GlaxoSmithKline: three billion lessons learned

With the dust settling on GlaxoSmithKline's record $3 billion healthcare fraud settlement in the US, it's a good time to reflect on the lessons pharmaceutical and medical device companies can learn from the case and how they can further protect themselves, says ***Retta Riordan***.

Much has been written about the $3 billion GlaxoSmithKline settlement announced in early July, the activities GSK is alleged to have engaged in and the laws the company is alleged to have broken. Two months on, it's a good time to reflect on the many lessons that healthcare companies can learn from the experience and how they can further protect themselves.

After providing a brief overview and discussion of some of the government's evidence regarding GSK's alleged off-label and kickback activities, this article will focus on certain extraordinary and novel elements of the settlement, including the corporate integrity agreement (CIA). The article will conclude with some thoughts about how companies can shore up their compliance programmes to ensure they do not end up writing a check to the government for $3 billion.

The settlement, which will not be final until approved by the courts, is worthy of note not only because of the multi-billion dollar price tag, but also because of what it addresses. Firstly, it takes into account numerous products across therapeutic categories; secondly, the remedies that have been fashioned make clear that the government is focusing on inappropriate financial incentives, from the top of the organisation (executives) and farther down the chain (field force).

While many of the offending activities took place as long ago as the late 1990s, some occurred more recently.

Background

To put the discussion in context, on 2 July 2012, GSK agreed to plead guilty and pay $3 billion to resolve both criminal and civil liabilities of unlawful promotion of various of its prescription drugs and its failure to report certain safety data, and its civil liability for allegedly engaging in false price reporting practices. This resulted in what the US government has termed "the largest health care fraud settlement in U.S. history and the largest payment ever by a drug company" (see text boxes for details of the alleged wrongdoings and the products involved).

Two of the allegations levelled against GSK – promoting products off-label and providing kickbacks – have become commonplace in recent settlements of this kind. Two additional allegations – withholding of safety data and false price reporting – appeared in this settlement.

Alleged wrongdoings

Off-label promotion
Kickbacks
Withholding of safety data
False price reporting

Products involved

Paxil (paroxetine), Wellbutrin (bupropion), Advair (fluticasone and salmeterol), Lamictal (lamotrigine), Zofran (ondansetron), Imitrex (sumatriptan), Lotronex (alosetron), Flovent (fluticasone) and Valtrex (valacyclovir)

The evidence

In reviewing the documents associated with the case, one cannot help but be struck by the candour with which employees openly discussed off-label promotion of products and devised and used ways to convince doctors to use the products for those unapproved uses. From product launch meetings to direction to the sales representatives, numerous examples of off-label promotion and offerings of activities in exchange for business from a healthcare professional (HCP) seem apparent. For example:

- For Advair (approved for moderate to severe asthma): designed the "Myth of Mild" campaign intended to promote the product for all degrees of asthma, including mild.
- For Advair: developed a national strategy entitled "Establish Advair Diskus as the Physician's First Choice for the Treatment of ALL Persistent Asthma".
- For Wellbutrin (approved for treatment of depression in adults): touted the product for numerous quality-of-life conditions such as obesity and sexual dysfunction, earning it the nickname of the "happy, horny, skinny pill".
- For Paxil (approved for adult use): samples to doctors who primarily or exclusively treated children.

Sales representatives openly discussed in their call notes their efforts to have doctors prescribe their products (these are all direct quotes, including typographical errors):

- After taking doc and wife to Cardinals game, rep asked for business. "he laughed. I didn't really see the humor in it. How could he think I wouldn't ask for the business when I've treated his family to a day at the ball park."
- "Tkts to Crosby Still Nash. Asked for business in return."
- "doc very into QUID PRO QUO wants to be taken care of for his business."
- "Gained commitment to increase his use. Will do this every three weeks, great ROI, very cheap."
- "I have spent a lot of money on him and it has paid off."
- "he really can be bought."
- Doctor "said he could take care of us if we take care of him."

