

Drug Shortages – Causes, Progress, and Strategies

EMS Drug Shortages Summit
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Disclosure

- This presentation represents my own opinions.



National Shortages and University of Utah Drug Information Service

- UU DIS provides drug shortage content to Novation and ASHP
- Public website at www.ashp.org/shortage
 - Partners since 2001
 - Receive voluntary reports submitted via web
 - Collaboration is key to success
 - Frequent communication with FDA drug shortage team



Shortage Website Differences

ASHP

- www.ashp.org/shortage
- Drugs impacting clinical practice (biologics, devices, dosage forms)
- What is available at NDC level
- How to access
- Frequent updates
- Alternatives

FDA

- www.fda.gov/cder
- Medically necessary drugs
- Information from manufacturer



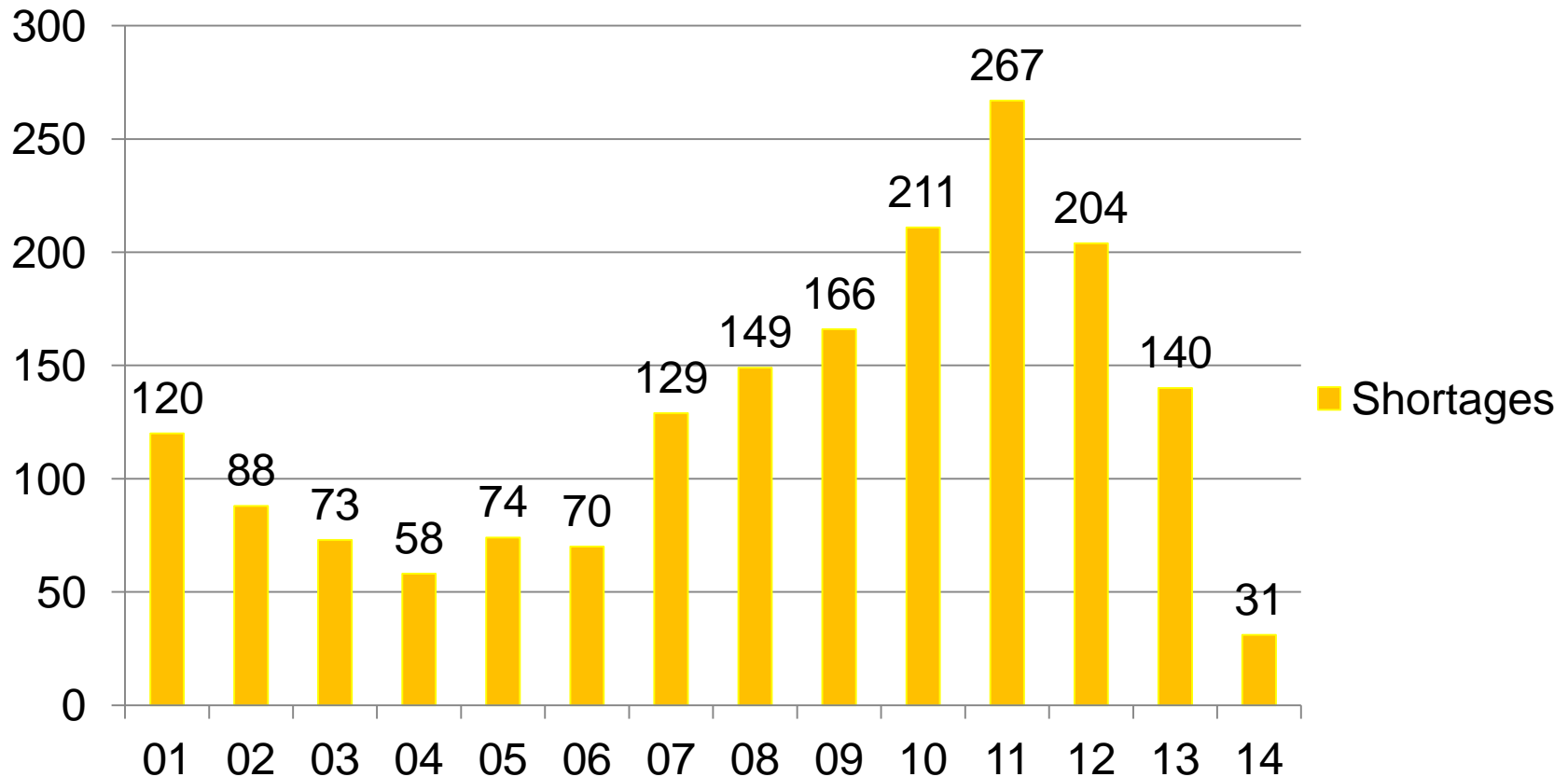
Current Trends



National Drug Shortages

New Shortages by Year

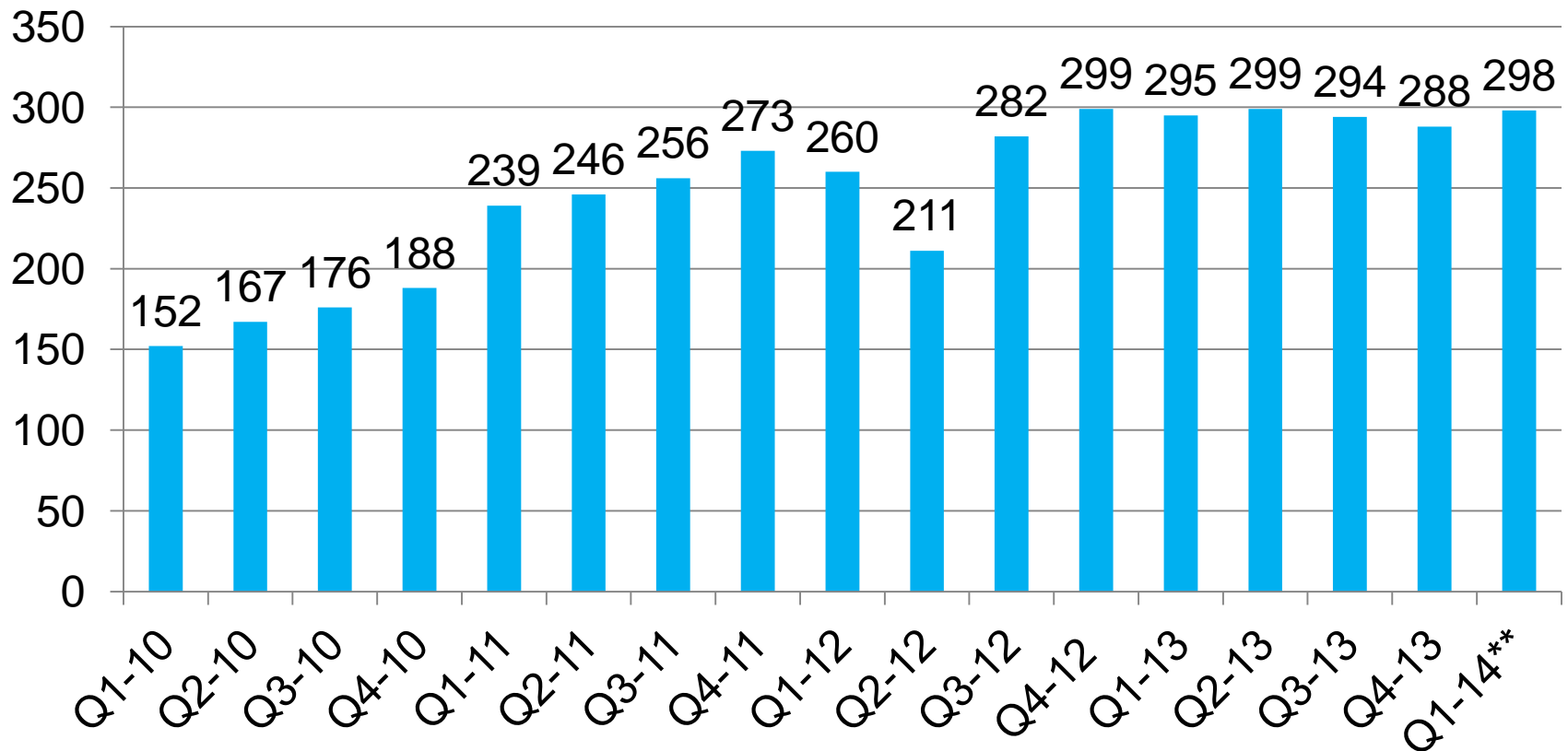
January 2001 to February 28, 2014



Note: Each column represents the number of new shortages identified during that year. University of Utah Drug Information Service

National Drug Shortages – Active Shortages by Quarter

Active Shortages



Note: Each column represents the number of active shortages at the end of each quarter. Q1-14 are data through 2/28/14.

