- Is the product coded with a lot number

Responsibilities of Recalling Firm

Preparing for a Recall

- Review available recall guidance
- Develop a recall plan
- Maintain manufacturing and distribution
- records in a manner to facilitate a timely and effective recall
- Identify finished products with a lot number/code

Responsibilities of Recalling Firm

Communicating with FDA

- Notify FDA and provide information in a timely manner (A current list of FDA recall coordinators can be found on FDA's website at: http://www.fda.gov/ora/inspect_ref/iom/iomoradir_monitors.html#recall)
- Info needed by FDA includes: product (identity, size and type of containers, brand names, lot numbers, whether refrigerated/frozen/shelf stable), codes, amount manufactured and amount distributed, number of and types of consignees, area of distribution, reason for recall

Responsibilities of Recalling Firm

Communicating with FDA

- Discuss recall strategy with FDA (including disposition of recalled product)
- Let FDA review text of phone notifications, written recall notifications, press releases (follow models provided in FDA guidance)
- Provide FDA with consignee list
- Provide actual labels or clear photos of labels

Responsibilities of Recalling Firm

Communicating with Consignees

- The timely dissemination of communications about recalls of FDA-regulated products, important drug safety information, and other important product safety information is essential for the protection of the public health.

Responsibilities of Recalling Firm

Communicating with Consignees

- The FDA's current thinking interprets the provisions of 21 CFR 7.49 and 200.5 to allow the use of e-mail and other electronic communication methods, such as fax or text messaging, to accomplish any recall notification or distribution of important safety information.

Responsibilities of Recalling Firm

Communicating with Consignees

- Be brief and to the point
- Identify clearly the product, size, lot number(s), code(s) or serial number(s) and any other pertinent descriptive information to enable accurate and immediate identification of the product
- Explain concisely the reason for the recall and the hazard involved, if any

Responsibilities of Recalling Firm

Communicating with Consignees

- Provide specific instructions on what should be done with respect to the recalled products
- Provide a ready means for the recipient of the communication to report to the recalling firm whether it has any of the product
- Provide sub-recall instructions (if necessary)

Responsibilities of Recalling Firm

Recall Monitoring/Closure

- Maintain record of responses and re-contact non-responders
- Maintain record of units
- returned/reconditioned/destroyed
- Maintain returned product under quarantine
- Destroy/recondition product under FDA supervision
- Make corrections to minimize probability that problem will repeat

Responsibilities of the FDA DISTRICTS

- Submit a 24 hour alert of the recall to the affected FDA centers
- Collect information on the recall
- Offer guidance on recall (recall strategy & communications)
- Submit a recall recommendation to the affected FDA Center
- Monitor the recall

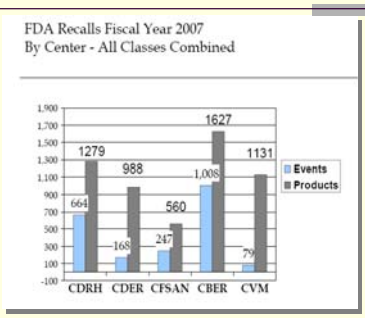
Responsibilities of the FDA DISTRICTS

- Witness product destruction or monitor the completion of an FDA approved reconditioning plan
- Initiate & monitor recall audit checks
- Notify the firm of recall classification and termination
- Terminate Class II and III recalls

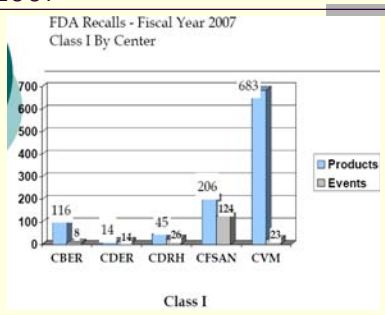
Responsibilities of the FDA Centers

- Receive & review recall recommendations
- Initiate Health Hazard Evaluations (HHE)
- Review and evaluate the firm's recall strategy
- Update FDA's recall database with recall classification, strategy and recommendations.
- Place recall information on the FDA Enforcement Report (weekly notice of recalls)
- Terminate Class I recalls