In reading one sales representative's emails disagreeing with the directives given to him, the employee's frustrations in not being heard are palpable:

I have had some serious complaints, regarding my DM [district manager] taking disciplinary action against me for refusing to participate in obvious violations of company policy regarding mainly, but not limited to speaker events/promotion etc.. These events contine with no response whatsoever back to me from Human Resources, who has been given most of the material evidence (not all).

The sales rep continues that HR had not responded, in violation of the company's published policy:

Please check this out, TAP Pharm. recently had to pay almost 1 billion dollars for similar conduct, yet this company will not even acknowledge my existence. My DM . . . has had full knowledge of the conduct, yet I was the one reprimanded by him for reporting it to him and refusing to participate. I suggest that someone inform me of the status of the matter. . . . After over two months with no response, and my reputation and employ at stake, I hope this can be referred to someone who has the ability to oversee HR. I have tried all I can to no avail.

In another email, the sales rep, says:

This is not some minor violation of policy, the conduct I have attempted to report could result in severe legal and monetary penalties if left unchecked. I think that should be very evident and need no further explanation. I do not want to be the one responsible for a child's injury or worse because we PAID a physician, who wrote a book on ADHD, to tell others that Wellbutrin SR was a great drug for ADHD. Nor do I want to be responsible for paying a Nurse Practitioner to tell 200 others that Amerge is a great drug for Pediatric migraine. Further I will not take part in paying for an expensive lunch, and day at the SPA ($350) for 25 physicians and physicians assistants, just for listening to what they already know about Wellbutrin SR for 1/2 hour.

I also believe expensive programs now

approved and pending by [my] DM-re: Ski bus trips to Breckenridge, Dinner and tickets to Avalanche games with a "guest" for physicians is no more than "buying the business through bribery." Is this the "high road"?

. . . "Well just imagine the call I received ten minutes ago from a physicians assistant, not a physician, ordering 1) 65 minute deep tissue massage a 2) a 60 minute Colorado cleansing facial 3) a 30 minute foot reflexology and 4) a pedicure and French manicure. This would be after her "lunch at the Broadmoor" and 30 minute lecture by Brendan Montano, MD who flew in from Connecticut for several thousand dollars to talk about weight loss and the benefits of Wellbutrin SR !!!! I want to promote the benefits of my products, but this sickens even me."

This sales rep became one of the whistleblowers whose actions led to the federal investigation that resulted in the July 2012 settlement. [There were four whistleblowers for the issues involving off-label promotion and kickbacks. The other two allegations involving safety data and pricing did not stem from whistleblowers.]

Extraordinary and novel provisions

The settlement and accompanying CIA include the provisions of settlements and CIAs of old, but the government and GSK agreed to incorporate several extraordinary and novel provisions.

The settlement

Of course, the most visible provision in the settlement is the sheer magnitude of the financial resolution: $3 billion, of which $1 billion is attributed to the criminal component of the settlement. How the $1 billion criminal fine was derived may be of interest; to paraphrase former US President Bill Clinton, it's simple arithmetic. Following the US sentencing guidelines, the government calculated the maximum penalty for each of the three counts: delivering two misbranded drugs – Paxil and Wellbutrin – into interstate commerce; and failing to report data relating to clinical experience and other data and information regarding Avandia (see Table 1 for details – in addition, each of the counts included the possibility of probation of up to five years and restitution to victims of the offence).

Gasps over the size of the $3 billion settlement continue, but there are some who assert that the number is too low, particularly in light of the sales the drugs involved generated. Avandia, for example, reportedly had $10.4 billion in sales, Paxil had $11.6 billion and Wellbutrin sales were $5.9 billion during the years covered by the settlement. "So a $3 billion settlement for half a dozen drugs over 10 years can be rationalized as the cost of doing business," Patrick Burns, a spokesman for the whistle-blower advocacy group Taxpayers Against Fraud, said.

