CASE AUTH/2699/1/14

ANONYMOUS, NON CONTACTABLE HEALTH PROFESSIONAL v MERCK SHARP & DOHME

Promotion of ezetimibe and sitagliptin

An anonymous, non-contactable complainant who described him/herself as a practicing clinician with an advisory role at a clinical commissioning group (CCG) complained about a meeting with two representatives from Merck Sharp & Dohme. The complainant stated that the representatives asked him/her to look at a computer programme (MIRROR) in his/her CCG capacity. The complainant stated that the computer programme purported to hold information about hospital admissions; the representatives focussed in particular on non-elective hospital admissions in patients with heart disease and diabetes. Merck Sharp & Dohme marketed Ezetrol (ezetimibe) as adjunctive therapy to reduce cholesterol levels in patients with, *inter alia*, primary hypercholesterolaemia and Januvia (sitagliptin) for use in adults with type 2 diabetes to improve glycaemic control.

The complainant stated that with regard to heart disease the representatives used MIRROR to discuss non-elective admissions for a variety of coronary events and focussed on the number of these events that occurred in patients with cholesterol levels above the quality outcome framework (QOF) targets. They claimed that the coronary event had been as a result of cholesterol levels being too high and that if the complainant treated his/her patients better and reached not only the QOF target but even lower, he/she could help to save money. The complainant explained that his/her practice achieved as close to target as possible. The complainant was then told that if he/she used Ezetrol then more patients would reach a lower cholesterol level and stop the coronary events. The complainant was unaware of any data that showed that Ezetrol reduced coronary events or death and when challenged the representatives conceded that there was no data available but there soon would be. The complainant stated that the representatives insisted on selling Ezetrol as a medicine that would stop coronary events just because it lowered cholesterol and that studies had shown the lower the level the better the outcome; but they could not provide any outcome data. The complainant alleged this was misleading and potentially dangerous.

The complainant was similarly concerned about the representatives' discussion on diabetes, which focussed on hypoglycaemia and that such attacks precipitated even more serious issues including fractures. The blame for these events was placed on sulphonylureas as a class despite the complainant's challenge that poor insulin control was more likely the problem. The complainant was told that if he/she used Januvia then he/she would stop patients having hypoglycaemic events and needing hospital treatment and was referred to a couple of clinical trials that showed a lower incidence of hypoglycaemia with Januvia compared with a number of sulphonylureas. The complainant asked to see the effect of reducing hospital admissions from these data and was told the studies did not look at that and they covered all grades of severity of hypoglycaemia. The representatives conceded that only severe events would need hospital attendance but could not quantify how Januvia did against comparative medicines. However the representatives asserted there would be a reduction in urgent admissions if Januvia was used instead of sulphonylurea but were not able to provide clinical trial data to support it. Again the representative dismissed the importance of insulin related hypoglycaemia.

The complainant stated he/she was alarmed at the way in which this information was presented to health professionals. As the information could be presented to practices with their specific practice information the complainant was even more concerned that this presentation or programme was being used widely and alleged it was misleading. The use of such material brought the pharmaceutical industry into disrepute. Presenting data and making false claims was a disgrace.

The complainant alleged that there was disguised promotion of Ezetrol and Januvia in the presentation and that claims for the medicines could not be substantiated. The linking of the medicines to this computer data made a clear link between the perceived problem and that the Merck Sharp & Dohme medicines could prevent or reduce the problem, which was not so. The programme included prescribing information but the products had no data or licences for the prevention of the issues that the programme purported to identify. The complainant stated that this must be wrong. The complainant alleged that the Merck Sharp & Dohme representatives had promoted the medicines for unlicensed uses.

The detailed response from Merck Sharp & Dohme is given below.

The Panel noted that the complainant was anonymous and non-contactable. Such complaints were accepted and like all complaints judged on the evidence provided by the parties. The complainant bore the burden of proof. It was not possible to contact the complainant for further information.

The Panel noted that point 1 of the information which Merck Sharp & Dohme stated representatives had to read through and discuss with customers before they proceeded further with the MIRROR tool stated, 'Merck Sharp & Dohme ("MERCK SHARP & DOHME") has developed this MIRROR tool for

the purpose of promoting its products. Prescribing information for relevant MERCK SHARP & DOHME products can be found at the prescribing information tab found at the top of each page'. The Panel noted that it had not been provided with the complete MIRROR tool. Screenshots all included a link to prescribing information and reports generated at a customer's request would have prescribing information attached. The Panel did not know in what context the meeting in question had been set up but as the complainant had clearly considered that Ezetrol and Januvia had been promoted it did not consider that the use of MIRROR amounted to disguised promotion. No breach of the Code was ruled.

