ARTICLES

cGMP Violations may be the Basis for QUI TAM Lawsuits in the United States

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Summary

Pharmaceutical manufacturers continue to battle with the Food and Drug Administration (FDA) over compliance with current Good Manufacturing Practice regulations (cGMP), which outline the requirements that drug manufacturers must follow for the manufacture, processing, packing, and holding of a drug. Pharmaceutical manufacturers have already been the target of successful Federal False Claims Act (FCA) prosecutions, mostly due to pricing and kickback issues raised in qui tam lawsuits. Qui tam lawsuits are brought under the FCA by private citizens who sue on behalf of the United States (US). In exchange for their efforts, the US law provides that the private citizen is entitled, generally, to 15 to 30 % of the recovery generated by the qui tam lawsuit.

Kenneth J. Nolan, a top qui tam attorney says that in the last several years, total payouts by manufacturers to settle qui tam lawsuits have amounted to over USD 2.0 billion.

Key Words

pharmaceutical manufacturing; cGMP; good manufacturing practice regulations; federal false claims Act; FCA; kickback; qui tam

Introduction

In August 2001, the FDA http://www.fda.gov issued its 'Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients' ('Guidance'). The Guidance was developed within the current Good Manufacturing Practice (cGMP) working group (Q7A) of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). This marked the first recent step by the FDA to better clarify its cGMP regulations. One year later, in August 2002, the FDA announced a high profile initiative to re-evaluate cGMP policies. But the battle between pharmaceutical manufacturers and the FDA about compliance with cGMP continues.

The US Code of Federal Regulations (CFR), parts 211–226 of Title 21, contain the cGMP regulations. They describe the requirements that drug manufacturers must use for 'the manufacture, processing, packing, or holding of a drug to assure that such drug meets the requirements of the act as to safety, and has the identity and strength and meets the quality and purity characteristics that it purports or is represented to possess.' The focus of the cGMPs is on quality – and with quality, the cGMPs are satisfied.

Strictly speaking, failure to comply with any of the cGMP regulations renders such drug to be 'adulterated' under the Federal Food, Drug and Cosmetic Act. A drug or device is 'adulterated' if

1. Its manufacture, in processing, packing, or holding do not conform to or are not operated or administered in conformity with current good manufacturing practice to assure that such drug meets the FDA requirements as to safety and has the identity and strength, and meets the quality and purity characteristics, which it purports or is represented to possess;
2. Its strength differs from, or its quality or purity falls below, the standard set forth in

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the applicable compendium or New Drug Application (NDA)/Abbreviated NDA (ANDA); and
3. It consists in whole or in part of any filthy, putrid, or decomposed substance.

To prevail on an adulteration charge under 21 USC §§ 331 and 351 on the ground of failure to conform to cGMP regulations, the United States does not need to establish that any particular drug is actually deficient as a result of nonconformance.

The Federal False Claims Act

The Federal False Claims Act (FCA) http://www.nolanlawfirm.net/false-claims-act.html is the United States Government's most powerful and most utilized tool to fight fraud. The FCA was originally enacted by US Congress in 1863, as a response to widespread abuses by government contractors against the Union Army during the Civil War. The Act was scarcely used in the interim years until 1986, when Congress enacted amendments to the Act, which strengthened the law and increased monetary awards. When hearings were held in 1985 and 1986, the climate was favorable for strengthened anti-fraud legislation, as Congress received reports that approximately 10 % of government spending was lost to fraud.

A company that violates the FCA is liable to the US Government for a civil penalty, plus three times the amount of damages, which the Government sustains. For example, if a drug manufacturer causes the submission of false claims of USD 10 million to the Medicaid program, it is potentially liable for damages of up to USD 30 million, plus a civil penalty of up to USD 11,000.00 for each patient claim for reimbursement submitted.

The FCA also authorizes *qui tam* enforcement. The *qui tam* provisions allow any citizen, called a 'Relator', who has knowledge of fraud that has taken place against the government to bring a civil action in Federal Court in the name of the United States. In return for his/her and his/her attorney's efforts, the citizen is entitled to share in the proceeds of the recovery.

Qui tam is shorthand for the Latin phrase, *qui tam pro domino rege quam pro seipso*, meaning 'He who is as much for the King as for himself.' *Qui tam* statutes date back to 13th century England. The actions were a means of enabling private parties to allege the King's interest and therefore gain access to the Royal Courts.

If the government intervenes, the Relator is entitled to 15–25 % of the total recovery, depending upon the extent to which the Relator 'substantially contributed to the prosecution of the action'. If the Government declines intervention, the Relator is entitled to 25–30 % of the total recovery.

Since the 1986 amendments, *qui tam* suits have proven successful beyond even Congress' expectations. According to Department of Justice, recoveries to the United States Treasury as a direct result of *qui tam* suits have exceeded USD 7.8 billion. Of this amount, approximately USD 362 million has been recovered from *qui tam* lawsuits in which the government has declined intervention. While cases filed have exceeded 4200, the Department of Justice has elected to intervene in approximately 750 cases. Relator awards in intervened cases now total over USD1.3 billion (source: US Department of Justice Statistics as of September 2003). (http://www.usdoj.gov)

Potential Violations to Steer Clear Of

Pharmaceutical manufacturers have already been the target of successful FCA prosecutions, mostly due to pricing and kickback issues. In the last several years total payouts by manufacturers to settle *qui tam* lawsuits have amounted to over USD 2.0 billion. Fraudulent conduct as it relates to the cGMPs is potentially violative of the FCA and will no doubt center on false representations in the written record-keeping requirements. Potential violations include the following:

1. Accepting and validating drug products that failed to meet established standards or specifications and any other relevant quality control criteria (i.e. dissolution rates,

content uniformity, purity, potency), and then falsely recording the untruthful data as if the drug products did not fail.
2. Accepting and validating the stability characteristics of drug products, and then falsely recording the untruthful data as if the drug products did not fail.
3. Documenting the examination and review of labels, when in truth and fact no review occurred (which results in inaccurate labels distributed with drugs).
4. Falsely documenting any components of master production and central records.
5. Falsely documenting any component of the batch production and control records.
6. Falsely describing testing methods when no (or inadequate) testing methods were performed.
7. Failure to accurately make a written record of all written and oral complaints regarding a drug product, and/or certifying that investigations were performed when they were not, falsely certifying that the findings were negative when they were not, and so on.
8. Falsifying records, which would indicate manufacturing changes, which require approval by the FDA.
9. False representations that contain statements of fact in correspondence sent to the FDA addressing violations in an inspector's Form 483, or the subsequent Establishment Inspection Report.

The use of the False Claims Act is not a stretch. The basis of liability is that a fraud, or false claims have occurred, resulting in monetary damages to the United States. The monetary damages result because the payer (in this case, the US) is potentially paying for substandard drugs due to the cGMP violations – later covered up by false claims. It makes sense, too – the cGMPs are a set of regulations, which, by their very nature, are designed to ensure that drugs are manufactured in such a way that they meet the requirements of the Federal Food, Drug and Cosmetic Act as to safety and have the identity and strength and meet the purity characteristics that they purport or are represented to possess.

The FDA, using its own enforcement powers and regulations, in recent years has collected hundreds of millions of dollars for violations of the cGMP regulations, in cases against Wyeth-Ayerst (USD 30 million) and Schering-Plough (USD 500 million). Under the term of each Consent Decree, payments were made to the U.S. Treasury. In each instance, the FDA used the theories of 'restitution' or 'disgorgement' of ill-gotten profits as a basis for collection.

Unsafe or Ineffective Products Should not be Paid For

False representations concerning minor or technical violations will not be the basis for FCA liability. Distribution of products that are not totally cGMP compliant (but have been falsely documented to be) does not necessarily result in unsafe (or sub-potent) products. Substantial violations of the cGMPs, later covered up in writing, however, will be the basis for FCA liability. Examples of potentially actionable violations are set forth in the previous section. The common thread through each violation is that the violation is severe enough so that the drug product that finally reaches the public arguably is, or is foreseeably likely to be, less safe or less effective than if the cGMPs were not violated. Simply put, false statements that hide cGMP violations that are substantial enough to result in unsafe or less effective products are likely to be the basis for FCA liability.

Medicare and Medicaid, the two major government healthcare programs in the United States, operate under the express provisions that they will only pay for medical services and products that are 'reasonable and necessary.' Unsafe or ineffective drug products are neither reasonable nor necessary. Accordingly, as the theory goes, the United States suffers monetary damages if it pays for unsafe or less effective products. Such damages would be the amount it paid for the drugs – an amount that is likely to be in the 10 if not hundreds of millions of dollars.

Written records are required to be kept as set forth in 21 CFR Part 211.180 to 211.208. Highlights are as follows:

§ 211.180 General requirements

(a) Any production, control, or distribution record that is required to be maintained in compliance with this part and is specifically associated with a batch of a drug product shall be retained for at least 1 year after the expiration date of the batch or, in the case of certain OTC drug products lacking expiration dating because they meet the criteria for exemption under § 211.137, 3 years after distribution of the batch.
(b) Records shall be maintained for all components, drug product containers, closures, and labeling for at least 1 year after the expiration date or, in the case of certain OTC drug products lacking expiration dating because they meet the criteria for exemption under § 211.137, 3 years after distribution of the last lot of drug product incorporating the component or using the container, closure, or labeling.

§ 211.182 Equipment cleaning and use log

A written record of major equipment cleaning, maintenance (except routine maintenance such as lubrication and adjustments), and use shall be included in individual equipment logs that show the date, time, product, and lot number of each batch processed.

§ 211.184 Component, drug product container, closure, and labeling records

These records shall include the following:

(a) The identity and quantity of each shipment of each lot of components, drug product containers, closures, and labeling; the name of the supplier; the supplier's lot number(s) if known; the receiving code as specified in § 211.80; and the date of receipt. The name and location of the prime manufacturer, if different from the supplier, shall be listed if known.
(b) The results of any test or examination performed (including those performed as required by § 211.82(a), § 211.84(d), or §211.122(a)) and the conclusions derived therefrom.

§ 211.186 Master production and control records

To assure uniformity from batch to batch, master production and control records for each drug product, including each batch size thereof, shall be prepared, dated, and signed (full signature, handwritten) by one person and independently checked, dated, and signed by a second person. The preparation of master production and control records shall be described in a written procedure and such written procedure shall be followed.

§ 211.188 Batch production and control records

Batch production and control records shall be prepared for each batch of drug product produced and shall include complete information relating to the production and control of each batch.

§ 211.194 Laboratory records

Laboratory records shall include complete data derived from all tests necessary to assure compliance with established specifications and standards, including examinations and assays ...

§ 211.198 Complaint files

A written record of each complaint shall be maintained in a file designated for drug product complaints.

Conclusion

The use of the FCA based upon violations of cGMP reporting requirements will become a reality in the coming years. Responsible pharmaceutical manufacturers whose products affect the health and well-being of the public should welcome the use of this law. Used responsibly and judiciously, FCA enforcement would benefit the industry as it would no doubt increase the quality standards in the industry if manufacturers of products are held monetarily accountable for false statements in cGMP required records. Moreover, competitors who are adhering to cGMP are put on a more level playing field. Even more, there will be less risk to the public, as far more companies will be deterred from falsifying cGMP record-keeping documents if they know that the FCA can and will be used against them.