Table 1. GSK's $1 billion criminal fine… it's all in the numbers

	Violation	Maximum penalties	Criminal fine imposed
COUNT 1	Delivery into interstate commerce of a misbranded drug (Paxil)	$200,000 fine or 2X/gross gain (Gain was $99,855,000; maximum possible fine: $199,710,000)	$159,768,000
COUNT 2	Delivery into interstate commerce of a misbranded drug (Wellbutrin)	$200,000 fine or 2X/gross gain derived (Gain : $346,521,000; maximum possible fine: $693,042,000)	$554,433,600
COUNT 3	Failure to report data relating to clinical experience and other data and information (Avandia)	$200,000 fine or 2X/gross gain derived (Gain: $151,633,000; maximum possible fine: $303,266,000)	$242,612,800
SUB-TOTAL (Criminal fines)			$956,814,400
Forfeiture			$43,185,600
TOTAL			$1,000,000,000

Clawback provision

In recent settlements and CIAs, the government has been focusing more carefully on individuals, holding them liable for their actions and those of their subordinates. Interestingly, in this settlement, the government has looked at the drivers of illegal or inappropriate behaviour by the individuals – financial incentives.

GSK is required, under its CIA, to institute a financial recoupment programme that, at its essence, allows GSK the right to recoup or cause the forfeiture of up to three years of an executive's annual performance pay who is discovered to have been involved in any "significant misconduct". The annual performance pay includes the executive's annual bonus as well as long-term incentives. The provision applies to both current and former executives.

To be subject to the clawback provision, an executive must have personally engaged in "significant misconduct", defined as a violation of the law, regulations, or a significant GSK policy. Additionally, the provision may be triggered if one of the executive's "subordinate employees" engages in "significant misconduct". There are two important restrictions. First, the incident must be more than "an isolated occurrence". In addition, the executive must have known or "should have known" that the activity was occurring. [Note: The "should have known" standard is also used in applying the Park (or Responsible Corporate Officer) doctrine.] The government incorporated the concept into the CIA.

It is important to note that the recoupment will not be paid to the government, but to GSK.

Field force financial incentives

In a major shift, GSK has significantly changed how it compensates (and disciplines) its field force. In place of providing incentives to its sales representatives and their immediate supervisors based on the volume of their territory sales, GSK has begun to compensate its field employees on the basis of business acumen, customer engagement and scientific knowledge about GSK's products.

Prior to the settlement, GSK had implemented the new field force compensation system, termed "Patient First" programme.

Manufacturing

In what appears to be a first, the Office of Inspector General has incorporated into this CIA a mini-CIA involving GSK's manufacturing processes. The manufacturing CIA contains numerous provisions similar to those found in CIAs, for example:

- Appointment of a compliance officer for global manufacturing and supply (GMS) who has responsibility for establishing policies and procedures relating to current good manufacturing practice (cGMP) activities and the CIA.
- Annual certification by the GMS compliance officer to the OIG that GMS is materially in compliance with cGMP requirements and the CIA.
- Establishment of a compliance committee consisting of senior management.
- Oversight responsibilities by the board of directors over cGMP and CIA-related activities, including a resolution that the

board has made a "reasonable inquiry" into the GMS compliance programme and believes, "to the best of its knowledge", that GSK has implemented an effective compliance programme.
- Development of a code of conduct to be distributed to all manufacturing employees, who must certify to it.

The mini-CIA contains novel provisions relating to cGMPs activities including:
- Training on cGMP activities and requirements of the manufacturing portion of the CIA and GMS's compliance programme, and training of board members. Each person trained must certify to the training.
- Requirement that the Food and Drug Administration notify the OIG if GSK fails to comply with cGMP requirements. Remedial actions may involve the recall of the product.
- Reporting of "manufacturing reportable events" (MREs), including a significant violation of laws applicable to cGMP activities. [Note: Certain areas are specifically not considered to be MREs, such as observations contained in Form 483 reports and field alert reports.] The report must include the relevant facts and people associated with the MRE, the actions GSK has taken to correct the MRE and the future actions GSK will take to prevent the event from recurring.

The requirements are applicable to a wide swath of people, from the president of GMS and all members of the GMS executive team to the senior vice-president of GMS quality and all members of the quality executive team. It also extends to numerous other employees, distribution centre employees and contractors.

