Transcription of a meeting at MHRA about Seroxat

29 April 2008

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KW: First we'll introduce ourselves and explain our role in all this. And just to give you a bit of general background about how the agency operates. And perhaps you could introduce yourselves and your interests. I'm Kent Woods and I'm Chief Executive here and I have been for the last four and a half years. My background is in clinical medicine, NHS consultant for twenty plus years. And came into the agency from a clinical NHS, university job. And I have no industry background. I've worked since I qualified for the Medical Research Council, for two universities and the NHS.

So I emphasise that my place in this is not at all from an industry perspective. And my concern is that the agency should contribute to the healthcare and good clinical practice, using the regulatory mechanisms, to ensure that patients get access to the most effective and safest treatments that can be contrived. Sarah, perhaps you could say a bit about yourself?

SM: My name is Sarah Morgan. I have worked in the MHRA for the last fourteen years in the pharmacovigilence and risk management side.

JC: My name is James Cook. I'm a solicitor. My background isn't in medicines regulation, it's in criminal law. First of all in private practice doing defence work. I joined the civil service about eight years ago where I worked for the Department of Work and Pensions as a prosecutor, prosecuting benefit fraud. I became the manager of one of the London offices doing that. And on 5th January 2005 I was recruited from the Department for Work and Pensions to the MHRA to lead their investigation in respect of failure to report information from paediatric clinical trials of Seroxat. I was brought in because the case was clearly taking on a very legalistic and regulation heavy quality to it, and they needed a lawyer to cut through that and to be able to define the issues.

JS: Pity they didn't tell you then. [laughs]

JW: John Watkins, communications division. Quite a varied, long background but before MHRA was formed I was for many years in the Medical Devices Agency.

DS: I'm Derek Scott. And I was on Seroxat for four years and it almost killed me.

JS: I'm Janice Simmons. Coordinator of Seroxat User Group.

PM: I'm Patricia Martin, I'm principal of Field Martin, solicitors. I'm the legal advisor, it's a pro bono role I took on, advising Seroxat Users Group. I've done this now for about just over a year. So I defer to Janice when it comes to the more technical issues such as how the MHRA and all the various agencies actually work together. And also her far greater depth of knowledge of Seroxat and the side effects of it.

KW: How would you like to use the time?

PM: Well, I'm going to start… I mean, I'm not quite sure, we haven't come with a formal agenda, other than we all know we're here to discuss the decision by the MHRA in conjunction with the various agencies not to prosecute GSK. And I've read through the report only once, and again this morning on the train coming up here. And I actually drafted up some questions which I'm happy to leave with

you by hand delivery which I'd quite like some written answers on, if that's okay? So if I could perhaps give you those.

And I'm quite happy… I think it might be a good idea if we actually run through the… some of these are obviously more serious questions than others. But can we just start by this issue as to why in fact it was in fact the MHRA? I'm not quite sure who I address that question to, why the MHRA rather than the CPS for example?

KW: I'll kick off and then enlist John's [NB: should have been James'] help if I need to. I mean, the MHRA has got the statutory responsibility under the medicines legislation to investigate potential breaches of medicines legislation. And so it's absolutely laid down in statute whose responsibility it is to do this work. And…

PM: But presumably if the conclusion had been different then there would have been a referral to not the CPSIC but in fact more the prosecution division of the Pensions and…

KW: Can I clarify that particular point? Because we are the investigating agency. And there is a separation between the investigation and the decision whether or not to proceed to a prosecution. And as you've referred to, the decision is made not by us, it's made by the prosecution division of the Department of Work and Pensions, government legal service. And that separation is, if you like, analagous to police investigating a crime and the Crown Prosecution service deciding whether to take it to court.

JC: It's not uncommon in government for regulatory bodies and government departments to conduct the criminal offences which cover their area of business. So for instance the Inland Revenue do the criminal investigations and prosecutions in respect of revenue fraud. The Department of Work and Pensions investigate and prosecute benefit fraud. The Environment Agency investigate things like illegal fly-tipping and prosecute it. The MHRA has a statutory responsibility, as Kent says, to investigate medicines fraud. And our cases are prosecuted by Department of Work and Pensions. Which may seem…

PM: It does sound a little…

JC: It does seem odd, but there are historical reasons for that. You'll recall that years ago there was a single very large government department called the Department for Health and Social Security. That split into the Department of Health and the Department for Work and Pensions. But the legal department didn't split, but remained a single body. And it just so happens that the lawyers within that single body, who prosecute our cases, the Department of Work and Pensions, largely because they have a large stock of criminal lawyers for benefit fraud, it's a large area of criminal practice, they prosecute about 12,000 cases over the year. So with criminal lawyers in that large legal department on the Department of Work and Pensions side of it.

PM: So James, you haven't been doing this for very many years, but have you ever prosecuted? Has there been a prosecution of the drug companies under the regulations?

JC: There have been two or three investigations. I think we've yet to have a case where a large drugs company have been prosecuted.

PM: So isn't it a bit unknown territory to you guys in some respects, then?

JC: It's new. The law that we're using was passed in 1994 and I don't think there's been yet a big prosecution for pharmacovigilence offences. Largely because referrals are relatively rare. You could count them on the fingers of one hand, quite easily.

PM: This must have been the largest investigation that's been conducted then?

JC: This is the largest investigation that the MHRA has conducted of any sort. And certainly the largest pharmacovigilence investigation. It's also, I think, of its sort unique more or less in the world. All the European countries that use the same legislation as we do, the directives from the European Union, don't all enforce in the same way. Some want to use criminal sanctions and others don't. In many jurisdictions there'd be no prospect of having a criminal prosecution simply because they don't have those criminal offences. Where jurisdictions do prosecute through the criminal route… and I'm fairly sure we're the only country in the world that have attempted criminal investigation or prosecution in respect of these facts.

PM: That's not actually true, I don't think. I don't know what the outcome has been. But certainly Eliot Spitzer.

JC: That's not a criminal case. That was a civil case.

PM: It is. It was fraud. No, it's fraud. It's the people of the State of New York, the Attorney General, and the allegation is… the cause of action is repeated and persistent fraud.

JC: As I understand it, that's a consumer affairs type case and was settled by way of a financial agreement in the way that civil cases are.

PM: This was looked at, I did the background to this.

JC: I read… I recognise the…

PM: You recognise the… I don't know… the outcome was presumably before Mr Spitzer got side tracked in other matters.

JC: It was, it was quite a long time ago. [laughter]

KW: And that was settled out of court?

PM: By GSK.

JC: That case related to medical information which has been passed by GSK to prescribers in the States, rather than being what the main focus of our investigation was about, pharmacovigilance, the reporting of adverse reactions.

JS: But surely before this investigation began even, you knew that it was going to happen, say. I mean, you knew that law didn't exist anyway. You knew they were going to wriggle out of it. So what was the point in spending all that money on the investigation?

JC: I wouldn't say we knew the law didn't exist; the law is there, but it's very complicated. And it's never been tested before in the criminal courts. With all

new legislation, it's not until it's gone through the court process a few times [that] it gets fleshed out and the courts make decisions to clarify the meaning of the law and how it's likely to be interpreted.

JS: It's just that now, the way it looks to us, it was all very clear-cut and simple, no law, they're off. And it seems very easy to us. Because the evidence has been there for so long and it should have been seen without such a massive investigation, to us. Because the evidence was there for so many years and you chose not to look at [it].

JC: The evidence… there's a huge mass of evidence. And some of it would have been seen by the MHRA and some wouldn't. There are specific requirements under European legislation as to what results have to be submitted to MHRA and which do not. The clinical trial evidence from which this safety signal emerged, which the criminal investigation looked at (and whether they reported at the time or not), not all of that clinical trial information, in fact the overwhelming majority of it, didn't have to be provided to the MHRA, and wasn't. So we hadn't had that information. We hadn't seen.

JS: Yes, but…

JC: Of the nine studies that were looked at in order to find the safety signal in respect of suicidality in under-eighteens, only one of those studies had been submitted to the MHRA. Because the regulation only required that one of them should be.

PM: Is that because the study was in this country?

JC: Yes. Yes, it had… well, one of the centres using the study was in this country and that created a regulatory responsibility on the GSK to submit that study.

PM: So one other thing is, you're going to be looking to change the [coughing] responsibility that they provide you with clinical data that they glean from other jurisdictions; is that what you're intending?

JC: I'd probably reserve for answers on points of developments in law to subsequent… the written responses that you've asked for.

PM: Yes.

JC: But as I understand it, I think you're correct in saying the clinical trials regulations which were introduced in 2004 will make it a requirement now for the sort of information that wasn't supplied in this instance to be supplied in future. So in a way, that gap in the legislation which has been exposed has already [been] filled. And has now been filled for three or four years. Other reforms will be brought about which are explained in the papers that were released with the announcement.

PM: If we can just… that answers the first question I think. The second one is more of a procedural thing. Again, this is very much because I don't… I'm not familiar with this area, my main area is commercial litigation. Can you explain to me what the procedural… I don't know again who should do that, but the procedural aspects of the clinical trials? I mean, it seems to me as if these trials are different numbers of individuals who are actually involved. Are there regulations, or will there be regulations that will govern the number of trials? I mean, a trial could be ten people or it could be a million people. I mean, it's…

KW: I can have a crack at that again, perhaps James can join in. I think there are two elements, as I understand to this question. Firstly, what are the requirements of the clinical trials directive, as transposed into UK law, for how clinical trials should be done? And there are two bits of European legislation which have been transposed. One is about the directive itself and the other one is about what constitutes good clinical practice in trials. So that is quite carefully set out and has been passed into UK law in the medicines for human use clinical trials regulations of 2004.

But the other question which I think underpins this is how big a trial, or how many trials do you need, to be able to persuade, for instance, a regulatory agency to grant a marketing authorisation. Now, that's a bit different from the pharmacovigilance question, but the answer is that there are general principles about the number and the size of trials that are going to be needed to convince an agency, whether it's us or the European agency, to give a marketing authorisation. It is customarily expected that there will be two what are called phase three trials done in sufficiently large groups of patients. [coughing]

But there is no rigorous specification: 'you shall study 392 patients'. Because it depends on the condition, it depends on the nature of the treatment, it depends on the size of the treatment effect. And you will not get in legislation that degree of specificity. There's a great deal of legislation about how the trials should be done.

PM: I understand what you're saying, and we can't have one size fits all when it comes to legislation. But as far as the governing body, the MHRA is concerned, is it intended that going forward the MHRA, when it comes to licensing certain drugs, will have… I don't want to be contentious here when I say, 'will learn lessons from the past'. Because one of the issues that I think the general public has, is that they fear there's been a lack of transparency in a lot of the proceedings, in a lot of the information that's been released into the public domain.