University of Utah Drug Information Service

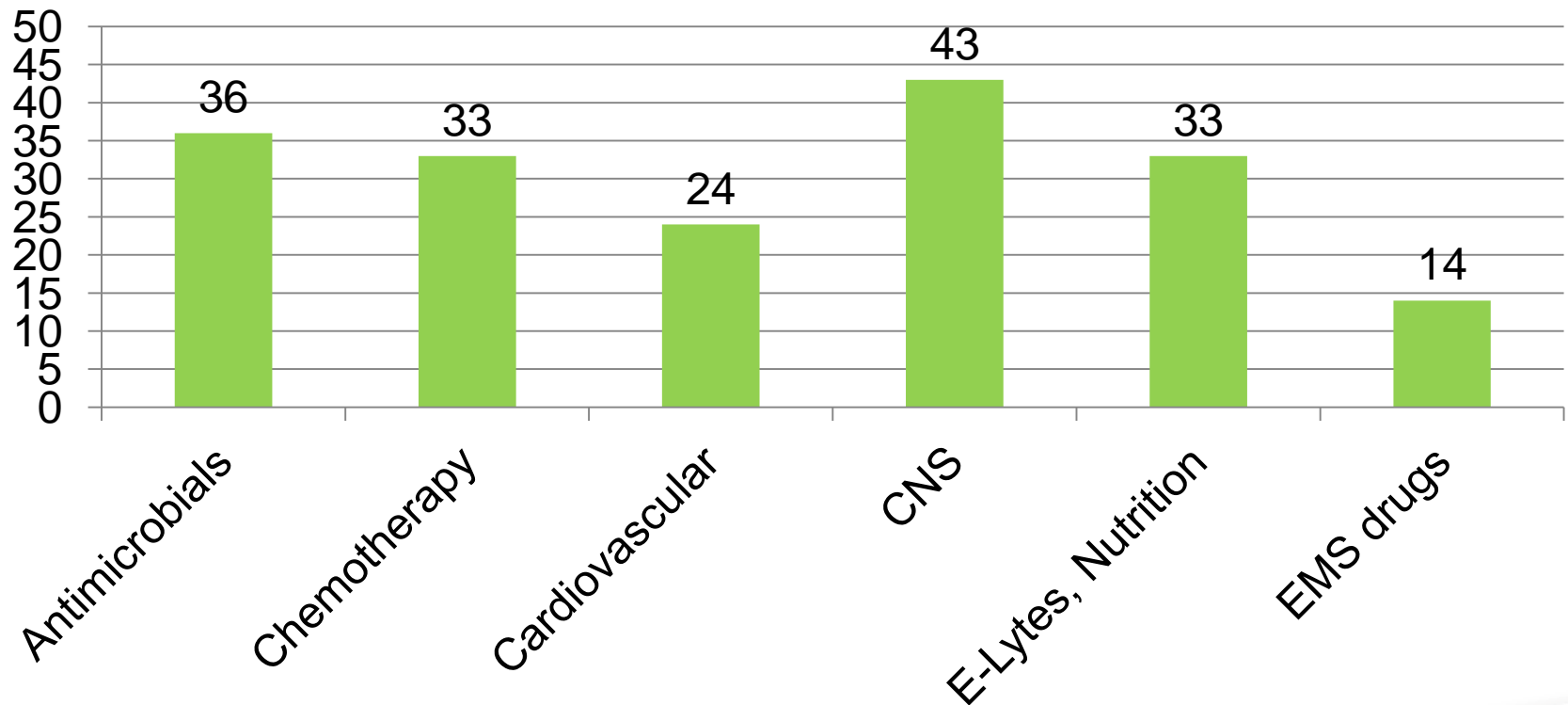
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Active Shortages By Selected Drug Classes

