Blowing the Whistle on cGMPs: The Next Big Challenge for Compliance

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Why This Matters Now

- Increased potential for use of whistleblower laws in exposing violations of drug manufacturing regulations (cGMPs), both in the US and abroad
- High profile cGMP whistleblower actions since 2010: GlaxoSmithKline and Ranbaxy: total $1.25 billion in criminal and civil recoveries
- Manufacturing violations need to be part of corporate compliance programs -- beyond Quality Assurance

What are cGMPs?

- cGMPs = current Good Manufacturing Practices for drugs, 21 CFR Parts 210 and 211
- Contain minimum requirements for the methods, facilities, and controls used in manufacturing, processing, and packing drugs; designed to ensure that product is safe and has the ingredients and strength it claims to have
- Drugs are adulterated if not made in compliance with cGMPs. 21 USC Sec 351(a)(2)
- Drugs are adulterated if the strength, quality, or purity differs from description in official compendia. 21 USC Sec 351(b)

False Claims Act *Qui Tam* Whistleblower Law

- Federal and thirty State FCAs create civil causes of action for fraud on the government, broadly defined
- Treble damages and penalties of $5,500-$11,000 per violation
- Action can be brought both by the government and by a private citizen in the name of the government (the *qui tam* "relator")
- Relator is entitled to receive between 15% and 30% of the proceeds (with exceptions) plus attorneys fees and costs

U.S. et al. *ex rel.* Cheryl Eckard v. GlaxoSmithKline and SB Pharmco Puerto Rico

- *Qui tam* case filed 2004 by former GSK Manager of Global Quality Assurance
- Allegations of system-wide cGMP violations at GSK's Cidra, Puerto Rico, facility, including:
  - Chronic product mix-ups
  - Super- and sub-potent diabetes drugs
  - Infant antibiotic and injectible drugs for cancer patients contaminated with microorganisms
  - Air handling systems created potential for cross-contamination
  - Investigations of non-conforming product not done
  - Ineffective Quality System

U.S. et al. *ex rel.* Cheryl Eckard v. GlaxoSmithKline and SB Pharmco Puerto Rico

- $750M settlement and criminal plea October 2010
  - $600M civil: GSK sold the government drugs made at Cidra that were adulterated
  - $150M criminal: GSK subsidiary SB Pharmco released batches of those drugs in interstate commerce with intent to defraud and mislead
- Largest drug seizure in FDA history
- Consent decree
- Plant shut-down

U.S. et al. ex rel. Dinesh Thakur v. Ranbaxy USA, Inc., et al.

- Qui tam case filed in 2007 by former Director of Research Information & Project Management at Ranbaxy
- Allegations of systemic cGMP violations at the Paonta Sahib and Dewas facilities in India affecting hundreds of generic products included:
  - Falsified bio-equivalence data and studies to get approvals for generic drugs
  - Bioequivalence studies conducted on innovator drugs that were ground up and represented as generic formulation
  - Fabricated stability studies filed with FDA
  - Sub-standard API mixed with good API to make it pass

U.S. et al. ex rel. Dinesh S. Thakur v. Ranbaxy USA, Inc., et al.

- $500M settlement and criminal plea May 2013
  - $350M civil: Ranbaxy sold the government, including PEPFAR (foreign aid program), drugs that did not conform to their purported properties or were not made according to approved formulas, and made false statements to FDA
  - $150M criminal: with intent to defraud and mislead, Ranbaxy: released non-conforming drugs in interstate commerce; failed to file Field Alert Reports with FDA; and made false statements to FDA in Annual Reports
- Consent decree
- Import bans

DOJ Broad View of FCA liability in cGMP Cases

- FCA liability may arise "where the [cGMP] violations are significant, substantial, and give rise to actual discrepancies in the composition or functioning of the product."

- "Moreover, in some situations, manufacturing deficiencies may affect the strength, purity and/or quality of the affected drug such that the drug is essentially 'worthless' and not eligible for payment by the government."

DOJ Statement of Interest filed in US *ex rel.* Rostholder v. Omnicare, No. 1:07-cv-01283 (D. Md. Nov. 18, 2011)

DOJ SOI in Omnicare, cont'd

- "[W]here the defendant has engaged in a fraudulent course of conduct involving [cGMP] violations, the touchstone is whether the defendant's conduct compromised 'the reliability and trustworthiness of a claim' such that it might cause the government to actually refuse payment."

- "[T]he core question for 'falsity' under the FCA is whether the government received the benefit of its bargain."

Increased DOJ Scrutiny on cGMPs

- "[W]hen companies fail to follow current good manufacturing practices, they often place patients at great risk of harm that neither they nor their doctors have any way of mitigating or even recognizing. We are very concerned any time it appears that a company is gambling with patient health for monetary gain …"
- "We will … be taking an especially hard look whenever patients are placed at an unacceptably high risk of harm by those violations of current good manufacturing practices…"
- "…GMP will be one of our top areas of focus…"

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2013 CBI Pharmaceutical Compliance Congress

Companies Increasingly Exposed to cGMP Whistleblower Cases in the US and Abroad

- False Claims Act:
  - GSK and Ranbaxy show DOJ will use FCA as enforcement tool for cGMP misconduct both in the US and overseas
  - 2009 FCA amendments: liability extends to funds administered by the US even if not US funds, e.g. foreign aid
- SEC Whistleblower actions under Dodd Frank 2010:
  - Conduct involves company publicly traded in the US and material information has been concealed from investors
  - Conduct can be outside of the US
  - Foreign Corrupt Practices Act: bribery of foreign officials by US company is a securities law violation

How Big Is the Problem?

- 7,021 FDA-registered drug plants in the US
  - inspected by FDA on average every 30 months
- 3,525 foreign drug plants registered in FDA database
  - Inspected on average every 9 years
  - 374 inspected in 2012 (10.6%)

cGMPs are now in Corporate Integrity Agreements

- In 2012 GSK entered into 5-year Corporate Integrity Agreement with HHS OIG
  - Requires cGMP Compliance Officer, Program and senior executive Committee
  - Board of Directors must attest to effectiveness of cGMP Compliance Program
  - Must allow HHS-OIG access to all documents related to cGMP activities and report annually to OIG
  - HHS OIG may require GSK to initiate recalls – failure to do so is a "material breach" which may result in exclusion
  - Must report cGMP-related "probable violations" to OIG
  - Covers products made in foreign plants and released in US