And GSK have got themselves to blame for this. We've seen this in the report that you have published into your investigation. And I can appreciate that it's had to distil an awful lot of information. But there is enough of a flavour of commercial interest of GSK being put first and foremost. And there is a reference actually in this letter to one of the – just pieces of information that's referred to here – that there is an internal communication from GSK, where they put the commercial importance of not damaging the brand of Seroxat to allow knowledge that in fact there are contra-indications, especially with paediatric trials to be made… to get into the public domain.

JS: But it's not only GSK, is it?

PM: Is it not part of the MHRA's, shall we say, lessons to be learned or in fact views that have been formed as a result of this investigation, to be far more vigilant in future as to what in fact you are going to require before you license any drug?

KW: There are several themes there which need to be disentangled, need to be dealt with separately.

PM: I'm sorry.

KW: I think they're all important themes but we need to separate them out. In terms of lessons to be learned, I think it's fair to say that the whole business of medicines regulation is a continually evolving and developing area, going back to the Medicines Act in 1968. And the scale of clinical trials data required now to achieve market authorisation is vastly more demanding than was the case when the legislation came in. In fact, from '64 to '68 the whole system was voluntary anyway. But there's been a progressive increase, not only in the quantity of data which are required to get a marketing authorisation, but the quality of data too.

And I think the second thing I'd just like to pick out from what you said is that in this instance we're talking about the use of Seroxat specifically in children and adolescents, for which there had never been a marketing authorisation sought or granted. And the nubbin of the legal issue has been essentially around the obligation of the manufacturer to provide data in relation to the use of a product for which they've never sought or obtained a marketing authorisation.

PM: But they were aware it was being… they had to have been aware it was being prescribed, and that is really the crux of this whole issue, isn't it?

KW: It is the crux of the issue. And I think it distinguishes, in my mind anyway, the distinction between what I consider to be the moral and ethical responsibility of the company to make available the information on which prescribers and patients can make informed decisions. Even if there isn't a legal obligation on them to make that information known, I think there is a distinction between the ethical and the legal requirement. And clearly with abuses taking place, those two will narrow. And the point I made on this accordance was that if companies won't accept an ethical responsibility then…

PM: They've got to be regulated.

KW: …it has to be spelt out, line by line, in statute, what they should have to do.

PM: I'm delighted to hear you say that, because in fact it came out loud and clear in the MHRA report that although you may have drawn the conclusion (we'll come onto the basis on which you did draw those conclusions), that [sic] you couldn't prosecute for legal reasons.

KW: Well, the government legal service drew the conclusion, but yeah.

PM: I'm using short-hand here. But the point is, though, it came through quite loud and clear to me that even if GSK had complied with the letter of the law they certainly had not complied with the spirit of the law.

KW: Well, the spirit of the law, the broader ethical responsibility for a company marketing pharmaceutical products, I think, is the same as an ethical responsibility on any other provider of healthcare if you like. And it is more demanding than simple legality. But there's an interesting point I'll just flag up here. The actual evidence of harm in relation to children and suicidal behaviour came not from any individual trial, it came from the pooled analysis of all the trials that there were. Now, that is a [pause]… [a paper is passed to KW] I'll have to read this separately but this is the… I recognise what this is but…

JC: The trials that they are, are well known and that's been published.

KW: So the company's ethical responsibility is to interrogate all the data to which it has access. But the legal requirements are actually very much based on the trial by trial requirement to notify us of what the trial showed. And so the more demanding and the more flexible research methods become, the more the company can actually dig and dig and dig and see what they can find from the totality of the information. And the legislation is running along behind and trying to catch up with the reality. Meta-analysis, for instance, didn't appear until 1984. And so the techniques get better, the analytical approaches get more discriminating and the law is running along behind. And that's why I think there is always going to be an ethical requirement on the company because the law can't keep up.

PM: And also just the nature of the beast, quite frankly. These are commercial enterprises, they're driven by profit. First and foremost their responsibility is to their shareholders. And there's always going to be tension between profit and, shall we say, the greater good of the general public.

KW: Yeah, that may…

PM: Well, you just have to take the one internal document that in fact was identified in your report, that came into the public domain. You know the one I'm talking about.

KW: Absolutely.

PM: Where, I mean, that was an internal GSK management document, dated October 1998. It would be commercially unacceptable to include a statement that efficacy had not been demonstrated, because this would undermine the profile of Paroxetine.

KW: Yes. I wouldn't even begin to try to defend that. I think it exactly highlights the issue about legal requirements and ethical responsibility.

JS: There's one thing that really bothers me about this whole thing. And that is that you've… well, they say that these drugs are dangerous for under-eighteens, dangerous for under-twenty five, dangerous for under twenty-nine, dangerous in the elderly.

KW: Ah, can I come back to you on that? Because I think those statements are a bit over-inclusive. We're talking… we're always talking in this agency about risk benefit. If we're looking for safe drugs, basically it's a vanishing concept. There is no drug which doesn't have the potential to cause somebody harm.

JS: No, of course.

KW: So we'll always have to look at the trade-off between the potential risks and the potential benefits to the individual.

JS: But the problem being, I don't think the general public are made aware enough…

KW: You're quite right, Janice, you're absolutely right.

JS: …of the risks.

KW: And one of the things that we did soon after the MHRA was formed was to set up a communications division inside the agency so that we can do more to put out information to prescribers and users, and it's essential. It's as large a part of our job as a regulatory agency to get that information out as it is to actually say to a company, yes you can or, no, you can't market this product.

JS: It's like your promotion of the yellow card system, for instance. I mean, I think you're trying hard to promote that, and that's good. But the way it's being promoted is that it is quite okay for us because we know what's going on. But for an ordinary member of the general public who trusts their GP totally, I don't think it's good enough.

PM: And even the GPs quite frankly, again the GPs, often a lot of the information they had came from the salesmen from GSK, which is another issue altogether. It's a can of worms.

KW: You raised an issue which goes back to something Janice was saying, why did it take us so long to investigate? We needed to know what the company was saying throughout this whole period of years, through its sales force, to prescribers. That's one of the reasons why it took so long. It's not a simple matter of saying, oh, let's go and look at the legislation, the legislations are unclear, let's just drop this case. We needed to know whether in fact the company was making claims or misusing data in their promotional activity.

JS: And now you know they are, what happens to them? They get a rap on the knuckles, you know. I mean, it's disgusting, absolutely appalling. They did get a stiff letter, didn't they, and that's about it. I mean…

PM: Well, they had the prospect of criminal proceedings hanging over certain individuals for some time. There is no such thing as a bad company, only bad executives of a company.

KW: I think this has actually produced a bit of a shockwave to be honest. I think the fact that a company of the size and reputation of GSK has been subjected to a criminal investigation running over years... And this report, which does nothing at all for their professional reputation, or their company reputation, is not trivial.

And the reason I say that is because even in the last two or three years companies… and GSK has been prominent among them, have moved much further and much faster about transparency. For instance, the principle of putting all their trials into the public domain is now accepted. And that's a voluntary industry wide-activity which GSK are very keen to take up on.

PM: To be cynical about it, you can say that they were… they embraced that concept because they knew it was going to be forced upon them.

KW: Well, I think that is if you like the… one of the spin offs of this whole process of rigour. That to an extent, getting a conviction is less important than getting compliance with good ethical practice.

PM: I think in the long term I agree entirely. I think in the short term, people like Derek for example, who have real grievances as far as this drug is concerned.

DS: I feel very angry about Seroxat. It's really damaged my life.

KW: And angry in that you felt that you did not have information that would have influenced your decision?

DS: Yeah. I've actually got a Yellow Card here. [produces document] That's what that drug did to me.

JS: I think we all feel very angry about these drugs. It's how we communicate with other people about it.

PM: I have to say I know that Panorama have done a number of exposés on this drug. This drug, of all of the drugs that the MHRA govern, shall we say, has had a very high profile in the public consciousness since 2002 when the first Panorama programme went out. I have to say, and it's picked up in my letter, if you want to follow the questions through, and I'm not sure to what extent we need to, because you've got it here anyway and no doubt you'll be able to respond. But to what extent was it because of the Panorama programmes that the MHRA appeared then to get more interested in this?

You say in the report that in fact you had been monitoring the situation. But the timing of this, it's quite clear when you see it set out, the dates, when you actually called for meetings with GSK, all seem to follow on key moments from the airing of the Panorama programmes. Now, it's not a criticism if that is indeed the case. Because it's not surprising that in fact the MHRA would want to be seen to be responding to high public…

KW: I think should respond – not so much *seen* to respond – should respond to what appears to be new information.

PM: Yes.

KW: And the whole story going back to 1990 or thereabouts has been that we've had external expert advisors, our Commission on Human Medicines, Committee on Safety of Medicines, revisiting the risk/benefits of SSRIs as a class, since they were first authorised. And there had undoubtedly been a situation where if Panorama presents information which appears to be new, then we revisit. But the whole field has been examined and re-examined and new advice has been put out. I mean, this is in Sarah's area. But we have put repeated advice and guidance out to prescribers to help them to use this class of drugs to the best effect.

PM: But surely it's only because Panorama went looking for… because they were responding clearly to a heightened public concern, people like Derek, that Panorama even investigated. But these are investigative journalists. The MHRA, sorry, it's your job surely to be… I mean, isn't part of your job to continue to monitor the licensing of drugs?

KW: Absolutely. And it happens routinely for every product which is on the market. We have a continuing monitoring process. And if there are areas of concern, either coming from reports coming in from companies or from the field or from patient reports, we will as necessary go and get fresh external expert advice. It's ongoing, it's continuous.

JS: But if you're only getting ten percent of reports back by yellow cards – only ten percent, you know, what good is that? You're not getting…

KW: Well, now that's a good question.

JS: …the right information, the true information, are you?

KW: There is at least one large country in Europe which technically has a legal requirement on doctors to report adverse drug reactions.

JS: That would be good.

KW: Yeah, well, I'm afraid…

JS: [laughs]

KW: …in France, which is the country I'm thinking of, they have no more success in getting spontaneous reporting in than we do. How can you make a legal requirement on somebody to report a suspicion of something?

PM: Well, how do you enforce it, is the point?

KW: Absolutely, it's unenforceable.

JS: Yeah, but the doctor has to take the oath.

PM: The Hippocratic oath, yes. But I understand the point you're making, that it's rather difficult to enforce.