Active Shortages 2/28/14

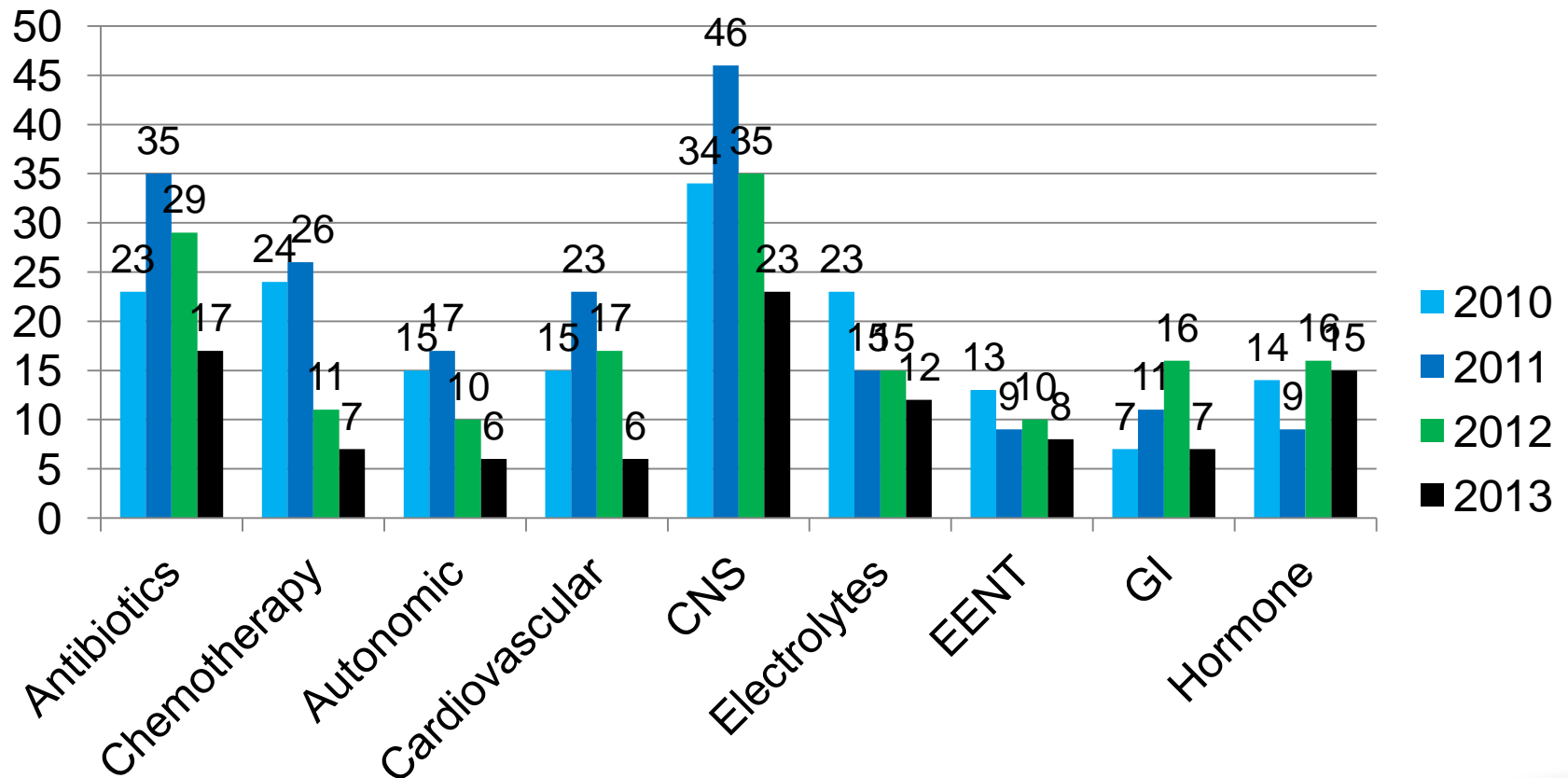


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Common Drug Classes in Short Supply – 2010 - 2013



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What do these numbers mean?

