

Editorial

Quality Products at a Reasonable Price

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Low-cost manufacturing may come at a steep price.

It is no secret that companies from all sectors of the pharmaceutical industry have been accelerating an Eastward march to position research, development and manufacturing operations in developing countries. While there is no doubt that companies are jockeying to capture their share of the fast-growing consumer markets, the other side of the coin is that increasing competition and the public's incessant demand for inexpensive medicine is pushing branded, generic, and biotech manufacturers to outsource and "off-shore" operations in an effort to reduce costs. Pharmaceutical manufacturers are only the latest of many industries to source operations in developing countries, where they are attracted by tax incentives, less-complex environmental standards, and lower wages.

In a March 2007 World Pharmaceutical Frontiers article,¹ Joseph Acker indicated that the US General Accounting Office estimated 80% of our active pharmaceutical ingredients (API) were imported. During this period of realignment, the strength of the global pharmaceutical quality assurance system is more of a concern than ever. Unfortunately, persistent limitations on the international inspection capacity of the FDA, along with the policies of countries which sometimes require FDA to provide notice well in advance of inspections, may provide incentive for companies to locate offshore for the purpose of reducing the cost of compliance.

The recent recall of a popular heparin product brings to the forefront such recurring questions regarding the regulation of overseas pharmaceutical manufacturers. While the actual cause of the quality problem at the root of the heparin recall has yet to be determined (as this is written), well over 300 adverse reactions, including 4 deaths, are suspected to have been caused by active pharmaceutical ingredient (API) from an overseas plant that was never inspected by the FDA. The importance of risks to patient health posed by such quality problems, as well as the potential for supply disruptions due to the recall of lifesaving medications, should not be discounted.

While regulatory authorities and manufacturers alike promote Quality by Design (QbD) as a philosophy that promises to improve product quality, appropriate quality control systems must be maintained to protect our nation's drug supply. The complex supply chain that pharmaceutical manufacturers sustain in today's world, coupled with the current inspection process, have caused a situation where foreign manufacturing facilities may present increased risk to a safe drug supply. Technologies facilitating rapid quality measurements could enable the development of supplemental cGMP inspection protocols which might be applied to products (including raw materials) being shipped from countries where FDA does not currently have total operating freedom.

Improvements in the safety of our drug supply could be achieved through development of modern technologies for rapid *in situ* characterization of pharmaceutical raw materials and finished goods- techniques such as XRD, solid state NMR, NQR (nuclear quadrupole resonance), Raman, and near infrared spectroscopy would enable *in situ* analysis of pharmaceutical materials for the detection of counterfeit, adulterated and degraded drugs.

Despite the cost-savings that pharmaceutical manufacturers can achieve by off-shoring, good reasons exist for maintaining a strong domestic manufacturing industry. Advanced manufacturing technologies, such as continuous processing and PAT, have the potential to drastically reduce production costs and environmental footprint, which would go a long way toward reducing the incentive for shareholders to seek offshore production in low-wage, environmentally-lax countries. Furthermore, while populist sentiments are on the rise, and recent surveys show that consumers' favorability of "big pharma" is only slightly above "big oil" (and below HMOs),² we can scarcely afford another reason for our industry to be fingered as a scapegoat for the problems in healthcare.

Today's pharmaceutical products provide cost-effective therapies for the treatment of many diseases, thanks to the efforts of manufacturers and regulators. Innovator companies continue to invest heavily in the research that is required to identify and develop new life-saving medicines while the generic industry maintains its effort to provide low-cost alternatives for those brand-name products for which patents have expired. Regulatory authorities protect the public by overseeing drug development and manufacturing in a complex global marketplace. Certainly, today's pharmaceutical products must be considered safe and effective. However, if we are to maintain the public's trust, we are obliged to recognize new risks to our drug supply and take advantage of modern technologies in our efforts to provide quality products at a reasonable price.

¹ "Trouble With Trust," Joseph Acker, *World Pharmaceutical Frontiers*, March, 2007.

² "Views on Prescription Drugs and The Pharmaceutical Industry" (The Kaiser Family Foundation, 2005).

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