KW: It is impossible to enforce. And essentially over the time that the yellow card system has existed, since 1964, the reporting through that mechanism began with doctors and coroners and then it became extended to pharmacists and nurses and patients - we're constantly trying to find ways of expanding the reporting base.

PM: To harvest the information that's there.

KW: To harvest the information. But it is never going to be more than a proportion. It doesn't even have to be complete. All that system is there for is to give us signals which we can then investigate by better methods.

PM: But the impression I have had is often the anecdotal type evidence that Janice's Users Group has obtained has been somewhat downplayed by the MHRA. It's seen as something less than worthy than, say, the yellow card system. And I certainly know that Doctor Herxheimer, when he reviewed and vetted all of the emails as a result of the first Panorama programme, both he and Charles Medawar were, in certain sections anyway, criticised because this was anecdotal.

But the point is, that's nothing more than anecdotal half of the time. Because in fact you are not using standardised words. You're dealing with each individual GP who will report what, first of all, [is] his interpretation of what the patient is telling him. So he may talk about sleep disruptions or…

DS: I've actually got a letter here from my GP. [produces document]

PM: What was the point you wanted to make, Derek?

DS: It's just that my GP was actually making the point that I wasn't getting any better on the drug and I couldn't get off it.

PM: Yeah. Actually it's an interesting point. Because again, I mean, I'm not… I don't practise in this area, so I'm not familiar with the terminology. But for me, when you say that a drug is addictive, it means it is difficult for a patient to come off easily. It seems that the MHRA, in keeping with the pharmaceutical industry, uses a rather more euphemistic approach to… you don't call them withdrawal symptoms, you call them all sorts of…

DS: Discontinuation symptoms.

PM: Discontinuation syndromes and symptoms and whatever else. But your average patient who's looking at the patient information leaflets that he gets with his drug would look for words that they would recognise immediately. Such as, is this addictive, is this an addictive drug?

DS: It actually made me suicidal.

JS: But GSK removed that statement, didn't they? In 2003, this drug is not addictive. I wonder why?

KW: Well, there is a medical problem here in terms like 'addictive'. Because they do have quite a precise meaning, and they're not generally understood in the sort of lay sense. The worry… if you label a drug as addictive that isn't actually addictive, you can have the undesirable effect of actually discouraging people from using a treatment they actually need. And one of the problems that I faced in clinical practice over and over again, where patients clearly needed medical treatment for severe depression, the question would be asked of me, 'Is this an addictive drug?'

JS: But how do you decipher severe depression? There is no test.

KW: There is no test. But there's a pretty clear clinical diagnostic algorithm for diagnosing depression, a diagnostic manual. A diagnostic statistical manual sets out very clearly what constitutes the criteria for severe depression.

DS: But there have been recent studies that showed that antidepressants, all of them, were no better than placebo.

KW: No, no. I'd have to challenge you on that.

JS: Except in severe depression.

KW: Are you talking about the whole study, the amount of analysis that came out of it?

DS: Yeah.

KW: What that showed was… and it was a study that wasn't above criticism, it was criticised at the time, it certainly showed that the effectiveness of antidepressants was difficult to demonstrate in anything less than severe depression. But if you look at the marketing authorisation for antidepressants, it always says, 'indicated for major depressive disorder'. It's not for minor depression, it's not for unhappiness, it's for major depressive disorder. And what that study actually showed was to confirm the licensing authorisation; these are not drugs to be used for trivial indications. They really are not.

PM: But if you just look at the figures though, the total number of SSRIs that have been prescribed, you know you're not dealing… these are not being prescribed just for severe depression.

JS: Yeah, what I was going to say is that therefore that proves surely the point that the drug companies have given false information to health professionals regarding the drugs. Oh, they'll be okay for shyness, they'll be okay for this and that. And doctors have just prescribed them so willy-nilly.

KW: The company, by law, is not allowed to promote its product outside the terms of its licensed authorisation. And that's why we ploughed through these million pages of documents to see whether the company showed any documented evidence that it had encouraged its sales force to push their product for indications that they didn't have a licence for.

Now, there are two other players in this. Okay, there's the company which would quite like to sell its product. There's the prescriber who's trying to find the best solution for a patient, and there's the patient who wants the best treatment going. And I think there's this complex triangular relationship. And we shouldn't only focus on the push factor from the company, although that is sometimes taken to the limit. But there is the pull factor from patients and there's the pull factor from doctors who really want to do something useful for the patient. And I contrast the example of antidepressant treatment with the example of anti-hypertensive treatment or lipid load treatment. You don't see the same…

PM: Pullings.

KW: Pulling factor. You don't see the same grossly over prescribing.

PM: But what you're saying is the dynamics of the nature of the beast is at play, and the patient wants a quick fix.

KW: Well, it wants a fix. And let's not underestimate the seriousness of depression as an illness. It's a thoroughly unpleasant condition and it is not without its morbidity and its risks. And we can't forget that these are not tablets to be distributed for fun, they're being dispensed to treat conditions of distress.

PM: But surely then if we're talking about severe depression, you talked about that, this is something that you can clinically assess, depending on the various parameters. Surely then you should have to have a referral to a psychiatrist before in fact they are prescribed with an antidepressant? Because there are so many contra-indications now that people that are not severely depressed, perhaps just moderately, or in fact even low in mood, that have been clearly prescribed these drugs, have ended up with far worse problems to contend with – and Derek, I'm sure, will probably say he's one of them – than they have, than giving him nothing else than a kind word and encouragement.

DS: The letter actually states that it wasn't helping me.

PM: If anything, it was, well…

DS: It was making it worse.

PM: It was making it worse.

JS: My husband was prescribed them because his first marriage went wrong. I mean, and seventeen years later he's still on them.

KW: I guess the real problem is there is no one size fits all. And every patient is different and there has to be, if you like, a negotiation between the patient and the prescriber as to what is the best way forward. We don't have the powers, and we probably shouldn't have the powers, to dictate what the individual patients, individual prescribers, decide to do in that situation. We regulate the company, we don't regulate the prescriber or the patient.

JS: I think that's where it goes wrong.

KW: Well, it goes wrong. But if you think about it, Janice, how could it be different? I mean, I couldn't, from this office in central London, dictate how a patient in the north of England, being treated by a GP in the north of England, should be treated in detail.

JS: But you could talk to the GMC. Maybe you could communicate with the GMC and other organisations more closely.

KW: A lot of guidance does go out. Not just from us, but we work closely with NICE. And at the time of the report on antidepressants we worked very closely with NICE. So that their clinical guideline, developed by professionals, psychiatrists, patients, GPs, were actually linked into our advice from the safety point of view.

JS: One of the things we brought up, I think Sarah will remember this one, is that we would like to see coroners receive more information about SSRIs. Because we believe that we are not going to see the true suicide figures until all coroners are aware that these drugs can be linked to suicide. And we do see that you're… there is something on your website for coroners but we don't see enough.

PM: Well, Lord Hunt, before he changed jobs, actually undertook to raise this with the Ministry of Justice. I remember when they were reviewing the coroner's rules and we met in June last year. I don't know where that's gone; it would be nice to have an update. Since in fact we've been promised that he would look into that and whether in fact there would be a…

But to come back, sorry, to the question that I raised, which is, would it not, since in fact it is really only to be used for the treatment of severe depression, why would it not be thought a good idea to only have these prescribed by a psychiatrist as opposed to a GP? When in fact there has been… the point I'm getting at as well is, you know – and again, it's responding to one of the points you've just made about you can't regulate what the – the pull factor shall we say, from the patients.

But the point is, these are NHS prescriptions. And the government has every right to be more discerning in what is prescribed. Because it's a multi-billion pound industry. And if in fact the risk benefit analysis is not in favour of prescribing, why are we… why are you still… why is the government still allowing this to continue at a vast cost to the NHS?

KW: Allowing drugs to be prescribed to subsets of patients within the evidence of benefit is not sufficient. It comes back to this individual clinical judgement and patient preference factor. Now, you either try to mandate clinical care from the centre or you actually have to depend on the interaction between the patient and

the prescriber to reach the best solution in that individual case. And I've sat on both sides of the table on this one.

And my own view is that there is a limit to how you can circumscribe and specify prescribing decisions. And that goes across the board. I'm not just talking about prescribing for depression, but prescribing for blood pressure, prescribing for this, that and the other. There are very seldom situations where you can say it is absolutely one to one. You see this, you give that. You don't see this, you don't give that. And depression…

PM: I'm not suggesting that, though. I'm not suggesting that. What I'm suggesting is that if in fact it is accepted that these SSRIs should only be used for the treatment of severe depression and your average GP… it's clear from the number of prescriptions that have been written, they are not just prescribing for those with severe depression. They're prescribing for different varieties, low mood, all the way up to…

JS: My doctor's surgery at the moment, they don't prescribe anything other than Prozac and Venlafaxin and Cyprimil. They're the only three that they use. And to me, it's still not good. Because Venlafaxin as you know was only prescribable by psychiatrists for a time because of the risks and now it's… oh, it's okay now. And doctors seem to, I don't know, they only pick up on what they want to pick up on.

PM: Well, Kent, you've said, the patient themselves, the dynamics, there is a pull factor.

KW: There's a pull factor.

PM: There is a pull factor. And the patient wants a quick fix. He wants to go and get a happy pill. And that's how often they see this. What we're saying is, surely given the body of evidence now that there are a lot of cases – and I accept what you're saying – you're constantly monitoring the risk benefit, but there is enough anecdotal evidence, surely, to say at the moment, right now, that apart from severe cases of depression, these drugs ought not to be prescribed at all to patients? And we're getting away from just paediatric prescriptions now.

KW: The Royal College of Psychiatrists ran a campaign some years ago to improve the recognition and proper treatment of depressive illness on the grounds that they felt that there was under-treatment, under-diagnosis of depression. And that patients were being left in distress and sometimes at risk of harming themselves, because GPs were not sufficiently sensitive to pick up the rather treacherous signs of depressive illness. So there is this…

PM: But weren't they advocating at the same time that there would be more counselling? That the facilities in counselling, which of course is far more expensive...

KW: Well, it's more expensive, and also, I have to say, the evidence base is less. The one thing about drugs [is] you can expose them to decent size trials. And you have an authorisation step. But the trials of counselling, I think in principle it's a good idea, but the trials are less robust and…

PM: It's difficult to have an empirical calculation of counselling.

KW: Absolutely. You have to ask the question, well, it sounds as though it's a good idea but it's actually much harder to evaluate the role of counselling than it is the role of pharmaceuticals.

PM: I thought the Royal College of Psychiatry themselves have advocated more counselling.