- The rate of new shortages has decreased
- The ongoing shortages are not resolving
- Continued daily impact for patients, clinicians, health systems, health care

<http://www.gao.gov/products/GAO-14-194>



Why is this happening?



Cascade of Events

Early 2000's

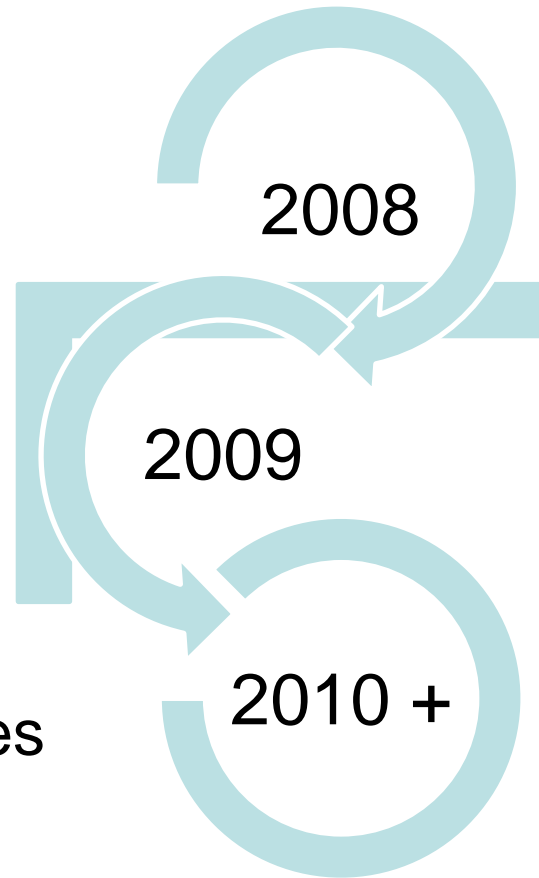
"Find efficiencies in drug production"

