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Seroxat and the suppression of clinical trial data: regulatory failure and the uses of legal ambiguity

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ABSTRACT

This article critically evaluates the Medicines and Healthcare products Regulatory Agency's announcement, in March 2008, that GlaxoSmithKline would not face prosecution for deliberately withholding trial data, which revealed not only that Seroxat was ineffective at treating childhood depression but also that it increased the risk of suicidal behaviour in this patient group. The decision not to prosecute followed a four and a half year investigation and was taken on the grounds that the law at the relevant time was insufficiently clear. This article assesses the existence of significant gaps in the duty of candour which had been assumed to exist between drugs companies and the regulator, and reflects upon what this episode tells us about the robustness, or otherwise, of the UK's regulation of medicines.

In October 2008, the Medicines and Healthcare products Regulatory Agency (MHRA), the body responsible for licensing medicines in the UK, announced an amendment to the 1994 Medicines for Human Use (Marketing Authorisations Etc) Regulations which is intended to address one of the gravest failures in pharmacovigilance since the Medicines Act 1968 came into force nearly 40 years ago.¹

This amendment became necessary following the MHRA's revelation, on 6 March 2008, that there would be no prosecution of GlaxoSmithKline (GSK) for withholding clinical trial data, which suggested not only that Seroxat was ineffective at treating childhood depression, but also that it increased the risk of suicidal behaviour in this patient group.

The MHRA's March announcement came at the end of a four and half year investigation into whether GSK had acted illegally by withholding this data from the regulator. In a press release published on 6 March, Professor Kent Woods, MHRA Chief Executive, said:

I remain concerned that GSK could and should have reported this information earlier than they did. All companies have a responsibility to patients, and should report any adverse data signals to us as soon as they discover them. This investigation has revealed important weaknesses in the drug safety legislation in force at the time.²

In the article, we examine the background to the failure to prosecute GSK, and reflect upon what this episode tells us about the robustness, or otherwise, of the UK's regulation of medicines. In the first section, we provide a brief history of the MHRA's investigation into GSK's failure to report data which revealed safety concerns as well as a

lack of efficacy. Secondly, we examine the defects in the legal framework which have enabled GSK to avoid prosecution. Finally, we suggest that these gaps in the law are not the only factor affecting the MHRA's ability to regulate effectively. We draw attention to the role of the agency's funding structure, and in particular its need to compete with other European regulators for licensing fees, as well as its desire to avoid "reputational risk".³ We conclude that the case of Seroxat and the missing trial data casts doubt upon that MHRA's capacity to fulfil its own "mission statement":

We enhance and safeguard the health of the public by ensuring that medicines and medical devices work and are acceptably safe. ... Underpinning all our work lie robust and fact-based judgements to ensure that the benefits to patients and the public justify the risks.⁴

Methodologically, the article draws on an analysis of the relevant legislation and regulations, and documents released by the MHRA, and Linsey McGoey's (LM) interviews with key individuals such as Kent Woods.⁵

THE MHRA'S INVESTIGATION INTO GLAXOSMITHKLINE

The MHRA's investigation into GSK was launched in October 2003, following GSK's submission, in May 2003, of data from Studies 329 and 377, clinical trials which tested the efficacy of paroxetine (Seroxat/Paxil) in children and adolescents in the mid-1990s in 11 countries. As soon as they were received, the relevant data were analysed by the Committee on the Safety of Medicines (CSM), which found that they provided clear evidence (a) that "there is no good evidence of efficacy in major depressive disorder in the population studied",⁶ and (b) that there was "a clear increase in suicidal behaviour versus placebo".⁶ Following this CSM review, the MHRA published advice to all doctors that Seroxat should not be prescribed to under-18s, and launched a criminal investigation into GSK's failure to submit this data in a timely manner.