KW: There is a strong lobby, and quite properly I think for the greater provision of counselling.

PM: Especially for…

KW: For people who don't meet the criteria for severe depression, I agree with you. But then if the resources available to a GP are limited there is a very strong urge to try and do something for a distressed patient and there's never been enough counselling available in the NHS to meet all these…

PM: Well, this is one of the issues that I know Janice has tried to raise on numerous occasions, about self-help groups. Even if the NHS cannot provide one to one counselling, then surely the NHS can look into… hopefully with the MHRA's sanction and encouragement, the number of self-help groups where people like Derek can go to be with people who have had similar experiences, you know, sharing their issues and their problems... And also then harvesting for the MHRA information which you can then use. The biggest problem…

KW: Yeah. And there's a huge role for patient organisations like that. I mean, seriously not just in terms of mutual support and advice, but in terms of an information source to us. These are what we draw on.

PM: But Kent, it can't be left to well-intentioned people like Janice to organise these things. Surely this has to come from the top down. That where in fact there are… that you identify that this is a major issue, there's no getting away from it, there is a major issue, there's a perceived problem now, what is going to be done. Making sure that the drug companies don't actually have a clear run in the future, yes, I agree, is a positive step in the right direction to ensure that there is a positive obligation to report any adverse reactions. But this issue – and depression is, and in fact with modern living, is going to become a more acute problem, not a less acute problem – what is going to be done to address the issue? I personally don't believe that it's a question of developing another drug that perhaps doesn't have the same contra-indications. But the self-help groups…

JS: You see, the main problem that we see, emails coming into the group, is people trying to come off the drug. That is the biggest problem. And doctors don't have a withdrawal protocol to help patients come off the drug. And there are many, many GPs out there instructing patients to come off the drug by taking the drug every other day. And that is not going to work for many patients.

PM: That could exacerbate the symptoms.

JS: I've seen what happened to John when we were told to try it that way. And that is very sad in my book, and they do need help. We put something on our website two years ago now, asking how many people would be interested in support groups. And we've had a really good response. Many people have said, 'Yes, it would be great to go somewhere where we can get proper advice

on coming off the drug.' That is your main problem, our main problem, everyone's main problem is coming off these drugs.

PM: And there has to be a cost benefit in this. I mean, instead of having people like John who's been on this drug for seventeen years, the cost to the NHS, to actually have a successful… maybe not in his case now, but to get people off these drugs. If they're not doing any good, then what happens is, it's quite clear that some people do benefit from them, others don't. And in fact, there are a lot of people who don't derive any benefit from this drug.

DS: And I'm one of them.

PM: Yes, Derek is one of them. Then he has to contend with the issues about coming off a drug.

JS: You've stated today in several instances that it would be difficult to do this and that. In Sweden they have a system where every suicide that happens that is preceded by antidepressant drugs or psychiatric drugs of any kind is recorded. Why can't we do that?

KW: Well, the data if you run a system like that, the data becomes really very difficult to make any sense of.

PM: It's a starting point I think though, Kent, surely. I know what you're saying; it doesn't mean to say… it's like saying that, you know, grey socks are dangerous for people because the vast majority of people are wearing grey socks.

KW: Wearing grey socks, that's right. I mean, the problems of drawing scientific conclusions from data like that are really very, very challenging. We possess, in this agency, the general practice research database. When we were looking at Seroxat we went and interrogated that database… these are data collected from six percent of UK general practice. Anonymised patient data. So we've got every prescription, every clinical outcome, every test done for a huge amount of clinical activity. You go and ask the question, what is the evidence of an association between Seroxat and suicide and Seroxat and self-harm? You come up against the problem of disentangling the effect of the treatment from the effect of the condition for which the treatment was given. And that's always going to be the way. And I think it's particularly difficult in relation to antidepressant treatment.

PM: But just because it's difficult doesn't mean to say you do nothing for it.

KW: Absolutely not. I'm not saying one shouldn't try to tackle the problem. But the fact is, it is scientifically very difficult to draw conclusions.

JS: When I spoke to you on the phone you said that you didn't believe that SSRIs caused suicide in adults.

KW: Yes.

JS: You don't believe that?

KW: No, I don't believe that.

JS: Well, I would like to put a really maybe rude question to you… I don't know, cheeky. If you think Seroxat and other SSRIs are safe for adults, would you consider taking it for three months?

KW: If I were depressed, I would certainly…

JS: No, no, they're not dangerous.

KW: I'm sorry.

JS: They're not dangerous.

KW: I don't know what you're doing.

PM: She's issuing you a challenge. She's issuing a challenge and…

KW: Would I take a treatment even if I didn't need it?

JS: Yes, but if it's not dangerous in adults and if many people have been prescribed it unnecessarily, who are not severely depressed, would you still take the drug?

KW: I wouldn't take any drug I didn't actually need.

JS: No.

KW: That's the whole basis of making a risk benefit decision. If I was depressed enough to feel I needed treatment, I would certainly consider an SSRI, tricyclic antidepressant.

JS: I think the way it comes over is, this drug is safe. It will not cause suicide in adults. Not if you're over thirty years old, you are not at risk of suicide.

KW: We have never said the drug is safe.

JS: Oh, no, I know you haven't actually said that. But I think… you see, I think we become different, we are not the same as the general public out there. We know a little bit more about drugs, etcetera, maybe… I obviously know a lot less than you.

KW: Sure.

JS: But the general public out there, they trust their GP. And that's the only person they trust when it comes to medicine. And the wrong impression is being given.

KW: Well, the alternative is not to trust their GP.

JS: Well, yes, but… I mean, I always [inaudible 54:10]

PM: Yes, people do.

JS: I mean, I wouldn't.

PM: My understanding is there was a test done that involved… and in fact it was… who, the chap up at Bangor?

JS: David Healey.

PM: David Healey referred to the test that was done on volunteers who took Seroxat. No previous history of mental illness. And there was even one suicide. And there were a lot of…

DS: Well, suicidal ideations.

PM: Yes, sure. As a result of… and that is… it addresses the point you made before that where you have an illness like depression, where you have the side effects, I'm using layman's terms now, that in any event are problematic and it's difficult to differentiate what's been caused by the drug and what's been the underlying problem. But where you have a test of that on perfectly healthy volunteers and you start seeing the sort of results that David… was it a test that David Healey actually did?

KW: Yeah.

PM: They actually had to discontinue. I'm not sure whether those results were made available.

KW: Yes, we've seen those studies. That's the only sort of context in which you can pick up an effect which is clearly not due to underlying illness.

PM: But it addresses the issue then that Janice has just asked you. Why do you believe that they don't cause suicide, when you have that sort of test result?

KW: The evidence that we've got from all sources does not support the view that in adults SSRIs themselves cause suicide.

PM: How do you explain that Healey study?

KW: That wasn't suicide. I mean, you're talking about undoubted psychological effects in a drug given to healthy volunteers. But that's not the same as saying that SSRIs cause suicide.

JS: [laughs]

PM: But they cause suicidal ideations, is what I understand.

KW: Well, in…

PM: But actually if you took someone who would be otherwise…

DS: Normal.

PM: …would not consider taking their own life.

KW: The logical conclusion of what you're saying, Patricia, is that on the basis of that evidence the drug should not be available?

PM: No, no. I'm just saying to what extent… I'm actually addressing the issue that you said, that you don't believe that SSRIs… you personally, Kent.

KW: I don't think… no, let me refine that down to, I don't think the evidence we have supports the interpretation that SSRIs cause suicide.

PM: That's somewhat different.

KW: Well, I can only work on the evidence.

PM: Okay.

KW: That's the way we are.

PM: The lawyer in me would actually say that's somewhat different. Because then the issue is surely the government should be actually sponsoring its own research into whether…

KW: It does. There's a large NHS R&D programme which funds trials, including…

PM: And what is… not trials, but I mean monitoring in the SSRIs? What is happening at the moment? Given that there is this body, a lot of it is anecdotal, some of it is clinical.

KW: What sort of data would you like to see that isn't being collected already?

PM: No, no, you tell me what is being done. Because I'm only responding as a lawyer to what you have just said. There is insufficient evidence available at present to make that statement that SSRIs can cause suicide, people to commit suicide or have suicidal thoughts.

KW: I take some reassurance from the observation that during the decade on war, when SSRI use was going up like that, the population suicide rate was going down. Now, that is an ecological argument, to use a technical term. It doesn't prove…

PM: It doesn't prove anything, that's my grey socks point. You'd have to look at all of the other sociological factors as well.

KW: Yeah. You'd have to argue quite strongly for special circumstances to explain if indeed SSRIs were themselves a contributor to suicide, why a quadrupling of the prescription of SSRIs accompanied chronologically a decline in suicide rate.

PM: Well, the whole study would suggest a placebo effect. But in some cases… I'm talking about non-efficacy, the whole study would suggest that a lot of people improved on SSRIs. Not because in fact the SSRI was working but because they thought it was actually making them better.

KW: That's undoubtedly the case. There is a very strong placebo effect in all areas of mental illness.

JS: Do you only consider trials done by drug companies, then, and nobody else?

KW: No, not at all.

JS: So why don’t you consider these other reports that are saying, such as David Healey's?

KW: We consider all the evidence that we can find.

JS: And you still say that they're not dangerous?

KW: We've looked at the Healey data, we've looked at the GP data, we've looked at the yellow card data, we've looked at the trial data.

JS: I can't believe that you still say that… I could show you so many emails from relatives and patients that have tried to commit suicide, that have harmed themselves.

PM: That have succeeded.

JS: Yeah. I could show you so many emails. And I have a copy of every single email that I have ever received through the SUG and I couldn't carry it here today.

KW: But Janice, do they get into the real problem that people are taking these drugs because they have depressive symptoms?

JS: Not always.

PM: Not always.

JS: Seventy-five percent of prescriptions for SSRIs are for mild depression. Only twenty-five for severe depression.

PM: The nice lady that now lives in Ireland, what's her name? The lady I spoke to.

DS: Steph Pratchell?

PM: Yes. Her daughter committed suicide. And in fact she was only prescribed Seroxat… she'd been taken to the doctors because her periods had not started at age sixteen. And the doctor asked her the question, 'Does this make you feel a bit down? I've got just the thing for you.' Prescribed her Seroxat. Within eight weeks she'd committed suicide. She had had no history of depressive symptoms even.

KW: And cases of that type are always at first sight very persuasive. But let me just draw your attention to something else that went through the media a few weeks ago. This cluster of successful suicides in South Wales, where the individual was concerned, the great majority gave no inclination they were suicidally inclined. This is a treacherous, unpredictable event in particularly the young adult population.

