COMMUNITY CATALYST

Protecting Seniors
by Ensuring Safe Drug Manufacturing

Seniors at risk from counterfeit or contaminated drugs

The use of prescription medications by seniors has risen by 39% in the last decade.[1] In fact **ninety percent of seniors rely on a prescription medication on a regular basis.**[2] As many as 40% of adults aged sixty-five or older use five or more different medications weekly, with 12 % of this group using ten or more different medications.[3] Overall prescription drug use by seniors accounts for a third of all prescriptions dispensed in the U.S.[4]

The U.S. pharmaceutical industry produces vital and innovative medicines that contribute to the health and independence of seniors. For instance, the availability of drugs to treat major chronic illnesses such as heart disease and hypertension have increased the use of prescription drugs by seniors significantly.[5]

However, vulnerabilities in the manufacturing processes and distribution system for these products have become a critical public health concern. As a result of manufacturing problems domestically and overseas, U.S. patients have seen shortages of critically needed products, pills with incorrect doses, mislabeled bottles of medicine, different drugs mixed in the same bottle[6], and contamination by mold, bacteria and viruses. Any one of these problems could cause a public health crisis.

Drug manufacturing has spread across the globe, beyond adequate inspections or industry quality controls.

The manufacture of pharmaceuticals has changed dramatically in recent years, due to industry globalization and outsourcing.[7] Currently, 40% of finished drug products and 80 % of the active drug ingredients and bulk chemicals used to make drugs are imported from 150 countries across the globe.[8] The number of registered foreign manufacturing sites -- 3,800 in 2009 -- now exceeds the number of domestic drug manufacturing facilities.[9]

This drive to outsource drug manufacturing has been fueled by the lower production costs overseas. For instance, the FDA reports that production of active pharmaceutical ingredients in India can cost between 15 and 40% less than in the U.S.[10] Unfortunately many of these overseas locations have weak regulations that allow inadequate or non-existent government oversight of manufacturing quality.[11]

Manufacturers' current audits of these overseas suppliers are insufficient protection in the increasingly complex global supply chain. In fact, as many 39% of drug manufacturers

themselves may be receiving inaccurate or false information about the origin and quality of the chemical ingredients they import to make finished drug products.[12]

Seniors at risk

The increased use of prescription medications among the elderly has created concerns about safety, as well as access and affordability. The heightened exposure to prescription medications and changes in pharmacokinetics (how the body responds to drugs) related to aging makes older adults more likely to experience medication-related adverse events.[13] Hence the consequences of adulteration of medications would be more severe upon more vulnerable seniors.

Higher rates of prescription drug use and increased vulnerability mean that the importance of the quality of prescription drug therapies to seniors cannot be overstated. Undetected impurities or contaminants introduced in the manufacturing process have the potential to cause serious harm to hundreds of thousands of the millions of seniors that rely upon needed drugs. The experience with contaminated Heparin illustrates this concern.

Seniors harmed or placed at risk by Heparin contamination

In 2007, over 300,000 people, primarily seniors, with end-stage renal disease received dialysis treatment.[14] Elderly patients with acute kidney injury (AKI) have an increased risk for end-stage renal disease.[15] In 2007 and 2008, numerous U.S. patients died, and many more suffered adverse reactions after exposure to contaminated Heparin, a blood-thinner that is nearly ubiquitous in these treatments.[16] The toxic ingredient was introduced by a supplier in China and was likely a deliberate substitution to lower production costs.[17] Suspect lots of Heparin were soon recalled, but contamination concerns have lingered, causing recalls as recently as October of 2010.[18]

As outsourcing overseas increases, so will risks

A special report from the FDA warns that economic pressure to maintain profits has driven the outsourcing of drug manufacturing to places like India and China, where drug manufacturing costs 30 to 40% less.[19] Even 'high risk' medical products such as vaccines and complex medical devices formerly manufactured primarily in the U.S. are now outsourced.[20] Furthermore, the dramatic outsourcing of the last eight years will likely increase as the dwindling number of new drugs in the pipeline creates more pressure to maintain profits on fewer products.[21] One major manufacturer has made public its plans to shift production of **all** its active ingredients to China and India.[22]

Such outsourcing, without strong FDA oversight, creates risks that quality may be sacrificed in the drive to cut costs. The agency currently does not have the resources to inspect these foreign plants at the level it does domestically (where plants are inspected every 2.7 years on average.) The GAO reported that at current levels of FDA staffing and resources, the agency could only inspect foreign facilities once every nine years, and that **some foreign suppliers may never be**

inspected.[23] The FDA warns that risks of counterfeit drugs (already a leading black-market industry globally), will increase as will the dangers of fraud and adulteration, as suppliers become more numerous and supply chains became more complex.[24]

Given the volume of imported drugs for the U.S. market, it is impossible to test all products at the border. Indeed it is impossible to test all products, whether made at foreign or domestic sites, before they reach patients. For this reason, companies must be held accountable for current Good Manufacturing Processes (cGMP), to ensure adequate oversight of all their processes, both in-house and outsourced, domestically and abroad.