In early 2004, suspicions of illegality were bolstered by the leaking of a confidential, internal GSK document that indicated that there had been a deliberate decision to withhold Studies 329 and 377 from regulators. The GSK document, dated October 1998 and entitled *Seroxat/Paxil adolescent depression—position piece on the phase III clinical studies* was first described in an article in the Canadian Medical Association Journal,⁷ and is now widely available on the internet.⁸ It stipulates that company representatives should be cautious in disseminating the results of Study 329 and 377,

stressing that “it would be commercially unacceptable to include a statement that efficacy had not been demonstrated, as this would undermine the profile of paroxetine”, and that it was necessary “to effectively manage the dissemination of these data in order to minimise any potential negative commercial impact” (emphasis added).⁸

It seems unarguable, then, that for five years, GSK deliberately failed to disclose clinical trial data which provided evidence that Seroxat should not be prescribed to under-18s. Given that, in 1999 alone, 32 000 prescriptions for Seroxat had been issued to children in the UK, it is clear that in the time-lag between the completion of the relevant clinical trials (1998) and the CSM’s warning notices (2003), tens of thousands of under-18s were prescribed a drug that was unlikely to work, and which carried an unacceptable risk of a serious, indeed fatal, adverse reaction. We do not know how many, if any, under-18s actually committed suicide between 1998 and 2003 as a result of taking Seroxat, but given the large number of children involved, it is certainly possible that deaths occurred which could have been avoided by prompt disclosure of this information.

It was the understanding of MHRA staff that the Medicines Act 1968 and Regulations which transpose a series of EU Directives impose a legal duty on pharmaceutical companies to give the regulator *all* clinical trial data which has a bearing on a medicine’s safety and efficacy. This point was stressed by Kent Woods (KW) during testimony before the House of Commons Health Select Committee on 9 September 2004, as part of the Select Committee’s 2004–2005 inquiry into the influence of the pharmaceutical industry on UK health policy:

Q39: Siobhain McDonagh MP: How many clinical trials does the MHRA examine before approving a drug application? Is the MHRA confident that it completely reviews all the findings necessary, both within and outside the public domain, before licensing a drug?

KW: The legal responsibility is on the applicant to ensure that in applying for a trial’s authorisation they do give us all the data, whether or not it is in the public domain. That is clearly spelt out in the medicines legislation, and, of course, it is fundamental to our assessment of a product that we do have access to all the available data. ... If we have evidence that there has been a breach of the regulations, then we have an inspection and enforcement division which will take the necessary action to pursue investigations; *the legal framework is clear, that we must have for the assessment process all the data which the applicant possesses* (emphasis added).⁹

In practice, however, as John Abraham has pointed out, the penalties for failing to submit clinical trial data, which include fines and imprisonment, remain untested, as to date in the UK no company has ever been prosecuted for withholding information that has a bearing on a drug’s safety profile.¹⁰ Woods confirmed this point during his interview with LM in January 2007:

LM: While you were a witness before the Health Select Committee, you noted there have been a number of instances when the MHRA’s enforcement group has been called in to assess whether there has been appropriate disclosure of data by industry. [Observers suggest] there has never been a prosecution of a company for suppression of data. Is that the case?

KW: I believe that’s the case. I’ve been in the agency for three years. In fact, I’m pretty certain that that’s the case. I would qualify that by saying firstly that our first stop is to achieve compliance and prosecution is very much a long stop. And secondly, industry has a very strong vested interest in not actually stepping over the line. ... The suppression of data would

clearly be a very serious matter. And one on which we would be particularly willing and able to take enforcement action. It is not something which is in a company’s best interest to do.

Given Woods’ assertion that the MHRA is committed to prosecuting breaches of the regulations, the Agency’s decision to refer GSK’s suppression of trial data to the MHRA’s Enforcement Group in October 2003 is not surprising. What is perhaps surprising is the length of time it took the MHRA to realise that prosecution would not be possible. Surely the five year time-lag between GSK’s completion of trials which revealed inefficacy and lack of safety, and their eventual disclosure—not to mention the fact that the disclosure in 2003 came in the form of a briefing paper about a possible future application to *extend* the indication for use of Seroxat in children, as opposed to an urgent risk/benefit alert—spoke for itself. It is hard to imagine any explanation of the non-disclosure of this data that did *not* amount to a breach of pharmacovigilance regulations. Yet, after a very long and complex investigation, during which the MHRA “obtained and examined over a million pages of documentation”,¹¹ the final decision was that the case could not proceed to prosecution.