JS: And do we know how many of them were on antidepressants?

PM: I don't know if any of them were.

KW: I'm not aware that any of them were.

JS: I think you'll find that they were.

KW: But these were people who were not thought to be depressed. But this was – it's always difficult to work from the media – but the fact is it is a treacherous event. And I personally have been taken by surprise by episodes of self-harm in patients who were not judged to be at serious risk.

JS: You see, we see the problem, you know the guy in Crete who threw himself off the balcony with his children. Now, you see, we all tend to think, and maybe it's wrong, I don't know… but as soon as an instance like that occurs we instantly think, ah, we know why he did it. And it wasn't until a few weeks after that incident that the truth was found out, from our point of view, that guy had

stopped taking his medication, which was Sertraline I believe, for two or three days before that incident occurred. He stopped it abruptly so he could drink, because he was trying to get back with his wife and they were on holiday, he wanted to have a drink. So he quite wisely, in some respects, stopped the medication.

PM: And that's an abrupt ending of a…

JS: And probably the alcohol with the Sertraline, is still in his system, that's what happens. And we see so many instances of this, you would not believe it. And if you look at a website, SSRIstrories.com, you will see absolutely thousands and thousands…

DS: And our site as well.

JS: Yeah. It's just not good what's happening. If you care for people, please, please listen to us. And please do something.

KW: What do you want to see done, Janice?

JS: I want support groups set up to help these people. That is my main objective at the moment.

DS: Funded.

JS: Well, yeah.

KW: So we're not talking now about the regulation of the drug, we're talking about something…

JS: No, no…

PM: It's a combination actually. There are a number of factors. One, it sounds as though you're already moving anyway to plugging the holes in the regulations, what would you like… I'd like the MHRA to investigate to what extent, rather than just what we've read in the media, to how many of those children in Wales, if in fact that any of them had been taking antidepressant drugs. Because you don't know.

JS: That's right.

KW: Well, this is the situation where a coroner's court is going to get all that information.

JS: Exactly. That's why we asked you the question earlier.

PM: Well, we did raise this actually last year as you know with Lord Hunt to see… again, it's about harvesting information.

KW: We do have access to some data coming through the coroner's system. For instance, there's a research unit at St George's which looks at the involvement… or the association between drug use and completed suicide in the majority of coroner's courts in the UK. And this is an ongoing study. And we've used it actually for a slightly different purpose, which is to look at the impact of some regulatory act to reduce the availability of large amounts of amphetamine type products. And Coproxamol, which is another painkiller. We took the regulatory

decision to phase out Coproxamol. We wanted to see whether that had achieved the intention of reducing completed suicides using Coproxamol. Going to the coroner's system and looking at those data, a sharp reduction in suicides associated with the use of Coproxamol. So that's, from our point of view, a clear indication that the regulatory action has achieved the desired outcome.

PM: Can I just challenge you on that, though?

KW: Sure.

PM: You actually said that you think there wasn't a link between… that just shows in fact that if they can't get hold of Coproxamol they may use another method to kill themselves.

KW: There is always a possibility of method substitution. It's been looked at in great detail in relation to aspects of Paracetamol itself. And when there was a decision that Paracetamol should only be available in packs of a small size, to get round the problem of impulsive overdose, not only was there a reduction in Paracetamol-related suicide, but also a reduction of Paracetamol-related liver injury, which is not necessarily fatal. And there was not evidence of a substitution of other means of suicide. It's like coal gas. When coal gas was phased out...

PM: But how do you actually find that evidence?

KW: Because you look at the total population suicide rate. If you can see a reduction in the actual population suicide rate, then you know that that has not been a substitution of one means for another.

PM: Have we got the statistics to show the number of suicides now in the UK, statistically over the last ten years? Is it rising?

KW: It's falling. We have got… the data would have to be interpreted with slight caution because the coroner's courts, as you probably know, are sometimes reluctant to give a verdict of suicide where the circumstances are not terribly clear. But if you lump together suicides and unexplained deaths, then the trend is downwards in, I think, all those groups. And that's been a phenomenon of the UK, I can give you the exact figures. But there is a very clear downward trend in suicide rates.

JS: Have you met with the… I mean, maybe you won't like to answer this question, but have you met with the two coroners that I can think of that have come out in this country and said that they think there's a Seroxat link to suicide? Because the media says that these coroners were going to contact the MHRA to make their reports.

KW: They might not necessarily have contacted me direct.

JS: No. [laughs]

SM: We have had reports.

KW: Yeah. But then the ones that we don't see are the suicides from patients who have not been treated.

JS: You know what I think would be a great idea. Like, it's been good to meet you today and the other people here, but it would be good if we could have a Health Minister, somebody from the Department of Health, somebody from NICE, all around the same table and have a discussion that way. A coroner, maybe. Because we have to keep jumping, we can only ask this question of this department and this question of that department. And there's no link between the whole lot. And I think that's where the whole thing falls down, is there's no communication between different bodies.

KW: Well, as I said earlier, we have worked closely with NICE, which is given the responsibility of providing guidance to the NHS use of treatments. We try to ensure that the guidance that they give is consistent with all the evidence that we've got, the risks and benefits. So there is a lot of work that goes on behind the scenes to make sure that these are joined up. There's no simple answer. I have said in public that I think there is over-prescription of SSRIs. I have said in public that I think people should be very discriminating in who they prescribe for.

And I've also said that in the early weeks of treatment, doctors should be particularly vigilant and relatives should be particularly vigilant, through this period. But that applies, as I said to you on the phone, Janice, to all antidepressant treatment, it's not specific to Seroxat. And one of the reasons SSRIs are so successful commercially, one of the reasons, was because they were perceived as being substantially less toxic than tricyclics.

PM: That was in overdose.

KW: But then depressed patients take overdoses. If I'm sitting across the table from a patient I've just diagnosed as depressive, and I'm thinking, what do I prescribe? Well, if the worst comes to the worst and this patient does decide to swallow the whole bottle, what's the safest bottle of antidepressants I can prescribe?

JS: But you see then… like I said to you earlier, twenty-five percent of prescriptions are for severely depressed patients. That twenty-five percent is minimal. They should be the ones that are looked at by psychiatrists. And the rest shouldn't have been prescribed at all.

KW: Well, it's difficult to second-guess an individual clinical consultation. But you'd be faced with the problem that an unhappy and depressed patient goes to see a GP and the GP says, ‘Sorry, I'm not going to prescribe you anything because the government says I can't.’ That's not the way it works. And this is why...

PM: Why not? If it actually… if in fact there is a risk… you've already admitted, there's always a risk with some drugs for some individuals.

KW: But all drugs carry a risk.

PM: Of course. So why prescribe any drug at all if in fact there's no efficacy?

KW: If I go to a GP with a painful knee because my osteo-arthritis is playing up, the GP might prescribe me an anti-inflammatory drug which is known to cause toxicity on the stomach and so forth. Now, you either say, ‘I'm sorry, you can't have any painkillers’, because they all have the potential to cause harm. Or you try to negotiate the best solution in terms of minimising risk and maximising

benefit. That's what it's all about. That's the skill of prescribing and it's not something I can second-guess from an office in London.

PM: I understand in your example of going in with your problem of your arthritic knee or whatever, but where you're talking about the difference between clinical, major depression and only low mood or mild depression, then surely it is down to the GP to ensure and to be told, either if it's the GMC or whatever that has to tell the GP, that they are not to prescribe the drugs. Because there is enough anecdotal evidence that there is no… there's no case for the efficacy of those drugs at that stage.

JS: Doctors don't seem to be ruled by the GMC anyway, only to a certain extent. Doctors are a law unto themselves basically.

KW: Well, I wouldn't actually agree with you.

PM: Well, I think they have to be. But, I mean… they have to be.

JS: To a certain extent.

KW: They have to have the opportunity to use clinical judgments and meet the need of the individual patient. And we talk over and over again about patient choice, about patient preference, about the individualisation of treatment so that the patient gets what the patient is happiest with. But you can't drive that by legislation, you just can't do it, it won't work, it's impossible. And I think we have to be a bit humble about what can be achieved from that sort of top down mandated healthcare system. I think patients would suffer more if there was not individual doctor discretion to negotiate with the patient the appropriate treatment in the circumstances.

PM: So can I just ask you this question then, Kent? You think that nothing else, apart from the regulatory tightening up on what needs to be done to ensure that this sort of information is actually at your fingertips when it comes to licensing these drugs, you don’t think there's anything else that can be done?

KW: I think what we need to see, we need to achieve, by legislation both in the UK and later in Europe, is a situation where it is absolutely clear that the manufacturer has got an obligation to tell us as the regulator everything they have which relates to the risk benefit of their products. Whatever those products are being used for, if they have information which is relevant to risk and benefit, we ought to know about it. And the reason we need to know about it is so that we can… in extreme circumstances we can change the marketing authorisation, but far more commonly so that we can give best advice.

PM: I agree with that entirely, but that's not my question. What else…

KW: What else? That's not enough?

PM: Yeah, what else needs to be done?

KW: In this specific case?

PM: In this specific case, given the wealth of evidence that there is. And some of it, you may want to say it's anecdotal evidence.

KW: I don’t dismiss anecdotal evidence; I just see it as part of the totality of evidence.

PM: Okay. Well, I don't know in other drugs, I've only been involved in Seroxat, but we've had a number of high profile Panorama programmes. When you see the SSRIs mentioned in the newspapers now, particularly in relation to Seroxat, it talks about the 'troubled', you know, drug, Seroxat, the newspapers have picked up on this. What else can be done? I mean, do you think there's nothing needs to be done?

KW: [pause] I think there are certain risks coming out of the media handling of this whole question. And the one that worries me most, to be absolutely honest, is the [pause]… the stigmatisation of the use of antidepressant treatment where it's necessary in patients who are depressed. And I think if you get to a situation where…

PM: Severely depressed.

KW: Sufficiently depressed to need treatment. I think if we get to the situation where doctors will not prescribe, even when they see a patient who is substantially depressed, the consequence is going to be firstly, you're going to have the unlimited misery of depressive illness, which is always debilitating, sometimes disabling, and occasionally fatal. It's a rotten, rotten condition. And if we actually try to inhibit the proper treatment being given to depressive patients then there will be more harm done by non-treatment.

JS: So basically…

PM: Sorry, can I just make one point. The point is this, you've already said now that your benchmark is to look at suicide figures.

KW: My benchmark?

PM: Well, you have said that…

KW: It is a part of the picture. It's part of the evidence…

PM: Okay, it's part of the picture.