The Panel noted that both Ezetrol and Januvia had been promoted within the context of a conversation about data held within the MIRROR tool. It appeared that field-based staff used the MIRROR tool to examine local health economy data and, within that context, promote a medicine. With regard to Ezetrol, the complainant had submitted that the representatives had discussed non-elective admissions for a number of coronary events and had focussed on the number of these events which had occurred in patients with cholesterol levels above the QOF targets. Merck Sharp & Dohme submitted that the MIRROR tool could conceivably be used to highlight the incidence of hospital admissions for ischaemic heart disease but that it would not be possible to attribute this to hypercholesterolaemia or to assert that the use of Ezetrol would result in fewer hospital admissions. In the Panel's view however, to promote Ezetrol, a lipid lowering agent, following a conversation about non-elective cardiovascular hospital admissions in patients with cholesterol levels above QOF targets, invited the customer to link the two conversations and assume that Ezetrol had a role in reducing such admissions. Although MIRROR briefing material stated that Merck Sharp & Dohme products must be portrayed accurately, fairly and objectively, and always within their licence, the Panel noted the MIRROR briefing document stated that:

> **'MIRROR can and should also be used with a customer(s) to highlight local performance gaps or disease management issues and to facilitate discussions to progress towards potential solutions.**
>
> **It is important to ensure that we maintain balance in these discussions. We may, where appropriate, suggest that our products might help to address an issue highlighted by the MIRROR tool but we cannot guarantee what the impact of our products will be and we should not suggest that use of our products will solve an issue completely.'**

An earlier briefing document stated:

> **'MIRROR can be used in calls with healthcare professionals to raise specific disease management issues and it is acceptable in that same call to then discuss how a treatment/ disease management strategy, involving therapy classes that involve 1 or more MSD products, could produce benefits for the patient and local health economy.'**

The Panel noted that the summary of product characteristics (SPC) for Ezetrol stated that a beneficial effect on cardiovascular morbidity and mortality has not yet been demonstrated. The Panel considered, given the statements above from the briefing documents, that on the balance of probabilities, concurrent use of the MIRROR tool and promotion of Ezetrol had given a misleading impression, which could not be substantiated, that use of the medicine would decrease non-elective hospital admissions due to coronary events. A breach of the Code was ruled. Further, the Panel considered that such an impression, given the statement in the SPC that a beneficial effect on cardiovascular morbidity had not been demonstrated, was inconsistent with the Ezetrol SPC. A breach of the Code was ruled. The Panel considered that Ezetrol had, in effect, been promoted for an unlicensed indication. A breach of the Code was ruled. The Panel considered that the representatives had not promoted the rational use of Ezetrol. A breach of the Code was ruled.

The Panel noted that although the complainant stated that he/she had asked for outcome data, as the claim for reduced hospital admissions could not be substantiated, none could be provided. In that regard the Panel ruled no breach of the Code, noting its ruling above of a breach of the Code.

The Panel noted the complainant's allegation that the representatives had suggested that use of Januvia instead of sulphonylureas would reduce urgent hospital admissions due to hypoglycaemia. The representatives had not been able to produce any data to support this claim. The Panel noted Merck Sharp & Dohme's submission that Januvia was associated with a lower incidence of hypoglycaemia than sulphonylureas and that to highlight this in a promotional call was acceptable, as was highlighting the scale of hypoglycaemia-related hospital admissions through tools such as MIRROR. The Panel noted its comments above and considered that to promote Januvia within the context of a conversation about hypoglycaemia-related hospital admissions would imply that the medicine had a role in reducing such admissions. The Panel considered that such an implication was misleading and could not be substantiated. Breaches of the Code were ruled. The Panel did not consider that such an impression was inconsistent with the Januvia SPC. No breach of the Code was ruled. The Panel considered, however, that Januvia had, in effect, been promoted for an unlicensed indication. A breach of the Code was ruled. The Panel considered that the representatives had not promoted the rational use of Januvia. A breach of the Code was ruled.