Importantly, however, this decision was not taken because the MHRA’s intensive investigation revealed that GSK had acted properly in relation to the data in question. On the contrary, as the leaked memo makes clear, GSK had deliberately suppressed data which revealed that Seroxat should not be prescribed to under-18s. Rather, once the evidence had been gathered, Counsel’s advice was sought in order to determine whether a prosecution should proceed, and the advice was “the legislation was sufficiently unclear as to make a criminal prosecution impossible”.¹¹

BARRIERS AND LOOPHOLES WITHIN THE LEGISLATIVE FRAMEWORK

This conclusion prompts a number of questions, the first and most obvious of which is that if it is indeed true that the law was insufficiently clear in March 2008, then it must also have been insufficiently clear in October 2003, when the decision was taken to launch a criminal investigation. Of course, if there was a degree of ambiguity in the law, then it might be especially important to spend time trying to assemble a clear-cut case of illegal activity on the part of GSK. But the important point about the MHRA’s March 2008 announcement was not that there was some slight ambiguity which could have been “cured” by decisive evidence of wrongdoing. On the contrary, as we see below, the defects in the law which were identified in 2008 are potentially so broad that, regardless of the robustness of the MHRA’s evidence of illegality, prosecution would be pointless. The existence of gaps in the law which make prosecution futile does not depend on the weight of evidence against GSK, rather it is an independent fact which, if detected by a competent lawyer in 2008, should have been detectable in 2003. If the law as it existed between 1998–2003 made a successful prosecution impossible *ab initio*, a four and a half year investigation into the possibility of prosecution may have been a colossal waste of time and money.

Secondly, was it, in fact, the case that the law at the relevant time was insufficiently clear? It is certainly true that the provisions which GSK were suspected of breaching consist, at least in part, of a shifting set of Regulations—the Medicines for Human Use (Marketing Authorisations Etc) Regulations

¹¹ Linsey McGoey interview with Kent Woods, January 2007.

1994—which have, over the period in question, implemented a number of new EU Directives. Without rehearsing every shift in the content of the 1994 Regulations between 1998 and 2003, two provisions are of particular importance.

From February 2002, para 8 of Schedule 3 of the Regulations provided that: “Any person responsible for placing a relevant medicinal produce on the market who fails to report to the licensing authority *any* suspected adverse reaction, or to submit to the licensing authority *any* records of suspected adverse reactions... shall be guilty of an offence” (emphasis added). More important still is para 10, which went further and required the qualified person to provide “*any* other information relevant to the evaluation of the benefits and risks afforded by a medicinal product” (emphasis added). The regulations do not apply retrospectively, so both these particular provisions applied to GSK in the time period between February 2002 and May 2003 (when the data were eventually disclosed).

The MHRA’s view, which we share, was that “the information eventually provided to the MHRA about adverse reactions experienced in the trials of Seroxat in children was clearly ... relevant to the risks and benefits of the product”.¹¹ On the face of it, then, the provision that there is a duty to provide “*any* information relevant to the evaluation of benefits and risks” does not look particularly vague or ambiguous, and would appear to capture precisely the non-provision of data by GSK. How then could the decision be taken that, contrary to appearances, this provision is “insufficiently clear” to justify prosecution?

In brief, the lawyers whose advice had been sought detected a number of possible loopholes, described below, which would have enabled GSK to avoid conviction, and this meant that a prosecution would have represented a further waste of public resources.

The first loophole relates to the duty to notify the MHRA of adverse reactions. This, apparently, could be read to apply only to adverse reactions “in the normal conditions of use of the product”. Though first licensed for adult use in the UK in 1990, Seroxat had not been specifically licensed for use in under-18s because enrolling children in clinical trials was not encouraged. As a result, its prescription as a treatment for childhood depression was effectively “off-label”, albeit that GSK knew that thousands of children were taking it, and had certainly not advised doctors against prescribing it to children. It should be noted that reluctance to enrol children in clinical trials means that off-label prescription to children is the norm rather than the exception, with obvious implications for patient safety. Until the CSM issued their warning notices in 2003, being under-18 was not listed as a contraindication to prescription of Seroxat, and so it could be freely and lawfully prescribed as a treatment for childhood depression.