KW: …to see what's happening to population suicide rates.

PM: And I understand, and it's a very important number. And you've said that that's going down. I'd obviously like to see the figures.

KW: Yeah.

PM: But how do you actually then make sure that you are aware of the whole panoply of other impairments, disturbed thoughts, everything short of suicide? The reason why I'm here today was because of a case that I got involved with where the girl in question did not commit suicide, she made false allegations against a family member. Because one of the other common side effects of Seroxat are these disturbed dreams that can seem very real. How do you actually ensure that that… that is actually… how do you get that information, if in fact you're only looking at the suicide numbers?

KW: I didn't say we were only looking at the suicide numbers.

PM: No, I know you didn't, but in fact…

KW: You are misquoting me. What I said was…

PM: And I apologise.

KW: ...that is an important part of the total evidence base. You cannot say that I ever said that we only looked at the suicide rate.

PM: You did actually say, though, that one of the reasons why you believe this on the whole – and it's your risk benefit assessment – is because the number of suicides have gone down.

KW: I think that you would have to have some quite convoluted argument to say that a fourfold increase in the use of this particular type of drug, unaccompanied by an upward movement in the suicide rate of the population, was compatible with the view that these drugs induce suicide. With individual patients, it is always terribly difficult, but if you look at the population effect of our total efforts to treat depressive illness, you have to consider the population suicide rate as a relevant statistic.

PM: And I agree with that. I do agree with that. What I'm saying is slightly different, and I apologise if I'm not making the point clearer. It's not just suicide, though, we're talking about.

KW: No, no, sure, sure.

PM: The side effects of these drugs are…

KW: But it's…

PM: …a whole range of… I mean, Derek himself can tell you about… he's sitting here, thank God.

DS: It was a very close thing. I almost did commit suicide.

JS: Derek, are there any questions that you really want to… you've come such a long way and you haven't…

DS: I've got some questions for the MHRA themselves. Why was the MHRA's Director of Licensing, Dr Ian Hudson, not interviewed as part of the investigation?

KW: James?

JC: He wasn't interviewed as part of the investigation because his name scarcely came up in the evidence we looked at. We had over a million pages of documents which were reviewed and Ian Hudson's name appeared once in the entire body of it. He didn't have an involvement in it. We selected individuals who we thought were the most closely involved individuals and wanted to interview them. We also wanted to interview people who were being viewed as representatives of the company, to get to the company's corporate…

DS: But he has admitted in an EMEA document, a copy of which we have before us, that he had ‘a significant involvement’ with Paroxetine until 2001 when he joined the MHRA in his current position.

JC: But he didn't have significant involvement in the paediatric clinical trials or the reporting of them or any of the…

DS: But he was involved as a world safety director, or class…

JC: I can't really get too far into the evidence of the case, but his name really didn't come up in the investigation at all. I come to this as a solicitor, no particular loyality to the MHRA, certainly none to GSK. My role is to carry out a thorough and impartial investigation of fact. I will quite happily follow those facts to wherever they lead. And if we had been required to investigate and interview Ian Hudson then I would have done. I considered it inappropriate on the evidence that we found.

DS: The question must be asked as to why Dr Ian Hudson was never interviewed by Department of Health enforcement officers during an investigation when he was well placed to answer questions related to the paediatric clinical trial 329. It was after all his previous job to know about the safety of Seroxat, or rather lack thereof.

JC: There was a huge number of people at GSK who were involved in the decisions as to whether or not they would report the findings of their paediatric clinical trials. There are several individuals who are more closely involved than Ian Hudson was. Ian Hudson frankly didn't really appear in the investigation at all. We had a vast amount of internal GSK documentation covering the subject and Ian Hudson scarcely appears in it at all. If he had done, I would have wanted to interview him. And certainly internally within the building I've never had any barrier placed in my way as to who I may wish to question or ask questions.

KW: Okay. I should point out two things actually, Derek. One is that the time period that… Ian Hudson worked for GSK was a relatively short period which doesn't actually coincide terribly well with the time the paediatric trials were being done. The second thing is, you refer to the EMEA declaration of a conflict of interest. Where there is any possibility of confusion as to whether somebody does or does not have a conflict of interest, then the advice is to declare it anyway.

This is what we do in-house, and it's what the EMEA chose to do and it's what Ian Hudson chose to do, even beyond the requirements of what the EMEA were asking for. We've taken a very stringent approach to conflict of interest in this building. I would emphasise that nobody with any conflict in relation to GSK got anywhere near this investigation. We were most meticulous. Neither James, nor his team, nor his scientific team working with them, nor the barristers externally who were consulted, had any reason to be conflicted in relation to GSK. And if there was a reason, then this investigation went nowhere near them.

JS: But I think the way it's looked at is that Ian Hudson was involved in the Donald Schell case, giving evidence in that case. Where GSK lost and had to pay out thousands of dollars, etcetera. And they feel that… then he came to work for the MHRA. So he knew the drug was dangerous and chose to keep his mouth shut. And I think that's, I think it comes down to... That's the sad part. He must have known…

PM: It's the appearance… whether… I think it's the appearance of what they're saying rather than that no allegations are being made, but the appearance is difficult.

JS: That's right, that's how it looks.

KW: James has to investigate the evidence.

PM: And where the evidence. I understand what you've said.

KW: I mean, we can't be driven solely by the external appearance which may, as you pointed out, be completely misleading. But I do assure you that there has been no conflict of interest allowed to enter into the way in which the agency has investigated this case. We've done it absolutely top to bottom. I moved the entire division, the group that James works in doing this investigation reported directly to me, not through any other division or director. For the simple reason there had to be a direct line of accountability and I have no conflict of interest.

PM: Apart from… can I just… I understand exactly what you've said as far as the investigation is concerned. But what about the ongoing monitoring of the drug for risk benefit analysis? What steps… are you going to make sure that, for example, this gentleman isn't going to be part of…

KW: Ian's division is concerned with the licensing of products when they first seek to enter the market. We have a completely separate division in which Sarah works, called vigilance and risk management of medicines.

PM: And he's got nothing to do with that?

KW: He's got nothing to do with that. And again, as a matter of policy, we have separated out the licensing function from the surveillance function. So nobody could ever say, 'I licensed this product, I'm going to look kindly on it through its surveillance.' They're separated out.

PM: Okay.

DS: Why was Dr Ian Hudson replaced by the Chairman of the MHRA? And why Dr Hudson, a former employee of GSK, saw Professor Breckenridge during the 2004/2005 parliamentary Health Select Committee investigation? Of the influence into pharmaceutical…

PM: Can you repeat that question, Derek? I don't think Kent heard it.

DS: Why was Dr Ian Hudson replaced by the Chairman of the MHRA? And why Dr Hudson, a former employee of GSK, saw Professor Breckenridge during the 2004/2005 parliamentary Health Select Committee investigation of the influence of the pharmaceutical industry, when the Health Select Committee specifically asked for Dr Hudson's input, with regards to Seroxat? I attended that particular evidence session and Dr Taylor appeared rather angry and perplexed that Dr Hudson was replaced.

KW: Yeah, that's interesting. I remember that Health Select Committee very well. And we discussed with the secretariat of the Select Committee as to who they would like us to put up to answer questions. I was there, June Raine was there, Alasdair Breckenridge was there. There were two evidence sessions at which we gave evidence. And it was never clear to me that the Select Committee wished to interview Dr Hudson specifically. They wanted to talk about the influence of the pharmaceutical industry…

DS: Well, I was there on the day. So I can remember Dr Taylor's face. And his body language.

KW: Well, we will put up in front of the Health Select Committee anybody that the Health Select Committee asks us to put up. But it relates to the questions that they're going to be expected to cover. And I can tell you that we discussed in some detail with the secretariat to the Committee who we should most appropriately send. And the people who were sent were the people most appropriate to answer the questions that were going to be put. I'm puzzled to know why there should have been a view expressed afterwards that somehow Dr Hudson was asked for and Dr Hudson didn't go. I really… you know, it was a source of irritation to me at the time that that allegation was being made. Because we work quite hard to support the Health Select Committee, with whatever advice…

DS: Here's one of the questions that was put by John Austin. 'I think it would have been useful if Dr Hudson had been here because, as far as I understand, he was at SmithKline Beecham and his department was responsible for the collection of adverse reaction information such as there was with Seroxat.' Professor Sir Alasdair Breckenridge, 'Yes, I know that.' And the last question, John Austin, 'So he would have been a very key witness.'

KW: Well, had that been known in advance, we could have put up different people. But it was something that actually only came out during the questions. And it wasn't clear from what we were told about what the Select Committee was going to cover.

PM: That was a bit unfortunate then, wasn't it?

KW: It was unfortunate. You know, we…

JS: It was a waste of time anyway, wasn't it? Because, I mean, they recommended that the MHRA become an independent body but nothing has happened.

PM: Well, they…

KW: They made all sorts of recommendations. Some which were acted on, some of which… well, the government responded. But the recommendations of the Health Select Committee didn't come to us, they went to the government, and the government responded. And one suggestion was that…

PM: Split the Department of Health, which was I thought the key in all of this. So that they didn't serve two masters.

KW: Yes. That's a matter of political policy which we don't lay down here. We're civil servants, we try to do what Ministers ask us to do. But that is a political question which the government responded to in the usual way.

PM: [laughs] To ignore it.

KW: There was a formal government response.

JS: We go and see Heath Ministers, etcetera, and all these Health Ministers, they seem to give standard answers which obviously come from yourselves. Or from the information that is provided by the MHRA. They haven't a clue, not a single clue, about the drug in actual fact. All they do is read and…

PM: Well, they take the briefing paper that the MHRA produces.

KW: That's government. But believe me the government… the Minister doesn't have to accept a briefing. It is not unknown for a Minister to bounce back a briefing and say, 'I don't believe this, I don't like this. Send me another one.'

JS: Yes, but I think that's if they take some sort of really good personal interest. It's like GPs. If they took a personal interest in finding out about… say they have ten people in a month report side effects of an antidepressant for instance, if they took it on themselves to look into it like we do.

KW: Ministers. If Ministers did. Of course the answer is that such is the complexity of government these days that a Health Minister has got a huge remit to cross, the NHS, service delivery…

PM: One more reason why they should split the two functions.

KW: I mean, there are five Health Ministers I think at the latest count. Yeah. You're talking actually about a general problem of government, Janice, which is the difficulty of Ministers to actually get down to the grass tacks of the issues they have responsibly for.

JS: I find it so irritating that they come over with this attitude, you know, of we know it all and you know nothing. And it's so irritating when we're dealing with the actual people.