The Panel noted that although the complainant stated that he/she had asked the representatives to substantiate the claim that Januvia would reduce hospital admissions, as the claim could not be substantiated no data could be provided. In that

regard the Panel ruled no breach of the Code, noting its ruling above of a breach of the Code.

The Panel was very concerned about the wording of the MIRROR briefing documents quoted above. In the Panel's view, to suggest that a medicine might help to address an issue or could produce benefits usually resulted in the impression that the medicine would definitely do so. MIRROR was used to establish a local health economy need or gap which, when followed by a promotional discussion, invited the customer to link the two and assume that the medicine would address that need or fill the gap. In the Panel's view the briefing material positively encouraged representatives to discuss medicines in relation to the local health economy data provided by MIRROR. The Panel considered that the use of the MIRROR tool to discuss healthcare issues was incompatible with the concurrent promotion of medicines unless those medicines were appropriately licensed or had relevant outcome data (eg reduced hospital admissions). In the Panel's view the MIRROR briefing material advocated a course of action which was likely to breach the Code. A breach of the Code was ruled.

The Panel noted its rulings above and considered that high standards had not been maintained and a breach of the Code was ruled. The Panel further considered that the use of MIRROR in conjunction with the promotion of medicines, and to brief representatives that it was acceptable to suggest that Merck Sharp & Dohme's products might help to address an issue highlighted by the tool, was such as to bring discredit upon and reduce confidence in the pharmaceutical industry. A breach of Clause 2 was ruled.

Upon appeal by Merck Sharp & Dohme the Appeal Board noted that the company had raised points about the veracity of the complaint, conduct of the meeting and use of the MIRROR tool that had not previously been submitted to the Panel.

The Appeal Board noted from Merck Sharp & Dohme's submission at the appeal that the company's field based area access leads (AALs) who used the MIRROR tool were separate from its sales representatives. The AALs had a promotional and non promotional role. Each AAL was experienced and had received specialist training. A call by an AAL to use the MIRROR tool would only be in response to a request from a health professional (payers, commissioners etc) usually elicited by a sales representative at a prior call. The way in which the AAL would use the MIRROR tool in each meeting was led by the health professional choosing which information he/she wanted to view in a chosen disease area and region. The discussion and extraction of data in just one disease area could take up to 2 hours. The Appeal Board noted Merck Sharp & Dohme's submission that the MIRROR tool examined the burden of illness and despite its description as a promotional tool, it was not designed to lead to a product discussion although this might happen.

The Appeal Board noted Merck Sharp & Dohme's submission that a call detailing the MIRROR tool concerning two different disease areas did not occur but if it had, it would take up to 4 hours to complete which would be impractical for most health professionals. The Appeal Board also noted that Merck Sharp & Dohme could find no record of an AAL detailing the MIRROR tool with another Merck Sharp & Dohme employee as described by the complainant.

At the end of detailing the MIRROR tool a report was generated for the health professional to keep. The Appeal Board noted that the complainant had not provided any additional evidence such as this report to support his/her allegations.

The Appeal Board noted its comments above and as, on the balance of probabilities, it was not satisfied that the alleged meeting took place it ruled no breaches of the Code in relation to the claims allegedly made about Ezetrol and Januvia. The appeal on these points was successful.

The Appeal Board noted that in the information which preceded the MIRROR tool, it was clearly stated that Merck Sharp & Dohme had developed the tool to promote its medicines. The company representatives at the appeal stated, however, that it was for use in a non promotional/health inequality/service improvement discussion but that if that discussion led into a promotional discussion the tool would nonetheless meet the requirements of the Code. The Appeal Board was concerned that the MIRROR tool thus appeared to have both a non promotional and a promotional purpose and in that regard it queried whether all of the Code requirements for each could truly be met.

The Appeal Board noted that the MIRROR tool launch materials, part of the briefing material provided by Merck Sharp & Dohme, referred to the core campaigns for both Januvia and Ezetrol. In the Appeal Board's view some of the slides appeared to positively encourage AALs to promote Merck Sharp & Dohme's products (eg the slide headed 'Value Proposition for key stakeholders'). This slide stated that Ezetrol should be an *essential* part of the management of patients with type 2 diabetes and CVD to reduce cholesterol and CV risk' (emphasis added). In the Appeal Board's view to describe Ezetrol as essential was exaggerated; it was indicated only as add-on therapy when patients had been inadequately controlled with a statin alone. A slide which detailed the payer proposition for Januvia stated that '…sitagliptin improves patient experience by reducing the complications of type 2 diabetes'. In that regard the Appeal Board noted from the Merck Sharp & Dohme representatives that there was no outcome data to show that Januvia reduced cardiovascular disease, skin conditions etc (ie the 'complications' of diabetes) and although it had a low incidence of hypoglycaemia, hypoglycaemic episodes were acute events/side effects of therapy, not complications of the disease.