Unusually then, GSK *had* conducted clinical trials of Seroxat in under-18s. This fact, somewhat ironically, led to the second legal loophole. Because the data which revealed an elevated risk of suicide did not emerge “during normal conditions of use”, but instead from clinical trials, again they were not captured by the regulations.

These two defects in the law might have been “cured” if instead the MHRA could have invoked the duty to report adverse reactions which occur during clinical trials, which is contained in Section 31 of the Medicines Act 1968, and governed by orders made under the Act. Yet, conveniently for GSK, there are two further loopholes here in that this duty applies only to trials conducted in the UK, and, at the relevant time, failure to comply would not have been a criminal offence.

An EU Directive which came into force too late—in May 2004—introduced a criminal offence for the failure to report adverse reactions which occur during clinical trials, but again this remains limited to trials which take place within the European Economic Area (EEA).

It is worth noting that pharmaceutical companies have always been *entitled* to rely on non-UK or now non-EEA trials when submitting applications for marketing authorisations. They have, in short, been able to benefit from the positive results of trials conducted abroad, while at the same time, it appears that they have not been under a corresponding duty to reveal the negative results of non-UK, or non-EEA trials.¹²

The existence of so many qualifications to what initially looks like a clear and comprehensive duty to submit “*any* other information relevant to the evaluation of the benefits and risks afforded by a medicinal product” is perhaps surprising. Certainly, two ordinary rules of statutory interpretation would militate against this conclusion. First, the words used in legislation are normally assumed to have their “ordinary language meaning”, unless otherwise specified. Use of the word “*any*”, according to the *Oxford English dictionary*, captures the idea of “indifference as to the particular one or ones that may be selected”, which would suggest that “*any* relevant information” should not, without a clear indication to the contrary, be qualified to mean “only information gathered in a particular setting”.

The second rule of statutory interpretation which is at odds with the existence of these legal loopholes is that, in the event of statutory ambiguity, it is legitimate to ask what the legislator’s intention was in drafting the provision in question. Here the intention was evidently to create a duty to report all relevant data, and in particular, to disclose suspected adverse reactions and other information relevant to the regulator’s evaluation of risks and benefits.

The interpretation of the law which has led to the decision not to prosecute would seem to subvert the intention of the creators of the regulatory regime, which was indubitably not to provide a series of “get-out” clauses for drugs companies who withhold, deliberately, evidence of lack of efficacy and serious side effects for a group of patients who are routinely being prescribed the drug in question.

Against this, it is of course true that there is a further rule of statutory interpretation according to which, where there is any ambiguity in the definition of a criminal offence, that ambiguity has to be interpreted in the defendant’s favour, and so, if the loopholes outlined above exist, the MHRA are clearly right that the prosecution of GSK would be likely to fail, and so embarking on it would be a further waste of time and money.

GAPS IN THE REGULATORY FRAMEWORK: NICE, MHRA AND ACCESS TO DATA

It now seems likely, therefore, that the legal framework which governs the licensing of medicines in the UK, set up by the 1968 Act in the light of the Thalidomide tragedy, has always been seriously defective. The duty of candour owed to the regulator, and referred to by Woods in his evidence to the Select Committee, to provide “*all the data which the applicant possesses*”, backed up by the possibility of criminal sanctions in the event of breach, has been revealed to be heavily qualified. It does not exist where adverse reactions become apparent in off-label use, even where that off-label use is both common and well known, or where they occur in clinical trials that took place

¹² We are grateful to Catherine Will for this point.

outside the UK (or, since 2004, the EEA). These are significant gaps in the regulatory scheme, which, as is apparent from the Seroxat episode, subvert the purposes of regulation, and undermine the powers of the regulator.

