Takeaways From Largest Drug Safety Settlement

Law360, New York (June 14, 2013, 12:07 PM ET) -- On May 13, 2013, generic drug manufacturer Ranbaxy USA Inc., a subsidiary of Indian generic drug manufacturer Ranbaxy Laboratories Limited, pleaded guilty to seven felony charges as part of a global settlement pursuant to which Ranbaxy will pay a total of $500 million to resolve criminal and civil False Claims Act liability.[1]

In pleading guilty, Ranbaxy admitted to manufacturing and distributing adulterated drugs made at two of Ranbaxy's facilities in Ponta Sahib and Dewas, India, failing to file required reports with the U.S. Food and Drug Administration and making material false statements to the FDA. Ranbaxy Laboratories Limited's press release following the settlement noted that the conduct at issue occurred several years ago and that Ranbaxy's current management cooperated fully in the U.S. Department of Justice's investigation.

The settlement follows upon Ranbaxy's 2012 consent decree of permanent injunction and represents the largest drug safety settlement to date with a generic drug manufacturer. The settlement also makes good on government threats to use criminal and civil enforcement tools, including the FCA, to address serious manufacturing violations.

However, significant questions exist regarding the viability of such violations as the basis for FCA liability.

History of Ranbaxy's Manufacturing and Data Integrity Violations

In January 2012, Ranbaxy Laboratories Limited, its senior vice president, head global quality and its managing director, as well as Ranbaxy USA Inc. and its regional director for the Americas, entered a consent decree of permanent injunction with the FDA, acting through the U.S. Attorney's Office for the District of Maryland.

The consent decree was filed along with a complaint for permanent injunction that alleges a history of good manufacturing practices (GMP) violations identified during FDA inspections, failures to file various reports with the FDA and significant deficiencies affecting the integrity of data submitted to the FDA. These various failures led the FDA to issue two warning letters to Ranbaxy in 2008 and another in 2009 and to place three Ranbaxy facilities in India on import alert in September 2008.

Pursuant to the consent decree, Ranbaxy is enjoined from manufacturing drugs at the Ponta Sahib and Dewas facilities until the facilities have been brought into full compliance with GMP. The consent decree also comprises notable data integrity requirements, including an audit of pending applications, the implementation of new procedures and controls to ensure data integrity and the withdrawal of applications found to reflect untrue statements of material fact or a pattern or practice of data irregularities.

Ranbaxy also agreed to relinquish 180-day marketing exclusivity rights for three

pending generic drug applications, and additional applications are at risk if the consent decree's deadlines are not met.

Terms of the Global Settlement

The May 13, 2013, settlement involves a number of Ranbaxy entities: Ranbaxy USA Inc. (the U.S. subsidiary), Ranbaxy Laboratories Limited (the Indian parent company), Ranbaxy Inc., Ranbaxy Pharmaceuticals Inc., Ranbaxy Laboratories Inc. and Ohm Laboratories Inc. (all of which are subsidiaries of Ranbaxy Laboratories Limited named in the qui tam FCA complaint).

The settlement also involves a number of government entities, including the U.S. Attorney's Office for the District of Maryland, DOJ Civil Division Consumer Protection and Commercial Litigation Branches and the U.S. Department of Health and Human Services Office of Inspector General, as well as certain states and the District of Columbia (which will enter Medicaid state settlement agreements with Ranbaxy).

Ranbaxy pleaded guilty to seven felony charges under the settlement. These include: one count of violating the Federal Food, Drug and Cosmetic Act (FDCA) by introducing adulterated drugs into interstate commerce with the intent to defraud and mislead; two counts of violating the FDCA by failing to file required reports with the intent to defraud and mislead; and four counts of violating 18 U.S.C. § 1001 by knowingly making material false statements to the FDA.

In addition to pleading guilty, Ranbaxy agreed to pay a total of $500 million in resolution of criminal and civil liability. That amount includes total criminal penalties of $150 million — consisting of a criminal fine of $130 million and forfeiture of $20 million — as well as total civil penalties of $350 million, of which the federal government share is $231.8 million, and $118.2 million will go to the states participating in the settlement.

Approximately $48.6 million of the federal share of the civil settlement will go to the qui tam relator, Dinesh Thakur, who was director of project and information management with Ranbaxy Laboratories Limited in Gurgaon, Haryana, India, from June 2003 until April 2005.