Clinical activities

The CIA establishes extensive requirements regarding the full, fair and accurate reporting of scientific data by GSK in various areas, including the following (GSK already had in place many of these processes at the time of the settlement):
- Development of procedures regarding GSK-sponsored post-marketing research as well as company-supported investigator-sponsored studies, including what is supported, how it is supported, publication of information including information about the research results and trial outcomes, and uses made of publications relating to research.
- Requirement that researchers disclose in any research publication the fact of GSK's support of the research and any financial interest the researcher has in GSK.
- Posting of clinical study results and protocols as well as registry of studies.
- Publication of results from and information about discontinued studies including the fact that a study has been terminated early.
- Registration or summary results from all applicable GSK-sponsored clinical trials of GSK products and reports on www.clinicaltrials.gov.
- Publication of study results in peer-reviewed, searchable journals.
- Acknowledgement of GSK as the funding source in company-sponsored research.
- Reporting of adverse event data.
- Requirement that investigators report study-related information and data, including data about adverse events before receiving final payment from GSK.
- Requirement that authors of GSK-sponsored research adhere to the International Committee of Medical Journal Editors (ICMJE) requirements regarding authorship; disclose any GSK financial support for the study and any financial relationship with GSK; and that to be designated as an "author" the individual must have made a substantial contribution to the study and have given final approval to the version of the publication that is published.

Other novel provisions

Social media. Reflecting changing times and companies' use of the internet to promote their products, to ensure compliance with the law as well as review and approval of all materials prior to distribution, GSK is required to develop processes governing how its materials and other information may be distributed or made available via social media and/or through direct-to-consumer advertising.
Notices. While most recent CIAs have required the company in question to provide notices to its current customers (HCPs and/or healthcare institutions (HCIs)) of the terms of their wrongdoing and settlements, GSK is required to also provide notices to payers with whom the company has a contract for formulary access or rebates (including state Medicaid programmes). The payer notice must include not only terms similar to the HCP/HCI notice, but also state that the company will pay rebates under the terms of its contracts with the payer, regardless of prior authorisation or formulary requirements (with certain exceptions).
Additional compliance personnel. GSK is required to install deputy compliance officers as well as "integrity champions" in the various business units to facilitate local implementation of the compliance programme.

Protecting your company

As each new settlement within the sector becomes public, companies should take the time to reflect on the current state of their own compliance programmes. The answer to all of the following questions should be "yes".
- Have you conducted a risk assessment recently?
- Does your senior management set a compliant tone at the top, signalling to employees no tolerance for illegal activities?
- Is your off-label promotion policy in writing? Are all employees trained on it?
- Do all employees understand fully what off-label promotion is as it relates to your products?
- Do you have in place relevant policies to govern all aspects of your business from sales and marketing to clinical to manufacturing? Have you recently reviewed and updated, as appropriate, your policies and procedures?
- Do you have an effective mechanism for receiving employee concerns? Is there a welcoming ear? Is the person receiving calls/concerns trained to handle them?
- Do you follow through with employee concerns?
- Do you take prompt, corrective actions if a problem exists?
- Do you conduct a thorough investigation on each concern raised?
- Do you conduct a root cause analysis of the problem?
- Do you close out the matter after the investigation is complete?
- Do you notify the concerned employee that appropriate action was taken?
- Do you revisit the issue within a certain period of time?
- Do you monitor activities, particularly high-risk areas such as off-label promotion?
- Is HR trained to recognise when it is important to send employee concerns to Compliance for further inquiry?
- Do you thoroughly review and approve all promotional materials, ads, field training materials, consultant meeting and speaker programme agendas?
- Do you review employee incentives to ensure they are appropriate for on-label uses?
- Do you review customer target lists to ensure they are appropriate for on-label uses?
- Do you train employees in how to receive and handle off-label inquiries?
- Do you have a qualified and effective compliance officer in place?
- Do you have a hotline to receive anonymous or identified calls to allow employees to express any concerns they may have?

References for this article are available on the scripregulatoryaffairs.com website.

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