Dr. Hamburg
FDA increases
scrutiny

Irvine plant closes

New York plant
closes

30% manufacturing
capacity is closed



Heparin

Warning letters,
483's begin to
document serious
quality problems

Ohio plant
closes



Fragile Supply Chain - Sterile Injectables



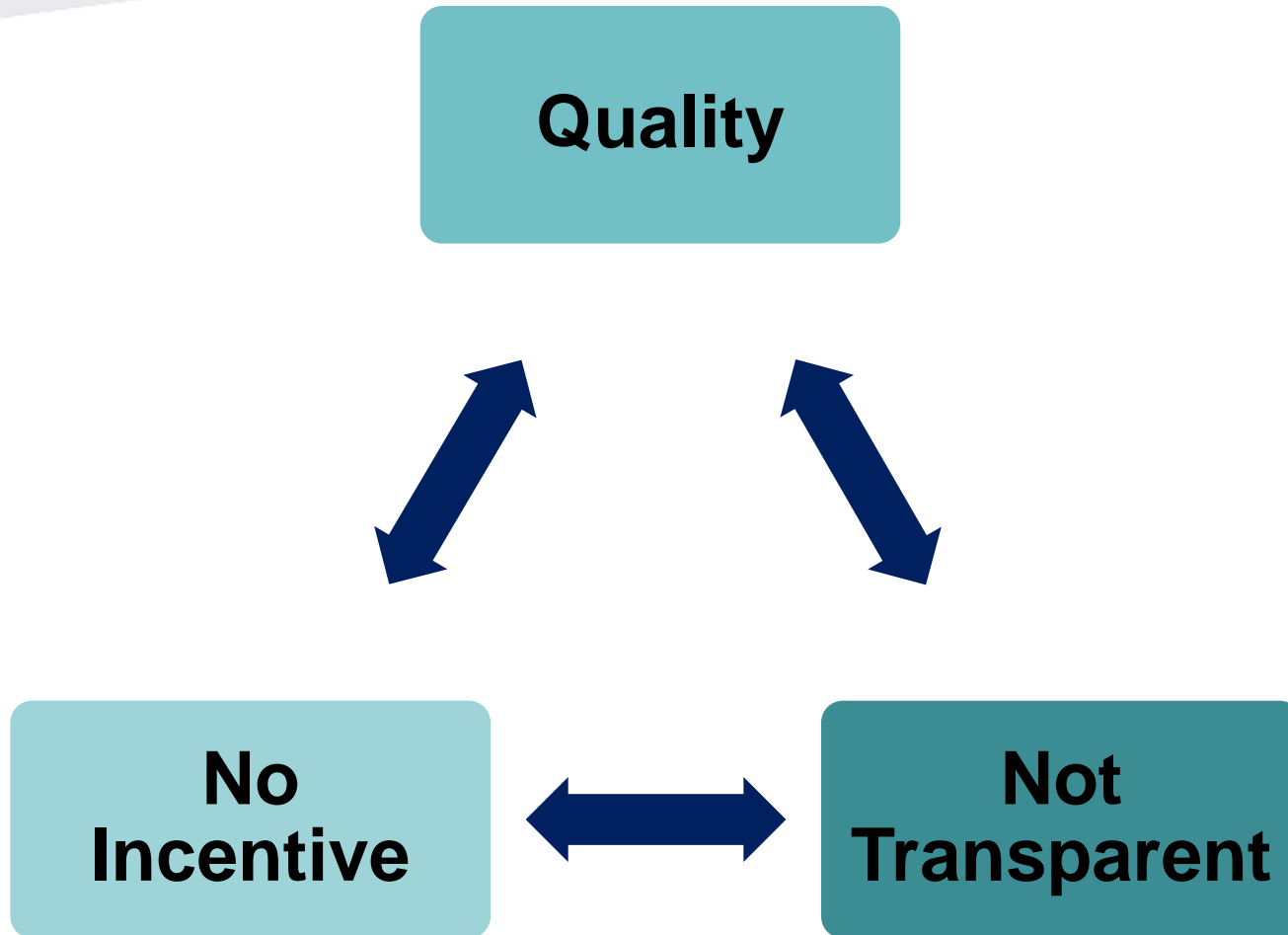
- Few suppliers (4 to 7)
- Lack of redundancy
 - Concentrated, “just in time” production, at capacity
 - Multiple products made on single line
- Complex manufacturing process
 - No simple fixes for quality problems
 - Problems typically affect multiple products
 - “Quality systems of manufacturing” – key cause identified by ISPE

<http://aspe.hhs.gov/sp/reports/2011/DrugShortages/ib.shtml>

<http://www.ispe.org/drug-shortages-initiative>



Economic Drivers



Clin Pharmacol Ther. 2013;93:170-176
Clin Pharmacol Ther. 2013; 93:145-147



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Law of Supply and Demand???

- Manufacturers produce on an ultra lean, just in time production schedule
- Number of products increased without additional capacity
- No suppliers to step in when others can't produce
- Patients, not suppliers



Example – Fragile Supply Chain

Electrolyte / Nutrition Shortage

Key supplier

Warning letter 2011

Closed in 2012

Trace elements*

Zinc, Selenium*

Sodium phosphate

Potassium phosphate

Calcium gluconate

Calcium chloride

Sodium bicarbonate

- Zinc shortage results in dermatitis at Children's National



Photo/S.A. Norton, Children's National Medical Center

Shortages of EMS Basics

- Frequent fliers
- 10 medications short > 50 times between 2001 and 2013
 - Dextrose, diazepam, epinephrine, fentanyl, lorazepam, morphine, ondansetron, nalbuphine, naloxone, promethazine



IV Fluids Shortage

- 3 suppliers
- All suppliers state “increased demand”
- “Real story” remains unclear
- Rolling shortages, unclear allocations (expect problems at least until June)
 - Available fluid type, volume will vary
 - FDA working on imported product



Minimizing Impact National Level



Summits

- ASA, ASCO, ASHP, ISMP – Invitation Shortage Summit – November 2010
- FDA Public Workshop on Drug Shortages – September 2011
- ASHP Drug Shortage Summit 2.0 – April 2013