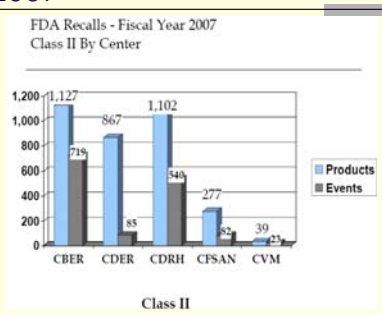
Recalls By FDA Center-FY2007



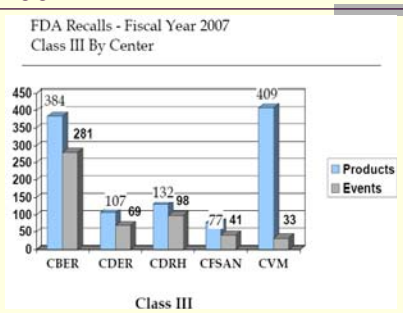
Class I Recalls By FDA Center-FY2007



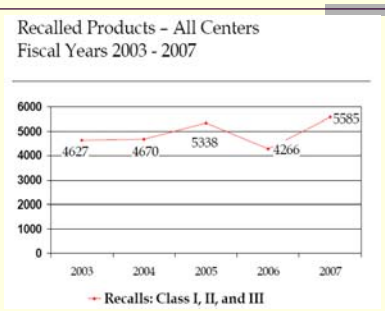
Class II Recalls By FDA Center-FY2007



Class III Recalls By FDA Center- FY2007



FDA Five -Year Recall Activity For All Centers



RESOURCES

- **WWW.FDA.GOV**
- **21 C.F.R. PART 7**
- **FDA REGULATORY PROCEDURES MANUAL, CHAPTER 7, "RECALL PROCEDURES" (MARCH 2006)**
- **FDA GUIDANCE FOR INDUSTRY, "PRODUCT RECALLS, INCLUDING REMOVAL AND CORRECTION" (NOVEMBER 2003)**
- **FDA INVESTIGATIONS OPERATIONS MANUAL, SUBCHAPTER 800, "RECALLS" (2008)**

Recall Contacts

- CDR Larry Howell
(949)608-4440
Larry.howell@fda.hhs.gov
- Tamala Bogan
(949)608-3504
Tamala.bogan@fda.hhs.gov
Food and Drug Administration
19701 Fairchild
Irvine, CA 92612
- A current list of FDA recall coordinators can be found on FDA's website at: http://www.fda.gov/ora/inspect_ref/iom/iomoradir_monitors.html#recall

California Department of Public Health Heparin Recall Inspection Findings

Loriann De Martini Pharm.D.
Chief Pharmaceutical Consultant
Center for Health Care Quality

Presentation Outline

- Overview of FDA Recall Process
- Regulatory Requirements – State /Federal
- Heparin Recall Notification Chronology
- CDPH Findings

FDA Recall Process

- "FDA has the responsibility for assuring the safety and efficacy of all regulated marketed medical products."
- Regulatory authority 21 Code of Federal Regulations (CFR) §§ 7.40 – 7.59
- Recall Policy

  To remove a product that is in violation of laws administered by FDA. [21CFR § 7.40]

FDA Recall Process: Health hazard evaluation and recall classification

- An evaluation of the health hazard will be conducted and will evaluate minimally the following factors:
  - "Whether any disease/injuries have already occurred
  - Whether any existing conditions could contribute to a medical situation that could expose humans to a health hazard.
- (3) Assessment of hazard to various segments of the population

21CFR § 7.41

FDA Recall Process: Health hazard evaluation and recall classification

- (4) Assessment of the degree of seriousness of the health hazard
- (5) Assessment of the likelihood of occurrence of the hazard.
- (6) Assessment of the consequences of the hazard.