Policies to ensure the safety and quality of drug manufacturing

The FDA's ability to keep pace with industry changes and protect consumers from unsafe drugs has diminished due to inadequate funding and authority. Legislation is needed to give FDA the means to protect consumers from these risks. We call on Congress to pass legislation to:

- Update standards to ensure industry supply chain control
- Improve FDA oversight of high risk plants, especially overseas.
- Give FDA updated authority to mandate recalls and to destroy adulterated products at the border
- Improve drug distribution security through a national system to track and authenticate drugs

Legislators, the FDA, senior and consumer organizations, and industry have all acknowledged the need to strengthen the pharmaceutical supply chain in order to protect patient safety and health. More information can be found at http://www.prescriptionproject.org/initiatives?id=0003 and at http://www.communitycatalyst.org/projects/prescription_access_and_quality/issues?type=drug-safety

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[1] Prescription Drug Costs: Background brief. KaiserEDU.org website. http://www.kaiseredu.org/Issue-Modules/Prescription-Drug-Costs/Background-Brief.aspx updated February 10, 2010. Accessed March 11, 2011.

[2] Agency for Healthcare Research and Quality. Prescription Medicines-Mean and Median Expenses per Person With Expense and Distribution of Expenses by Source of Payment: United States, 2007. Medical Expenditure Panel Survey Component Data. Generated interactively. (February 4, 2010); *See also* Patterns of Medication Use in the United States 2006: A Report from the Slone Survey Slone Epidemiology Center. Boston University.

[3] Avorn Jerry. Polypharmacy: A New Paradigm for Quality Drug Therapy in the Elderly? Archives of Internal Medicine/vol 164, October 2004.

[4] Families USA, Cost Overdose: Growth in Drug Spending for the Elderly, 1992-2010, at 2 (July 2000)

[5] Id. *See also* Goulding M.R. *Trends in Prescribed Medicine Use and Spending By Older Americans*, 1992-2001. National Center for Health Statistics, avail. at http://www.cdc.gov/nchs/data/ahcd/agingtrends/05medicine.pdf.

[6] U. S. Department of Justice, *GlaxoSmithKline to Plead Guilty and Pay $750 Million to Resolve Criminal and Civil Liability Regarding Manufacturing Deficiencies at Puerto Rico Plant*, Oct. 26, 2010, available at http://www.justice.gov/opa/pr/2010/October/10-civ-1205.html.

[7] Pew Health Group, *After Heparin: Protecting Consumers from the Risks of Substandard and Counterfeit Drugs.* July 2011, at 27, 30, and generally, available at http://www.pewtrusts.org/uploadedFiles/wwwpewtrustsorg/Reports/Health/Pew_Heparin_Final_HR.pdf

[8] FDA, *Pathway to Global Product Safety and Quality*, June, 2011, at 15, available at http://www.fda.gov/AboutFDA/CentersOffices/OC/GlobalProductPathway/default.htm. See also U.S. Government Accountability Office. (2007, November). Drug Safety: Preliminary Findings Suggest Weakness in FDA's Program for Inspecting Foreign Drug Manufacturers. (Publication No. GAO-08-224T)

[9] Autor, Deborah M., Esq. Director, CDER Office of Compliance. "Globalization: Challenges and Recent Case Studies." March 18, 2009. Presentation.

[10] FDA, *Pathway to Global Product Safety and Quality*, at 15.

[11] U.S. Government Accountability Office, *Better Data Management and More Inspections Are Needed to Strengthen FDA's Foreign Drug Inspection Program*, Sept. 2008, at 15, at http://www.gao.gov/products/GAO-08-970.

[12] Pew Health Group, *After Heparin* at 27, 30.

[13] Cornelius Christel. Drug use in the elderly: risk or problems. Current Opinion in Psychiatry 2004, 17:443-447.

[14] National Kidney and Urologic Diseases Information Clearinghouse, NIH, available at http://kidney.niddk.nih.gov/kudiseases/pubs/kustats/#2 (noting that in 2007, "368,544 U.S. residents with ESRD received dialysis.")

[15] Laurie Barclay, MD, et al. Acute Kidney Injury in Elderly May Increase Risk for End-Stage Renal Disease, Medscape Medical News, November 2008.

[16] The FDA initially reported 149 deaths at www.fda.gov/Cder/drug/infopage/ heparin/adverse_events.htm, based on patients with symptoms consistent with those caused by the contaminant. This represents a marked increase in deaths over the previous year, but some reports may have been stimulated by public awareness, and causality cannot be determined precisely.

[17] Pew Health Group, *After Heparin* at 16.

[18] Andrew Zajac, *Irvine Medical Products Company B. Braun Recalls Possibly Tainted Heparin*, L.A. Times, Oct. 27, 2010.

[19] FDA, *Pathway to Global Product Safety and Quality*, June, 2011, at 20, available at http://www.fda.gov/AboutFDA/CentersOffices/OC/GlobalProductPathway/default.htm.

[20] FDA, *Pathway to Global Product Safety and Quality, at* 18

[21] FDA, *Pathway to Global Product Safety and Quality, at 9.*

[22] Jarvis, Lisa M. *AstraZeneca Leaves Manufacturing: British firm looks to China for its pharmaceutical chemical production needs*. Chemical & Engineering News. Volume 85, Number 31, July 30, 2007.

[23] U.S. Government Accountability Office. (2007, November). *Drug Safety: Preliminary Findings Suggest Weakness in FDA's Program for Inspecting Foreign Drug Manufacturers*. (Publication No. GAO-08-224T)

[24] FDA, *Pathway to Global Product Safety and Quality* at 9, 21.