PM: Well, that's the arrogance of politicians. [laughter]

DS: In the interests of the public, who were the individual suspects the MHRA decided not to a) interview, and b) arrest?

KW: Again… well, James.

JC: If you haven't charged somebody with a criminal offence and much less convicted them, you have to consider whether it would be right or not to expose their identity publicly. Bearing in mind we haven't been able to prove or even officially accused them really of having done anything legally wrong. That being so, I think when we consider what we release and what we don't, we have to bear in mind would it really be appropriate to release their identity and expose them to the attention they would undoubtedly attract, if their names were given out. We thought about that long and hard and decided that the public know that GSK is the corporate entity that is involved here, and we don't really think it's necessary to go down to a level of sort of naming and shaming individuals when we haven't in fact been able to put an allegation to them for them to have the chance to answer publicly for.

PM: I have asked in my letter if you can review your decision not to publish the QC's opinion on this. Because although…

KW: We thought long and hard about that.

PM: It is confidential. But you can waive confidentiality.

KW: There is an issue here of wider government policy, about making publicly available…

PM: [laughs] Otherwise Goldsmith's opinion might have to be disclosed.

KW: But if… I'm not a lawyer, but as I understand it, the argument runs like this. If we actually made known the specific advice that we'd had in this particular area, it could actually be an impediment to us in taking forward a prosecution in a related area at some future date. Is that right, James?

JC: That's correct. But that's the general policy being run right the way across government and before Seroxat and before Goldsmith's opinion on Iraq, the government doesn't disclose its legal advice, and never has.

PM: I think you're wrong on that, I think they have in the past, when they've chosen to. And it may have been the wrong decision. But the point is I think there has been precedent where in fact they have disclosed opinions.

JC: The statutory general rule is that the government doesn't disclose legal advice. We're really adhering to that in not disclosing the QC's…

PM: Well, there are some other questions there that I've raised about the QC and perhaps, James, in due course you'll…

JC: What we needed for this really was a senior barrister that was external to the agency and to government that is going to take an independent and impartial view of the facts. And advise us on whether prosecution is possible or not.

PM: A relatively junior senior I would say. A junior leader. She hadn't taken…

JC: It is a contradiction in terms, isn't it, junior?

PM: No, I refer… no, I talk about senior juniors and junior leaders. In the commercial world we do. I mean, there's very much a pecking order as you know, if you look at the Chambers directory, you'll see where the pecking order lies. And she is a junior QC. She hasn't taken the silk that long. I'd just like to know, were you the person responsible for instructing her?

JC: It was a decision taken within our division, within our group, and in consultation with our solicitors at the Department of Work and Pensions as to who would be the best counsel to approach. We wanted a senior criminal lawyer. There aren't frankly any, we did look. There aren't any criminal lawyers who are experts both in the finer points of civil medicines regulation and in criminal law. So if you're choosing your leader you'd have to go for one or the other. And we thought the best approach would be to go for a senior criminal lawyer, which is what we did. With…

PM: I think if you'd have asked my opinion on that, I probably would have had a different opinion.

JC: But of course the Department of Health is blessed with its own specialist division of expert civil regulatory lawyers, many deal with draft and implement the regulations or at least they're instrumental in implementing them. The Department for Health has its own division which deals with all of that, so in a sense the government is its own authority on the interpretation and the application of medicines regulatory law. So for the person we're actually sending into court we'd prefer to find an expert criminal lawyer and that's what we did. The government has a list of lawyers from whom it selects, the ‘A’, ‘B’

and 'C' lists etcetera, for counsellors [inaudible]. Miranda Moore has a history of prosecuting high profile complex cases, technically complex cases.

PM: Fraud generally. But as you'll see there, I've raised questions about…

JC: Well, I think you're quite right. There is a sense in which this case could be approached as a fraud case. It's similar to complex fraud and it involves interpretation, analytical and evidential interpretation, but the vast bulk of the paperwork, the QC who may be great at prosecuting a murder or a kidnap won't necessarily be the one who you would use to prosecute a large documentary-based crime.

PM: But given that her background specialisation, according to Chambers anyway, is in fraud, I would be interested in knowing whether in fact she did consider the 2006 Fraud Act?

JC: We did consider the Fraud Act. I went and had a meeting with the Serious Fraud Office to see what their interest in this would be and if they had any guidance to offer us on the approach to such a large scale documentary case. Because it could be analysed in those terms. But I think the approach you have to take in the end, the MHRA is a medicines regulatory body, charged with the duty of protecting public health. And the real wrong here, and what concerns people such as Janice and Derek and others, is whether public health is being put at risk by what GSK did. And so to prosecute them for a fraud act offence and say they obtained money which they shouldn't have had, would not address the real wrongdoing then.

PM: I think it might address a lot of people's anger from that perspective. Which of course is one of the questions, why I've raised…

JC: What you would be prosecuting there would be for obtaining money they shouldn't have obtained by misleading people. It's a financial fraud.

PM: Absolutely, it's a financial gain.

JC: You wouldn't establish anything about them having put the public at risk or anybody having suffered harm as a result of that.

PM: Except the evidence would obviously have to be led as to why in fact you would be saying that they had committed fraud by doing what they did.

JC: But you wouldn't convict them in respect of those things.

PM: No, no, they're convicted of getting a financial gain.

JC: In any event, I'm not sure if bringing a prosecution for fraud would be [mobile phone rings] any easier than bringing one for the pharmacovigilance offences. We did consider fraud and a number of other charges, in general criminal law. But there were none that were really applicable and that worked with this case.

PM: Including the sections that I've highlighted here? There's a footnote at the end of the document. And it is in relation to the prescriptions that were written for the under-eighteens, even when they knew there was no…

JC: We did consider before that, and I think it was actually… I couldn't say for certain now without checking. We considered wider criminal law a fair bit.

PM: Well, I do actually see in the report you did. But anyway, look, I know time is moving on, so if I could have a written response to these questions, that would be great. But can we… we'd like to see some movement, something positive that comes out. Because this is now the third meeting I've attended. And people are very polite and they listen and we've listened very politely today. But I don't actually see that we're getting very far. Can I make two suggestions? Raise two points with you in a way. One is a follow-up with the coroners, the issue about whether the coroner should have a positive duty to report. And second, about the self-help groups which is, I think, what Janice particularly would like to see some movement on. Because in fact if you are concerned about the patients…

KW: I'll certainly take up the first one and look into this issue of the coroners. I suppose it's linked, that point about whether you make yellow card reporting on prescribers mandatory. You're really asking [that] the coroner should have a statutory obligation to report drug… suspicion of drug relevance to deaths.

PM: Well, even just the prescribing, what the patient had been taking, the medication they'd been taking at the time.

KW: We'll have a look at that and think about that. The second point you were asking was about the self-help groups. That's not really within our remit as an Agency. This is an NHS or a DH issue. I mean, I personally, as a clinician, am very persuaded by the value of self-help for patients. But it's not something that we can mandate from here.

JS: No, I understand you can't mandate it.

KW: What would you like us to do that we're not doing?

PM: What can you do in terms of, if we can say to the next layer of government that we speak to, that this actually carries the MHRA approval?

KW: Well, we regulate lots of things, but that's not one of them.

PM: I'm not talking about regulation; do you think this is a good idea?

KW: I do.

PM: We can quote, unquote?

KW: We draw quite heavily on patient groups to give us their views on a whole range of issues to do with for instance information for patients.

PM: And to harvest information that we've been talking about.

KW: We've been involved closely with patient groups in advising us on how we can make better use of the yellow card system. How we can get better quality information, more accessible information, out to people who need it. We use patient groups a great deal. And that, if you like, is our endorsement of the fact we think they're a good idea. I mean, they're not all equally good. And some of them, I have to say, are unfortunately close to the pharma industry. But nonetheless patient support groups are a constituency that we look to for help on a whole range of issues.

JS: You see, what we would like regarding coroners, is look at GSK's letter of 2006 with the suicide risks. We would like that sent to coroners. It should have been sent to coroners, in our view. And the warning letters from yourselves, if they were sent to coroners too. At the moment, they have nothing, they have no information really on the drugs at all.

PM: So it's down to the individual whether they think it's relevant.

JS: I know three people that have in the last year gone through coroner's court due to Seroxat or some other SSRI. And it's completely been dismissed, the drug has nothing to do with it, it's down to depression. How do they know that?

SM: If I could just comment on the…

JS: It could be possible but…

SM: On the communication with coroners, the 'Current Problems in Pharmacovigilance' was sent directly to coroners. And our new bulletin, 'Drug Safety Update', we make every effort to route through to coroners. So they do receive the warnings we send out.

JS: They do, excellent. Nice one, I'm really pleased about that. But it would be helpful, as well, if the drug companies maybe… I don't know if they do, as far as I know they don't, and that would be good if they sent information too. Because that letter from GSK in May 2006 about the suicide aspects of the drug, I think that's really informative, it's a really good letter. And it actually comes from the drug company, which means something.

KW: I guess it's a bit like prescribers; coroners ultimately have to reach their own decisions on the facts in front of them.

JS: Of course. But if they're not sent the facts, then they can't make a judgement.

KW: But they can seek the facts when they need them.

JS: Of course, yeah. [laughs]

KW: And they're qualified medically and legally so…

JS: I quite agree.

KW: And we send them, as Sarah has said, the publications that we think are relevant to… what they need to know. But otherwise we'd just deluge them with information they have similar…

JS: I just wonder what would happen to the MHRA if it wasn't funded by the pharmaceutical industry and it became funded by the government, by the tax payer?

KW: Do you think it would be any different?

JS: I do think it would be completely. [laughs]

KW: It could actually. Because the evidence is there, prior to 1988, before my time, a substantial proportion of the funding that went into medicines regulation came from central taxation. Medicines regulation was under-funded, it was under-

resourced, it was slow, it was cumbersome, it was inadequate. Government decided, and successive governments have confirmed, that they felt the best way to resource this properly was to do it by there being statutory fees. And every medicines regulator in the developed world uses fee income for most or all of its costs.

And the United States began with a federally funded, taxation funded FDA. They've progressively moved over the last twenty years to a fee-based funding regulation. And Janice, it's not just medicines regulation, but virtually every branch of government regulation depends on fees paid by the regulators. If you go to take a driving test, you pay a fee. You get your car through an MOT, you have to pay a fee. The person who's being regulated pays for the cost of regulation by and large. Medicines regulation is not that much different. And it works. Empirically it means that you get the resource in relation to the volume of work that needs to be done. And it doesn't in any way compromise the judgements that are made. We get the fee whether we say the product can or cannot have a marketing authorisation. It doesn't influence one iota the decisions that come out of this agency, I can absolutely assure you of that.