The Appeal Board considered that the MIRROR tool briefing materials were likely to encourage AALs to discuss Merck Sharp & Dohme products in relation to data generated by the MIRROR tool. It noted its comments above about the briefing material

and the absence of patient outcome data. The Appeal Board considered that the briefing materials advocated a course of action that was likely to lead to a breach of the Code and consequently it upheld the Panel's ruling of a breach of the Code. High standards had not been maintained and the Appeal Board upheld the Panel's ruling of a breach of the Code. The appeal on these points was unsuccessful. The Appeal Board did not consider that the circumstances warranted a ruling of a breach of Clause 2 and no breach was ruled. The appeal on that point was successful.

An anonymous, non-contactable complainant who described him/herself as a practicing clinician with an advisory role with a clinical commissioning group (CCG) complained about a meeting with two representatives from Merck Sharp & Dohme Limited. The complainant stated that the representatives asked him/her to look at a computer programme (MIRROR) in his/her CCG capacity. Merck Sharp & Dohme marketed Ezetrol (ezetimibe) as adjunctive therapy to reduce cholesterol levels in patients with, *inter alia*, primary hypercholesterolaemia and Januvia (sitagliptin) for use in adults with type 2 diabetes to improve glycaemic control.

COMPLAINT

The complainant stated that the computer programme purported to hold information about hospital admissions; the representatives focussed in particular on non-elective hospital admissions in patients with heart disease and diabetes.

The complainant stated that he/she had reflected on the meeting and was disturbed by what the representatives had said and he/she now considered that claims about Merck Sharp & Dohme's medicines had no substance. If this was standard practice by Merck Sharp & Dohme then the complainant was convinced that the company had breached the Code.

The complainant stated that with regard to heart disease the representatives showed a number of slides that looked at non-elective admissions for a variety of coronary events. They then focussed on the number of these events that occurred in patients with cholesterol levels above the quality outcome framework (QOF) targets. They claimed that the coronary event had been as a result of cholesterol levels being too high and that if the complainant treated his/her patients better and reached not only the QOF target but even lower, he/she could 'do his/her bit' to save money. The complainant stated that he/she explained that his/her practice had a very robust protocol for reaching targets as evidence of best clinical practice and achieved as close to target as possible with the medicines it used. The complainant was then told that if he/she used Ezetrol then more patients would reach a lower cholesterol level and stop the coronary events. The complainant was unaware of any data that showed that Ezetrol was proven to reduce coronary events and that there was no evidence for reducing events or death. In response to the complainant's challenge the representatives conceded that there was no data available but there soon would be. In the complainant's view this was odd. The complainant stated that the representatives insisted on selling Ezetrol as a medicine that would stop coronary events just because it lowered cholesterol and that studies had shown the lower the level the better the outcome; but they could not provide any outcome data. The complainant alleged this was very misleading and potentially dangerous.

The complainant considered that the representatives' slides on diabetes, which focussed on hypoglycaemia, were disconcerting. Figures were picked out to show that hypoglycaemic attacks precipitated even more serious issues including fractures. The blame for these events was placed on sulphonylureas as a class. The complainant challenged back with the view that poor insulin control was more likely the problem. The representatives pressed on with their assertion that it was only a problem of sulphonylureas. The representatives then told the complainant that if he/she used Januvia then he/she would stop patients having hypoglycaemic events and needing hospital treatment. The complainant stated that he/she again asked again for evidence and was briefly referred to a couple of clinical trials that showed a lower incidence of hypoglycaemia with Januvia compared with a number of sulphonylureas. The complainant asked to see the effect of reducing hospital admissions from these data and was told the studies did not look at that and they covered all grades of severity of hypoglycaemia. The representatives conceded that only severe events would need hospital attendance but could not quantify how Januvia did against comparative medicines. However the representatives asserted there would be a reduction in urgent admissions if Januvia was used instead of sulphonylurea but were not able to provide clinical trial data to support it. Again the representative dismissed the importance of insulin related hypoglycaemia.