GAO Report - 2011

- 1190 shortages between 1/1/01 – 6/20/11
- Average duration 286 days
- 64% of shortages were frequent fliers
- Strengthen FDA's ability to respond
 - Congress should require manufacturers to report to FDA
 - FDA should enhance ability to respond

<http://www.gao.gov/products/GAO-12-315T>



GAO Report - 2014

- Ongoing drug shortages remain a problem.
- FDA is working to prevent shortages
- FDA should enhance data analysis to focus on early identification of risk factors.

www.gao.gov/products/GAO-14-194



ASPE Economic Analysis 2011

- Limited capacity will take years to resolve
- Pricing
 - For 44 oncology products short since 2008, prices decreased by a mean of 26.5% between 2006 and 2008. Oncology products not impacted by shortages showed no price decreases.
- <http://aspe.hhs.gov/sp/reports/2011/DrugShortages/ib.shtml>



Government Action

- Executive Order – 10/31/11
- FDA Interim Final Rule – December 2011
- Senate and House Bills provide basis for language included in FDASIA / PDUFA

<http://www.ashp.org/menu/Advocacy/FederalIssues/DrugShortages.aspx>



FDASIA

- Drug shortage language around notifications
- Requires FDA Strategic Plan
- President signed into law July 9, 2012



FDA Strategic Plan

- Mandated as part of FDASIA law (2013)
- 2 key goals
 - Enhance mitigation efforts
 - Develop long-term prevention
- Suggestions for external stakeholders
 - Manufacturing incentives
 - Use quality data when purchasing
 - Capacity, redundancy

www.fda.gov/downloads/Drugs/DrugSafety/DrugShortages/UCM372566.pdf



Making a Difference?

- + FDA prevents hundreds of shortages
- + More suppliers choose to work with FDA early
- + Decreased rate of new shortages
- Ongoing shortages not resolving
- Manufacturing problems
- Continued patient impact



Coping



Strategies for EMS Shortages

- Make different purchasing and inventory decisions
- Use alternatives
- Consider compounded product
- Use expired product



Purchasing / Inventory

- Purchase from more than 1 source
 - Direct accounts?
- Can you buy a different form? (vials vs. prefilled syringes)
- Inventory strategies may minimize waste
- Consider quality?



Form 483 & Warning Letters

- 483 - documents inspection findings
- Warning letters – significant issues
- Worth reading!
 - Metal particles, mold, contamination
 - Insects, animals
 - Urine
 - Manipulating data, mixing failed API with passing API

<http://www.fda.gov/ICECI/EnforcementActions/ucm256377.htm>



Alternatives

- Check www.ashp.org/shortage for suggestions
- IV fluids shortage – may need to substitute a variety of products for NS, LR
- May require education, training, protocol reviews / adjustments
- Beware of dosing errors



Compounded Product

- Dating or refrigeration requirements may be a problem – will require logistics around inventory
- (Must) purchase from a registered outsourcing facility (check at FDA)
- Quality matters – poorly compounded product can be deadly

www.fda.gov/drugs/guidancecomplianceregulatoryinformation/pharmacycompounding/ucm378645.htm



FDA and Compounding

- Summary page provides links to actions, recalls, Med Watch alerts, inspections

CDER Statement: FDA alerts pharmacies to concerns with testing conducted by Front Range Laboratories