JS: And do we know how much… I mean, you're totally funded by pharma, are you?

KW: On the medicines side we have a fee recovery system which is reviewed by Parliament every year. Every February or so we take our fee proposals to Parliament. Every year they go out to public consultation for twelve weeks. Every year they go to the Treasury for approval. Every year they go to Parliament for approval. And never once in the last twenty odd years, as far as I'm aware, has the question of fee-based funding this agency been reopened in Parliament. I think it would actually be a detriment to us. We couldn't do our job properly if we were not adequately resourced.

JS: Of course not, no. I mean, I understand that. But I just think it's…

KW: If I went to Gordon Brown or Alistair Darling and said, 'We'd like to take fees out of this please to run this, that or the other', I think I can predict the answer, unfortunately. But why not, the fees… but the taxation could be better spent on patient care services. Why should this not be a fee-based regulatory charge to the industry?

PM: As long as they're not the masters.

KW: Absolutely not.

PM: And you've made it quite clear they're not.

KW: Absolutely not.

PM: So where the money comes from is irrelevant.

KW: Provided that there is proper governance of the way that funding comes into the agency, there is a proper mechanism in place to avoid any conflict of interest. We don't even have industry delegates on our private Agency Board. We I think are absolutely clean on that front, and I defend our processes to anybody.

PM: It's just a bit unfortunate, perhaps, that some of your people have been so closely associated with some of the drug companies – because of the appearance.

KW: Yeah, but deep beneath that, if you want to find a world expert on medicines manufacture, you don't go to a university, you go to somewhere where medicines are being manufactured. And you must draw on the best available expertise. And if you were to exclude industry experience as a disqualification, we would be impoverished, we couldn't do our job properly, if we did not have people who are sufficiently expert to have actually done it.

PM: I think it's a question of whether they're on the Board. I mean, that's the point. It's how close they are…

KW: Absolutely, yeah.

PM: …to the guiding mind and whatever.

KW: And we are a stubbornly independent body.

PM: Good.

JS: Can I just make one more statement, if you like, before we go. Would you be willing, if we provide you with as much information as we can about suicide, SSRIs, adults, would you be willing to look at it?

KW: We will look at all and every bit of information on this matter. And I think a large amount of it has come into VRMM already.

JS: We feel that we've been talking to you now since, I don't know, 2002 I believe. And it's a long time. And basically this is the way we feel, we were right, right the way through and we told you. And if you'd have listened…

KW: Told us what, Janice?

JS: We told you that the drugs were dangerous in under-eighteens and that they weren't licensed. We told you all the facts, basically, and we feel that we weren't listened to. Lives have been lost because people didn't listen when the information was there for everybody to see. And we just hope now that this meeting has… obviously we've had our say and you've had yours. And we hope that you will take a bit of notice of what we've had to say and just look into the situation for adults too. Because we know these drugs do cause suicide in adults.

KW: Well, I can only repeat what I said earlier, which is that we do keep risk benefit under continuous review. And we have done ever since these products were licensed. The other aspect I would mention is that we have to consider the alternatives. This is not the totally satisfactory class of drugs; no class of drugs is totally satisfactory. Where would you go instead? I mean, these products have been taken up as they have been, in part because they are safer in evidence than what went before. And if we… as has sometimes been suggested, if we said, 'Just take the SSRIs off the market', we would actually see a measurable mortality arising from that fact.

JS: I think… like I've had about five meetings with Alistair Benbow. And one of the questions that I realised… well, the main question that my husband and I raised to Alistair was, 'What happens to people who've been on these drugs for more than two years?' Nobody knows. That's what he told me.

KW: 'What happens', in what sense?

JS: Well, nobody knows what happens to them. What happens to their brain, what happens to their body.

PM: It's not just in terms of suicide, it's the other side effects. Studies have gone into the long-term…

JS: Long-term effects, that's what concerns me.

KW: There has been – and this applies to many classes of drugs which are intended for long term use – that the trials, the rigorous trials that are done, tend to look at short to medium term.

JS: But another instance of doctors receiving the wrong information or not enough information about the drug they're prescribing; because these drugs were only designed to be used short-term, for mild depression, or whatever, for depression...

KW: Severe depression.

JS: It should be severe depression, yeah. But it wasn't at the time.

KW: The other thing, of course, is the relapse rate of severe depression is quite high. And the clinical practice has tended to be to extend rather than shorten the use of antidepressants if they're working.

JS: I think what's happened is people, when they start to feel better after a year or eighteen months, they've been going back to the doctor, 'I feel better now, I want to come off the drug.' Then the withdrawal symptoms kick in because they are not instructed to come off the drug correctly. And then the doctor re-prescribes, thinking it's the original symptoms returning.

DS: Or increases the dose.

JS: And it's not. Or increases the dose, which can be dangerous, as we all know.

KW: We've talked a lot today, we have covered the ground.

DS: I've got one final question. When did the MHRA enforcement team and/or lawyers first realise that it was impossible to prosecute GSK because of a loophole in EU law – the dates, please?

JC: I can supply you with dates - I don't remember them off the top of my head. But I'm not sure if there ever really was an 'aha!' moment when we realised; it wasn't like you simply read a page and think 'I didn't see that line, we now know we can't do it'. It's a question of interpretation and considerations, It goes on over a long period of time. Lines going backwards and forwards that didn't approach it or attempt it. And in the end we had final views taken looking back on what we'd done so far and weighing it against the evidence, and seeing how we could apply the law to the evidence, the conclusion was eventually reached that we weren't going to be able to prosecute. Whether it was before this stage we realised that, I'm not sure. The body of people's work builds up to a final conclusion.

PM: Can I also make another suggestion. Since yellow cards are only anecdotal. Janice, you deal with all the emails that come into the Seroxat Users Group.

Would there be any harm in passing automatically a copy onto the MHRA, of anyone that's reported…

JS: We would have to ask them.

KW: Could you encourage your members to use the reporting scheme?

JS: We've actually got it on our website and it's been on there for some time now. A long time.

KW: I think that's the best you can do, isn't it really?

JS: Yeah.

KW: I mean, you can't pass on without…

PM: No, not without their approval. But in terms of where you have individual cases and who should you pass it onto at the MHRA?

JW: Janice, I mean, you've invited me to come to visit you on, I think, 19th May, I think was the date.

JS: I did, yeah.

JW: When you did that you said you thought you could perhaps show me some evidence. Would that be an opportunity for me to have a look?

JS: That's what I thought we would use the time for, as personal experiences. And show you how many emails we've got and…

JW: I'd like to see that and then come back and have a chat with…

PM: Would it be Sarah that in fact it… it should be you?

SM: Yes, you gave me some, I think, at the last meeting.

JS: I did, yeah, I give them out all the time. I didn't bother today because I get… it'd be like banging my head on a wall. [laughs] But you just feel, are they really read? Are these people listened to? And do you really, really…

DS: Well, Panorama said it was only one or two.

PM: It's a matter of record though. They can't ignore them, Janice. If you are willing to accept them…

SM: The reports on the yellow cards being…

PM: I understand.

DS: Which is the actual loophole.

PM: If I ask it slightly different. Are you happy that emails that Janice gets, not through the yellow card system but in fact the…

SM: Sorry, when I say the yellow cards, any report, whether it's a yellow card or the website.

PM: So you would treat Janice's emails in the same way that you would treat a yellow card?

SM: My only concern is the consent of the person. They would be reporting to Janice.

PM: I think that would be very helpful Janice, to do that as a matter of course.

JS: We could set that up on the website.

KW: There's another advantage of this. They do come in by yellow card, either electronically or on paper. Then they [are] formulated ready to go into database, so that it means not only do they get scrutinised as they come through, but they're actually pooled in a way that is analysable.

JS: That's the final thing I wanted to ask. Do you employ doctors to look at these yellow cards?

KW: We have a mixture of scientists.

SM: A mixture of scientists and doctors. And each of the weekly meetings…

JS: Oh, weekly they're looked at.

SM: …the cases are discussed.

JS: And can you tell me roughly how many you've received since the yellow card system has been open to the general public?

SM: I can get those figures for you, I don't have them with me.

KW: It's about two thousand a year, coming from the general public.

JS: Oh, and Sarah, one more thing. You know you sent me something about driving on SSRIs, a long time ago. My computer went down and I lost it. Would it be possible for you to send it to me again?

SM: Yes, of course.

JS: Because that is of particular interest to me, as my husband is an HGV1 driver. [laughs] There's so many different things… I could spend all day asking questions. But we're so grateful for the time you've given us.

KW: I hope it's covered the ground that you wanted to cover.

JS: It's been really great.

DS: What can the MHRA do to win back the public approval?

KW: Can I challenge your assumption about that? [laughter] We have actually MORI Market Research to test out what the general public thinks about medicines and medicines regulation. John has led on this project. And I think there is… I know, because we have got the data from 2000 individuals to prove it, but I think there is a majority of the public are confident that medicines regulation is done properly, seventy percent satisfaction rate.

JS: I'm not surprised.

KW: It doesn't mean to say one can be complacent about it. But if you ask me what can we do to restore public confidence, I'd say it's like, you know, one of those loaded questions. We monitor what the public thinks about the quality of medicines regulation. And I think certainly the percent could be a bit bigger and we hope to make it better.

JS: So you've got to consider how many people have complained about the SSRIs?

KW: All that information is…

JS: The rest of the general public and… we're outweighed I think slightly.

KW: Interestingly, all the survey information is on the website if you want it, the MORI survey.

JS: That's something I was looking at last night, was how to get the adverse reactions of Paroxetine. It used to be really simple, but where have they gone?

SM: We're uploading the daps, I can email them to you, I've got them. But we're in the process. I don't know where Paroxetine is in the line but we have to do it.

JS: I couldn't find Sertraline either. But I mean, they all seem to have disappeared, all the SSRIs.

SM: They're being put back on, up to date basically.

JS: Because what I was after was the suicide figures. And it said a hundred and… I think it was a hundred and ninety eight suicide related to Seroxat. I just was interested to see if that figure had changed at all because as far as I know it hasn't changed for about three years. And I just wondered why. [laughs]

KW: There's nothing sinister about this. We had a major IT rebuild and there was a time when these daps as call them, drug analysis prints, I think that's what it means, were not on the website, because we were rebuilding the IT system underneath. And that rebuild was finished last month and we are now repopulating the…

JW: And it's likely to give much more friendly…

JS: Lovely.

SM: User access.

JS: That's good. Thank you.

End of recording