In short, there can be no sanctions despite clear evidence that GSK withheld data which ensured that tens of thousands of adolescents have been prescribed drugs which do not work, and which may cause an elevated risk of suicide. In addition to the implications for patient safety, this also represents a huge waste of NHS resources: between 1998 and 2003, the NHS paid for hundreds of thousands of prescriptions of Seroxat for under-18s, despite the existence of (withheld) evidence proving (a) that it would not work, and (b) that it might cause a serious adverse reaction.

This latter question raises important issues for the National Institute for Health and Clinical Excellence (NICE). It might be argued that not only should the MHRA have had access to this evidence much earlier, on safety grounds, but that it would also be relevant to any guidance NICE might issue on the treatment of depression in children. Significantly, however, NICE does not have the same rights as the MHRA has always been assumed to have to require pharmaceutical manufacturers to supply clinical trial data. According to Kent Woods, the two bodies are exercising different functions. The MHRA decides whether a drug is safe—using the powers it thought it had to require the provision of “any relevant information”, and NICE can then rely upon that assessment in order to decide whether this safe and efficacious drug is *also* sufficiently cost-effective to justify prescription in the NHS. Woods elaborated on this point in his interview with LM:

LM: Would you like to see it move to a system where NICE policymakers had access to the same data as the MHRA?

KW: No.

LM: Why not?

KW: It's important to understand firstly what NICE is there for. NICE is an NHS organisation. And its job is to give advice and guidance to the NHS. I mean, the NHS is just a very large health maintenance organisation. We have a statutory responsibility to the nation as a whole, and therefore our remits are somewhat different... I think we need to keep separate in our minds the job that this agency does, which is about weighing up risk and benefit and quality, and what NICE does, which is about effectiveness and cost-effectiveness.

Yet it is not clear that the roles of the MHRA and NICE can be neatly separated in this way. If a drug does not work, then that information is critical to a decision about cost-effectiveness, since regardless of its cost, its lack of efficacy will make its prescription in the NHS a waste of money. It is also critically important that this two stage process for drug provision in the UK means that any failure by the MHRA to gain access to information about adverse reactions or lack of efficacy will be magnified by NICE's reliance on the robustness of the MHRA's conclusions on safety and efficacy. If the MHRA cannot detect that a drug is unsafe and inefficacious, because a drug company can withhold data without penalty, NICE's dependence on MHRA data analyses means that unsafe and inefficacious drugs may subsequently be widely prescribed in the NHS.

A positive result of the Seroxat episode may be that the inequality of access to data described by Woods may be revisited. Indeed, we understand the MHRA is currently negotiating with NICE about revising shared data arrangements. But restructuring access to data alone may not solve some of the problems that compounded the MHRA's inability to prosecute GSK. In the next section, we examine some further

structural factors that may be hindering effective drugs regulation in the UK.

MHRA, INDUSTRY RELATIONSHIPS AND REPUTATIONAL RISK

Fallout from the MHRA's decision not to prosecute GSK is not the first time that the Agency has attracted criticism. John Abraham^{12–15} has consistently highlighted the existence of a number of barriers that make it difficult for the UK regulator to effectively monitor the safety of medicines.¹⁴ The first is the MHRA's funding structure. The Medicines Control Agency (MCA), which preceded the MHRA, was established in 1989 when the UK government decided to make the drugs regulator semi-autonomous from the Department of Health. Unlike its predecessor, the new MCA, like the MHRA today, became entirely funded by fees paid by pharmaceutical companies in exchange for drug licensing services. Within the EU, this model of industry funding is becoming increasingly common.^{15–16} In comparison, the Food and Drug Administration (FDA), the US equivalent of the MHRA, originally received no private funding at all, and while its reliance on industry fees has grown, to about 50%, it retains a degree of financial independence from the pharmaceutical industry.^{17–18}

There is, as Breckenridge and Woods have pointed out, a logical reason for the MHRA's funding arrangements.¹⁹ Why should the UK taxpayer carry the burden of paying for the licensing process, when private companies profit from drug sales? And it is true that in many other sectors, the cost of regulation is borne by the regulated, rather than by the taxpayer. The particular problem industry-funded regulation poses for the MHRA is that, unlike most other regulators, the MHRA is effectively *in competition* for industry fees with other EU regulators.