According to his qui tam complaint, Thakur had responsibility for portfolio and product management and established a program management office that oversaw internal data created during the formulation and manufacturing of Ranbaxy's drugs. Thakur filed his qui tam action in April 2007.

Allegations and Resolution

The Ranbaxy settlement resolves allegations that fall into three general categories and are detailed in an agreed statement of facts:

- Violating the FDCA by manufacturing and distributing drugs deemed adulterated because they were not manufactured in compliance with GMP
- Violating the FDCA by failing to file required reports with the FDA
- Making material false statements to the FDA in annual reports.

The felony adulteration count is based on Ranbaxy's distribution of batches of Sotret (branded generic isotretinoin, used to treat severe recalcitrant nodular acne), gabapentin (used to treat epilepsy and nerve pain) and ciprofloxacin (broad-spectrum antibiotic) in 2005 and 2006 that were not manufactured in compliance with GMP.

Ranbaxy has further admitted significant discrepancies in stability testing at both

facilities. In particular, Ranbaxy admitted that it conducted stability testing several weeks or months later than the dates that were reported to the FDA in annual reports and also conducted stability tests that were required to be conducted at specified intervals (e.g., three, six and nine months) on the same day.

Ranbaxy also admitted to storing stability samples pending testing in a 4-degree C refrigerator rather than a stability chamber. This practice was not disclosed to the FDA; instead, Ranbaxy represented to the FDA that its stability testing program was being conducted in compliance with protocols submitted to the FDA.

Significantly, Ranbaxy admitted that its GMP and stability testing deviations were identified in 2003 and 2005 by outside consultants hired to audit its manufacturing operations. These stability testing deviations formed the basis for Ranbaxy's felony pleas to failing to timely file required reports and making material false statements to the FDA.

In particular, Ranbaxy admitted that it failed, as required under 21 U.S.C. § 314.81(b)(1), to submit a "field alert report" within three working days after receiving information concerning any bacteriological contamination, significant chemical, physical or other change or deterioration — i.e., failure to meet a specification established in an abbreviated new drug application — of a distributed drug product (in particular, Sotret and gapabentin).

Ranbaxy further admitted that it made materially false statements to the FDA regarding its stability testing program in annual reports filed in 2006 and 2007 relating to four antibiotics (Cefaclor, Cefadroxil, Amoxicillin and Amoxicillin and Clavulanate Potassium).

The settlement also resolves the allegations levied in the qui tam civil FCA action, United States ex rel. Thakur v. Ranbaxy Laboratories Limited, Civ. No. 1:07-cv-00962-JFM (D.Md.). In addition to alleging widespread GMP violations, the February 2010 amended complaint in that matter alleges that with the knowledge and approval of senior management in India and the United States, Ranbaxy filed marketing applications for its generic antiretroviral drugs that were not supported by formulation, bioequivalence and/or stability data or were supported by falsified data.

The civil settlement agreement ultimately resolves allegations that Ranbaxy knowingly caused the submission of false claims by manufacturing, distributing and selling drugs whose strength, purity or quality differed from their specifications or were not manufactured according to the FDA-approved formulations.

Ranbaxy's felony pleas under the FDCA subject it to mandatory FDA debarment pursuant to 21 U.S.C. § 335(a)(1). In addition, Ranbaxy's felony false statements pleas under 18 U.S.C. § 1001 subject it to mandatory exclusion from participation in federal health care programs, pursuant to 42 U.S.C. § 1320a-7(a)(3) (felony conviction relating to health care fraud).

The import of this debarment and exclusion is unclear, however, as Ranbaxy was purchased by Daiichi Sankyo Company Limited in June 2008.

Conclusion

The Ranbaxy settlement is significant in a number of respects. First, the $500 million total financial settlement represents the largest drug safety-related settlement with a generic manufacturer to date, and the seven felony guilty pleas reflect the DOJ's view of the severity of the allegations resolved.

Second, the settlement has broader implications for DOJ and FDA enforcement trends. Various DOJ and FDA officials have suggested that the government intends to focus on manufacturing issues in addition to the advertising and promotion claims that have historically dominated drug and device manufacturer government investigations and

settlements.