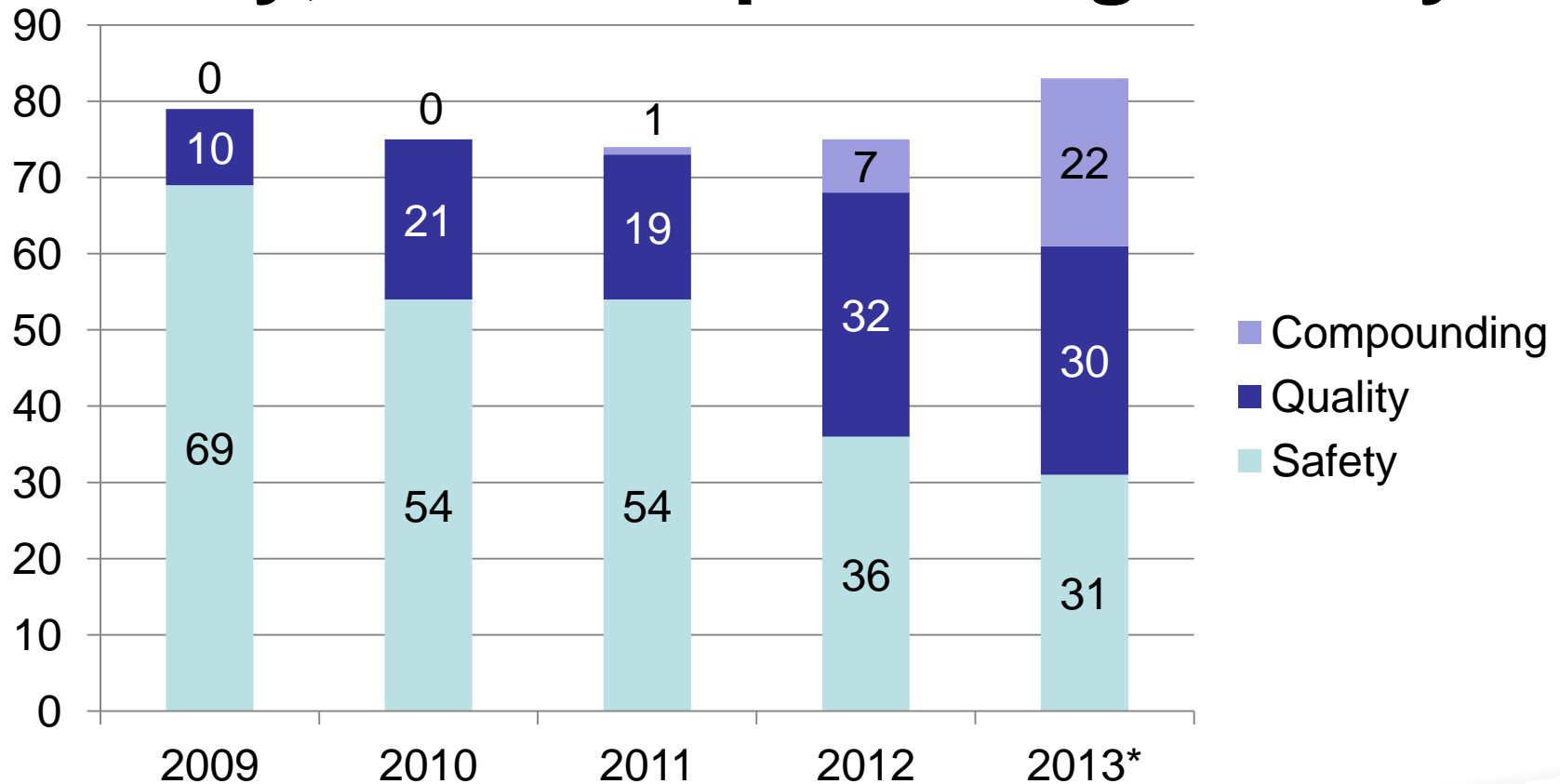
[8/21/13] The U.S. Food and Drug Administration is advising pharmacies of concerns about the adequacy of testing performed by Front Range Laboratories, Inc., in Loveland, Colo., a testing laboratory used by more than 100 pharmacies in 32 states, to verify quality, sterility, and expiration dating.

<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/default.htm>



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Med Watch Trends – Reports Related to Safety, Medication Quality, and Compounding Quality



<http://www.fda.gov/Safety/MedWatch/default.htm>



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Use Expired Product

- Last resort option
- Efficacy – may or may not be potent
- Consider each product, no blanket exceptions
- Standard approach



Crystal Ball Predictions



It's going to get worse before it gets better....

- FDA increasing inspectors in India
 - Many generic houses moving production
 - Ranbaxy, Wockhardt bans
 - Falsified data, shoddy product
- No new large suppliers (Ben Venue)
- Focus on biosimilars
- Who will make the basics that we need?



But there is some hope

- Trend of decreasing new shortages is real
- Some manufacturers are stepping up, new production models for quality
- Action is moving towards prevention, early identification of manufacturing issues