21CFR § 7.41

FDA Recall Process: Health Hazard Evaluation and Recall Classification

- Based on the health hazard evaluation the FDA will assign the recall a classification (Class I, II or III)
- Class I: A situation in which there is a reasonable probability that the use of or exposure will cause serious adverse health consequences or death.
- Class II: A situation in which use may cause temporary or medically reversible adverse health consequences or where the probability of serious adverse health consequences is remote.
- Class III: A situation in which use is not likely to cause adverse health consequences."

FDA Recall Process: Recall Strategy

FDA will review the adequacy of a [illegible] recall strategy developed by a recalling [illegible] and recommend changes as [illegible].

[illegible]nts of a recall strategy includes:

- (1) Depth of [illegible]
- (2) Public warning.
- (3) Effectiveness checks.

21 CFR § 7.42

FDA Recall Process: Recall Communication

- A recalling firm is responsible for promptly notifying each of its affected direct accounts about the recall. The recall notices informs that the further distribution or use of any remaining product should cease immediately.
- Responsibility of recipient. Consignees that receive a recall communication should immediately carry out the instructions set forth by the recalling firm.

21 CFR § 7.49

Regulatory Requirements - Drug Recalls

1. Unlawful for any person to manufacture, sell, deliver, hold, or offer for sale any drug or device that is adulterated. [HSC 111295]. A recalled medication is an adulterated drug [HSC 111285]
2. [illegible]lawful for any person to receive in commerce any [illegible]evice that is adulterated or to deliver or offer for [illegible]y drug or device. [HSC 111305]
3. No [illegible] or [illegible]ed drugs shall be available for use. [illegible] 63(q)(9)]
4. The P&T committee shall develop [illegible] and procedures for establishment of safe and effective [illegible] of medications [CCR Title 22 § 70263(c)(1)].

Regulatory Requirements - Drug Recalls

5. Take all reasonable steps to conform to all applicable federal, state and local laws and regulations including those relating to….safety measures. [CCR Title 22 §70701(a)(5)]
6. Outdated, mislabeled, or otherwise unusable drugs must not be available for patient use. [42CFR § 482.25(b)(3)]
7. Drugs maintained on the nursing unit shall be inspected at least monthly by a pharmacist. [CCR Title 22 § 70263(q)(10)]

Regulatory Requirements - Drug Recalls

8. In order to provide patient safety, drugs must be controlled and distributed in accordance with applicable standards of practice, consistent with Federal and State law [42 CFR [illegible]25(b)]
   - Comment: "Medications dispensed by the hospitals are [illegible]ved when recalled. Survey [illegible] does [illegible]spital retrieve and remove medications [illegible] for patient use when the hospital has been [illegible] of a drug recall. Does the recall include notification of patients who have been impacted and those that would order, dispense or administer the medication?

Regulatory Requirements - Drug Recalls

10. The recipient of a recall notification "should immediately carry out the instructions set forth by the recalling firm." [21 CFR § 7.49(d)]

Heparin Recall Notification Chronology

Jan 25- Mar 28

- Baxter
- American Health Packaging (AHP).
- B.Braun
- Covidien – "Formerly of Tyco"

May 2 CDPH issues an All Facilities Letter
May 5 CSHP posts AFL 08-14 to it's website
May 9 FDA issues an e-alert.
May 9 CMS issues an e-alert to all provider types
May 9 ASHP issues a "Special ASHP NewsLink"
May 12 Baxter issues an "important recall reminder"
May 12 CSHP issues an e-alert.
May 16 CPhA CEO Message

Heparin Recall Notification Chronology

May 2 CDPH issues an All Facilities Letter (AFL 08-14). "requesting that you immediately review all of your drug storage areas, including emergency kits, dialysis units and automated drug storage cabinets to ensure that all of the recalled heparin has been removed."