For instance, in a January 2013 speech, Deputy Assistant Attorney General Maame Ewusi-Mensah Frimpong, who leads the Consumer Protection Branch of DOJ's Civil Division, stated that when asked about the DOJ's "top areas of focus" for 2013, "the illegal conduct that came to mind was misbranding and adulteration of drugs."[2]

She continued to explain, "When 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."[3]

This tough talk, combined with Ranbaxy becoming the second example of a civil False Claims Act settlements based upon manufacturing and safety violations,[4] raise concerns that the DOJ intends to rely more heavily on the FCA as a tool for policing GMP violations. Notably, the two GMP-related FCA settlements to date have involved what the DOJ has characterized as egregious and persistent GMP violations stretching across many years.[5]

Moreover, the Ranbaxy civil settlement agreement premises the FCA settlement on Ranbaxy's alleged manufacturing and distribution of drugs, "(1) the strength of which materiality differed from, or the purity or quality of which materially fell below, [that which the drugs] purported or were represented to possess, or (2) that were not manufactured according to the approved formulation and were, therefore, unapproved new drugs, in violation of the FDCA, 21 U.S.C. §§ 331(d) and 355(a), and were not 'covered outpatient drugs' under 42 U.S.C. § 1396r-8(k)(2)."[6]

It is far from clear, however, that cases that do not rise to the level of the Ranbaxy matter can, or should, form the basis for FCA liability. As courts have recognized, GMP compliance is not an exact science but rather a standard with respect to which reasonable minds can differ.[7] It is well-established that the FCA is "not an appropriate vehicle for policing technical compliance with administrative regulations"[8] and that "differences in interpretation growing out of a disputed legal question are ... not false under the FCA."[9]

Equally significant, FCA actions generally lie only where compliance with the regulation at issue is a "condition of payment" by the government.[10] As a general matter, where GMP noncompliance does not impact the substance of distributed drugs, it is not a prerequisite to payment under federal health care programs.

Given these substantial legal questions, it is essential that the DOJ exercise enforcement discretion and not attempt to use the FCA "as a blunt instrument to enforce compliance" with all GMP regulations.[11]

For the vast majority of GMP violations, the administrative and civil remedies available to the FDA — which include Forms FDA-483, untitled letters, warning letters and consent decrees and are enforced by agency personnel with subject matter expertise — are a far more targeted, effective and appropriate enforcement mechanism for addressing GMP violations than an accusation that a drug manufacturer committed "fraud" on the government.

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[1] The information set forth herein is derived from publicly available sources.

[2] DOJ Press Release, "Deputy Assistance Attorney General Maame Ewusi-Mensah Frimpong Speaks At the 2013 CBI Pharmaceutical Compliance Congress," available at http://www.justice.gov/iso/opa/civil/speeches/2013/ civ-speech-130129.html (Jan. 29, 2013).

[3] Id.

[4] In addition to Ranbaxy, GlaxoSmithKline entered a $750 million criminal and civil settlement with the government in October 2010 that resolved alleged FCA liability premised on manufacturing violations. See DOJ Press Release, "GlaxoSmithKline to Plead Guilty & Pay $750 Million to Resolve Criminal and Civil Liability Regarding Manufacturing Deficiencies at Puerto Rico Plant," available at http://www.justice.gov/opa/ pr/2010/October/10-civ-1205.html (Oct. 26, 2010).

[5] For instance, the conduct alleged in the GlaxoSmithKline Settlement Agreement included that GSK's manufacturing deficiencies resulted in drugs that did not include any active ingredient, did not contain any controlled release mechanism, contained too much or too little of the active ingredient, were labeled as sterile but in fact non-sterile, or contained microorganisms. See http://www.justice.gov/usao/ma/news/2010/ October/GSK%20Settlement%20Agreement10_26.pdf.

[6] Dkt. 7-2, U.S. ex rel. Thakur v. Ranbaxy Laboratories Limited, Civ. No. 1:07-cv-00962-JFM (D.Md. May 13, 2013).

[7] See, e.g., United States v. Utah Med. Prods., Inc., 404 F. Supp. 2d 1315, 1319-23 (D.Utah 2005) (GMP regulations "have the virtue of generality and the vice of imprecision").

[8] United States ex rel. Burlbaw v. Orenduff, 548 F.3d 931, 959 (10th Cir. 2008).

[9] United States ex rel. Lamers v. City of Green Bay, 168 F.3d 1013, 1018 (7th Cir. 1999).

[10] See, e.g., U.S. ex rel. Chesbrough v. VPA, Inc., 655 F.3d 461, 468 (6th Cir. 2011); Mikes v. Straus, 274 F.3d 687, 697-702 (2d Cir. 2001). The exception to this rule is for so-called "worthless services" cases, where claims are knowingly presented for goods or services of no medical value. Id. at 702-03.

[11] Mikes, 274 F.3d at 699.