The reason for this is that drugs can be licensed throughout the EU through what is known as the “mutual recognition procedure”.²⁰ Drugs companies choose to apply to a national regulator, whose decision to grant a product licence will then be recognised throughout Europe. Because the majority of licensing fees go to the regulator to which the pharmaceutical company first applied, an internal EU market has emerged, in which national regulatory agencies compete for “regulatory business” by lightening the regulatory burden and speeding up approval times. In the first nine years of this system's existence, the average assessment time for new drugs in the UK fell from 154 working days to 44.²¹ While regulatory efficiency is, of course, to be welcomed, making regulators compete with each other in this way undoubtedly creates perverse incentives towards the minimisation of regulatory oversight, or a “race to the bottom” in medicines regulation.^{13–15}

Another factor at stake may be what Michael Power has described as the imperative to minimise “reputational risk”.³ The failure to gain access to Studies 377 and 329 is not the first time the MHRA has found that its decisions have been based upon inadequate or partial data analysis. During a 2003–4 investigation into the safety of all selective serotonin reuptake inhibitor (SSRI) antidepressants (including Seroxat), the MHRA's expert working group discovered that daily doses of SSRIs of more than 20 mg were no more effective at treating depression, regardless of its severity, than doses of 20 mg or less. At the time 17 000 individuals in Britain were receiving daily doses of SSRIs at 30, 40 or 60 mg, thus increasing their risk of suffering adverse effects,^{22–23} and increasing the costs to the NHS, without any improvement in efficacy. For our purposes, the important point about the new advice about safe dosing levels which resulted from this investigation was that it was not

prompted by newly submitted information, but following a *reanalysis* of data which had been in the MHRA's possession for over 10 years.¹⁴

Abraham has drawn attention to other examples of the MHRA's failure to act swiftly on evidence of the adverse effects of licensed drugs, such as its handling of Halcion, a triazolobenzodiazepine (tranquiliser) manufactured by Upjohn.²⁴ First licensed in 1978, the UK's Committee on Safety of Medicines began investigating reports of adverse effects as soon as the drug was licensed for use in the UK. Despite the existence of data dating back to the 1978 which proved that Halcion was not safe, the drug was only removed from the market in 1991. Far from being an aberration then, the MHRA's inability to gain access to all relevant trial data in relation to Seroxat indicates that there was a failure to learn lessons following the Halcion episode.²⁴ ⁱⁱⁱ This point resonates with recent work by David Demortain, who has suggested that one of the reasons why drug crises so often fail to produce any regulatory change is because accountability is "determined by the action of a group which, ironically, is likely to minimise the novelty of lessons publicly drawn from the crisis in an attempt to defend its ownership and minimise its responsibility".²⁵

It is worth noting that regulators in the US have a rather different record. There are obvious similarities between GSK's withholding of the Seroxat trials and a case in the US, 20 years ago, in which Eli Lilly had failed to report a number of fatal and serious adverse reactions, in UK patients, to the drug benoxaprofen (an anti-inflammatory drug marketed as Opren in the UK and Oralflex in the US). According to the US regulations, companies are required to report to the FDA any "unexpected side effect, injury or toxicity within 15 days" of receiving notice of such an event. In the case of benoxaprofen, because the adverse reactions had occurred in the UK rather than the US, Eli Lilly's lawyers argued that there was a lack of clarity over whether the regulations required the company to report them. Despite the existence of a degree of ambiguity, the FDA successfully prosecuted Lilly for failing to report four fatalities and six illnesses which were relevant to the safety of benoxaprofen. As Abraham as pointed out, in the US, the argument that non-US adverse reactions did not fall within the word "any" was given short shrift, and the spirit behind the regulations was decisive.²⁶

This episode is in sharp contrast to the MHRA's comparatively lax treatment of GSK. In the absence of any serious threat of sanctions for withholding data from the MHRA, have companies in the UK, in fact, always been free to hide negative trial results with impunity? Unlike the FDA, the MHRA has *never* prosecuted a company for failing to submit relevant data. As Tim Kendall, joint director of the UK's National Collaborating Centre for Mental Health, suggests in an interview with LM:

The 1998 GlaxoSmithKline memo, which suggested suppressing trial data on paroxetine use in children, is unlikely to be a lone aberration. I think it is absolutely necessary for physicians, psychiatrists and indeed the public, to publicly and forcefully say that this is completely unacceptable. This threatens the evidentiary basis of contemporary medicine. It's nothing short of a battle for the truth.²⁷

The failure to detect unsafe dosing levels; the failure to learn the lessons from Halcion, and the failure to prosecute GSK might all be said to cast doubt over the MHRA's ability to

regulate effectively, raising the prospect of risks to its reputation. For the regulator to reveal that it did not know of the existence of evidence which casts serious doubt upon the safety or efficacy of a widely prescribed drug immediately raises an inference that the regulator, which is under a duty to demand and analyse all such data, has not done its job properly. In relation to their inability to gain access to GSK's missing trial data, perhaps fortuitously, the MHRA has been able to manage this potential reputational risk by blaming the law itself.

CONCLUSIONS

We agree with the MHRA's conclusion that the legislation and regulations which cover drug safety in the UK have been revealed to be insufficiently robust to ensure that companies submit all data relevant to determining a drug's risks and benefits, and we would support measures, such as compulsory pre-trial registration, to ensure that trials with inconvenient or "commercially unacceptable" results, such as Studies 329 and 377, cannot simply disappear. We are also pleased to see that the Agency announced in October 2008 new amendments that aim to close the gaps in the law described above. When the Medicines for Human Use (Marketing Authorisations Etc) Amendment Regulations 2008 come into force, there will be a duty to provide "information arising from use of the product (a) in a country or territory outside the European Economic Area; and (b) outside the terms of the marketing authorisation, including use in clinical trials". It is to be hoped that the law will now be sufficiently clear to ensure that the duty of candour which had always been assumed to attach to information about a product's risk/benefit profile has teeth.

Where our analysis diverges from the MHRA's is with their assumption that the only problem this incident has revealed is the existence of loopholes in the legal framework. In our view, there are other factors at stake, which create incentives towards increasingly, and perhaps dangerously light-touch regulation of medicines in the UK. Many of these were highlighted by the House of Commons Health Select Committee in 2005, which found that:

The regulator, the Medicines and Healthcare products Regulatory Agency (MHRA), has failed to adequately scrutinise licensing data and its post-marketing surveillance is inadequate. The MHRA Chairman stated that trust was integral to effective regulation, but trust, while convenient, may mean that the regulatory process is not strict enough. The organisation has been too close to the industry, a closeness underpinned by common policy objectives, agreed processes, frequent contact, consultation and interchange of staff.⁹

Seen in this light, it could even be argued that defects in the regulatory scheme were convenient for the regulator. Instead of blaming its own structures and mechanisms, or, perhaps worse, having to face a high-profile criminal trial in which GSK's lawyers would skilfully pick over documents, memos and emails, in minute detail, in order to find fault with the regulator and its processes, the MHRA has been able to avoid these threats to its reputational status by blaming shoddy statutory drafting.

Kent Woods' letter to the CEO of GSK, Jean Pierre Garnier, informing him of the decision not to proceed to prosecution, suggests that a strengthening of the law "should be unnecessary in an industry which relies so heavily on public trust and aspires to high ethical standards".²⁸ The "moral responsibility" to provide data, Woods goes on to say, "*now* needs to be insisted upon by the unambiguous force of law" (emphasis added).

ⁱⁱⁱ See also McGoey 2007, p226 for further discussion of these points.¹⁴

Deftly, therefore, Woods criticises GSK for failing to meet their moral responsibilities, and the law for being too ambiguous. GSK has avoided prosecution, and the MHRA has avoided the intense negative scrutiny which would have been the inevitable consequence of a criminal prosecution. For both, then, could this almost be a win-win situation, four and half years in the making?

AUTHORS' NOTE

Following its acceptance in August, this paper was amended to include a reference to the announcement, in October 2008, that the Medicines for Human Use (Marketing Authorisations Etc) Regulations 1994 were to be amended.

Competing interests: None.

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