Heparin Recall Notification Chronology

May 9 FDA issues an e-alert. "Help FDA spread the word about recalls of heparin. Affected heparin products have been found in medical care facilities in one state. Although product recall instructions were widely distributed they may not have been fully acted upon. There have been many reports of deaths associated after heparin administration. We ask that health professionals and facilities please review and examine all drug/device storage areas, including emergency kits, dialysis units and automated drug storage cabinets to ensure that all of the recalled heparin products have been removed are no longer available for patient use."

Heparin Recall Notification Chronology

May 9 CMS issues an e alert to all provider types mirroring the FDA e alert. Ensure that all of the recalled heparin products are removed and no longer available for patients."

May 9 ASHP issues a "Special ASHP NewsLink" "FDA today asked health professionals and facilities to examine all drug and device storage areas. We're asking folks to rethink about all the places where heparin is placed," said Jason Woo, an associate director in the Office of Compliance at FDA's Center for Drug Evaluation and Research. Woo said follow up work by an FDA field office revealed recalled heparin products in "more than a handful" of California hospitals. The products were found in crash carts, surgical units, cardiac catheterization laboratories, and automated drug dispensing cabinets and on pharmacy shelves, he said."

Heparin Recall Notification Chronology

May 12 Baxter issues an "important recall reminder" sent to all hospitals and clinics nationwide. "Baxter has been alerted by the FDA that on site effectiveness checks by state regulatory agencies have revealed certain hospitals and other health care facilities have failed to remove all previously recalled Baxter heparin products from potential use in their facilities. As indicated in previous communications sent to Baxter customers on February 29, 2008 due to an increase in reports of adverse patient reactions, Baxter performed a recall. There should be no Baxter heparin products remaining in your facility. To ensure patient safety, you must immediately locate and discontinue use of these heparin products.

Heparin Recall Notification Chronology

May 12 CSHP issues an e-alert. "Executive Officer Virginia Herold of the California Board of Pharmacy met with the CSHP Board of Directors at its recent board meeting. She reported that the Board of Pharmacy would be conducting inspections for recalled heparin. Recently, members have stated that they have also been surveyed by the California Department of Public Health (CDPH) for heparin related issues.

Heparin Recall Notification Chronology

May 16 CPhA CEO Message. "Earlier this month, both the California Department of Public Health and the Board of Pharmacy issued provider notices indicating that certain lots of Heparin have been recalled because of contamination of the raw material used to produce the products. However, state surveyors are still finding the recalled Heparin in nursing facility emergency kits. Please read the CDPH letter (attached) and act according to its instructions--be sure to pull all of the recalled Heparin from the emergency supply kits and any automated drug delivery systems.

CDPH Inspections

Purpose: Ensure Patient Safety – recalled medications are not available for patient use.

- Assess facility's recall process
- Determine potential clinical impact on patients. .
- Ascertain if recalled medications are available for patient use.

Facility Type Investigations

- End Stage Renal Dialysis (ESRDs)
- Hospitals

Activities coordinated with CDPH Food and Drug Branch

CDPH Findings - Hospitals

87 inspections were conducted

- 84 - BOP referrals
- 3 - CDPH identified

Assessment for presence of available recalled medications included heparin, Digitek and Procrit

Inspection dates May 1 through August 12th

Average length of inspection visit – one day

30% of hospitals were identified with recalled medications available for patient use

CDPH Findings - Hospitals

More than one in four hospitals were identified with recalled medications available for patient use after the BOP inspection.

Total potential patient exposures from recall to removal of medication(s): Thousands

Average lag time following BOP visit – 13 days

- Range: 1 to 32 days

CDPH Findings - Hospitals

Majority of recalled medications found available for patient use was heparin and principally Baxter

Location of found heparin was primarily in patient care areas and at dosage formulations greater than 100 units/ml

On average Baxter heparin was found 67.5 days after February recall notice

Summary

Findings reveal systemic deficits in hospital's recall process and drug distribution system.

Patient impact

Costly

Opportunity for Improvement

- Identify root causes of these deficits
- Develop plans of action aimed at system deficits
- Goal: prevent a reoccurrence