The complainant stated he/she was alarmed at the way in which this information was presented to health professionals. As the information could be presented to practices with their specific practice information the complainant was even more concerned that this presentation or programme was being used widely and alleged it was misleading.

The use of such material brought the pharmaceutical industry into disrepute. Presenting data and making false claims was a disgrace.

The complainant alleged that there was clear disguised promotion of Ezetrol and Januvia in the presentation and that claims for the medicines could not be substantiated with any clinical trial data.

The linking of the medicines to this computer data made a clear link between the perceived problem and that the Merck Sharp & Dohme medicines could prevent or reduce the problem, which was not so in everyday practice.

The programme included prescribing information but the products had no data or licenses for the prevention of the issues that the programme purported to identify. The complainant stated that this must be wrong.

The complainant alleged that the Merck Sharp & Dohme representatives had promoted the medicines outside of the products' licences and for unlicensed uses.

When writing to Merck Sharp & Dohme, the Authority asked it to bear in mind Clauses 3.1, 3.2, 7.2, 7.4, 7.5, 7.10, 9.1, 12.1, 15.9 and 2 of the second edition of the 2012 Code of Practice.

RESPONSE

Merck Sharp & Dohme refuted the allegations and strongly believed that it had not breached the Code by the use of the MIRROR tool generally and/or by any individual specific interaction between any Merck Sharp & Dohme employees and a practising clinician.

The MIRROR tool, which because it relied on highly interactive access to a very extensive database, could not be provided electronically, in full, to the Panel. However, Merck Sharp & Dohme provided representative screenshots of the most recent active version of the tool which demonstrated the variety of information that could be accessed, together with screenshots of information about the tool itself that must mandatorily be presented to health professionals each time it was used. These were the screenshots used in training the Merck Sharp & Dohme market access leads who used the tool in the field. Merck Sharp & Dohme also provided the relevant approval certificates.

Merck Sharp & Dohme explained that the MIRROR tool was an interactive database of information derived from Health Episode Statistics (HES) data, supplied to the company via a commercial reuse licence by the NHS Information Centre (NHSIC). The tool was used by specifically trained health access leads with NHS personnel who might be interested in the data contained within it.

The tool brought together various categories of information, including local hospital admission data; out-patient data; attainment of QOF targets and practice-level prescribing information. All data was anonymised at the patient level. The tool was used to enable better understanding of the use of local resources for specific disease entities, to help identify areas of concern and to map healthcare needs and usages geographically. At the customer's request, reports could be generated and printed for their use, subject to various compliance restrictions detailed below. By the terms of the licence with the NHSIC, access to the tool could not be provided independently to health professionals; it could only be used in conjunction with a trained market access lead.

Merck Sharp & Dohme stated that careful examination of its customer relations database, which recorded all interactions between company personnel and health professionals, did not identify any call which would fit the parameters outlined in the complaint. Merck Sharp & Dohme was confident in the credibility and integrity of its field-based employees, and did not accept that any of them would deviate from the training and briefing related to the use of MIRROR. Without precise information from the complainant about where the alleged call had taken place and/or the Merck Sharp & Dohme employees concerned, the company could not investigate any specific employees and/or specific activity. Accordingly, its response focussed on the training and briefing information provided to employees who used the MIRROR tool (certified copies of the original and subsequent MIRROR tool briefing documents and copies of the slides used in training sessions on the tool were provided).

Merck Sharp & Dohme noted that the first screen following the log-on screen contained a summary of important information about the tool. The briefing document stated, under 'Important information': 'Prior to demonstrating the MIRROR tool, the important information shown below should be read through and discussed with customers'. In the same document, under 'What can I do and what can I not do…' was the statement: 'The first page contains important information about the tool. It highlights that MIRROR has been designed as a promotional tool; sets out an overview of the sources data used in the tool; and stipulates limitations on the use of data outputs. Customers need to be made aware of this important information at the outset'.
The first paragraph of the 'Important information' screen within the tool itself stated that Merck Sharp & Dohme 'has developed this MIRROR tool for the purpose of promoting its products. Prescribing information for relevant MERCK SHARP & DOHME products can be found at the prescribing information tab found at the top of each page'.

Further users were instructed that 'When generating local reports to send to or leave with customers, MIRROR will attach the important information section and the appropriate prescribing information and these must be included when the reports are sent to or left with a customer'.

Merck Sharp & Dohme submitted that it was thus clear that its personnel were trained and briefed specifically to ensure that health professionals knew from the outset that the tool was intended for promotional use, and the tool itself complied with all relevant clauses of the Code for promotional materials. Merck Sharp & Dohme did not accept the complainant's allegation that use of the tool represented disguised promotion and it denied a breach of Clause 12.1.

With regard to more general compliance briefing, Merck Sharp & Dohme noted that the original briefing document stated that 'MIRROR is a flexible and interactive tool and it is extremely important that you ensure it is used in line with the core principles of the Code, ie it must be used in a manner that portrays Merck Sharp & Dohme products accurately, fairly and objectively. As always we must also ensure that discussions of Merck Sharp & Dohme products are always within their licence indications'. A subsequent briefing document, issued following updates to the tool, and which supplemented but did not supplant the original briefing, additionally stated that 'It is important to ensure that we maintain balance in these discussions. We may, where

appropriate, suggest that our products might help to address an issue highlighted by the MIRROR tool, but we cannot guarantee what the impact of our products will be and we should not suggest that use of our products will solve an issue completely'.

Additionally, the MIRROR training slides reinforced these points; and, in particular, stated that 'As with all interactions, we must be fair and balanced in these discussions and ensure that they are within the terms of our product licence'.

Merck Sharp & Dohme considered that it had thus taken sufficient opportunity in its briefing and training materials to remind MIRROR users that all conversations relating to the tool must be undertaken in compliance with the principles of the Code, and, especially, that any promotion of Merck Sharp & Dohme products must be in accordance with their respective licences.

Ezetrol

Merck Sharp & Dohme noted the complainant's allegation that Ezetrol was promoted to him/her, in conjunction with use of the MIRROR tool, as a treatment that would 'stop the coronary events' highlighted by the in-patient data. He/she further alleged that the Merck Sharp & Dohme personnel insisted on selling Ezetrol as a medicine that would stop coronary events just because it lowered cholesterol and that, whilst they acknowledged that no cardiovascular outcome data was available for Ezetrol, 'there soon would be'.

Merck Sharp & Dohme submitted that it was difficult to respond to a one-sided report of a conversation from an anonymous complainant. However, it found it extremely unlikely that the employees concerned would have made the alleged statements, as they would directly contravene explicit training and briefing instructions. In the case of Ezetrol, not only would they contravene the principles referred to above, but they would go against a clear reminder in the training slides that Ezetrol was not licensed for reduction in cardiovascular outcomes. Furthermore, all Merck Sharp & Dohme sales personnel knew from general training that they were not allowed to proactively raise ongoing outcome studies, and that any enquiries about such studies from health professionals should be referred to the medical or medical information department (see below).

In this context, the MIRROR tool could conceivably be used to highlight the incidence of hospital admissions for ischaemic heart disease, but it would not be possible to attribute underlying causation (eg to hypercholesterolaemia), nor to ascertain (or assert) that lowering cholesterol with Ezetrol would necessarily lead to a reduction in hospital admissions or, indeed, the incidence of heart disease. Merck Sharp & Dohme reiterated that personnel were clearly instructed not to make or suggest such inferences. It would be a matter for the individual health professional's clinical judgement as to the weight to give to these various considerations.

Merck Sharp & Dohme was confident in the credibility and integrity of its employees in relation to this point and, as such, it strongly refuted the allegation that it had used the MIRROR tool to promote Ezetrol for cardiovascular outcomes, outwith its licensed indications.

Merck Sharp & Dohme explained that the forthcoming data about Ezetrol and reduction of coronary events was from the IMPROVE-IT trial, a cardiovascular outcome study set up to evaluate any reduction in risk of occurrence of a composite endpoint of cardiovascular death, major coronary event or stroke in subjects with stabilised high-risk acute coronary syndrome treated with an Ezetrol/simvastatin combination, compared with statin alone. The study was close to completion, and was expected to report at the end of 2014 or early in 2015. The sales force was instructed not to raise the existence of the trial proactively. If asked about it by a customer, it was instructed to respond 'It is an ongoing clinical trial, and I am not able to discuss it with you. If you have questions about this study, I can submit a medical information request for you, or arrange a meeting with one of our MSLs'.

Januvia

Merck Sharp & Dohme noted the complainant's allegation that unwarranted assumptions were made concerning the potential reduction in hypoglycaemia-related hospital admissions if Januvia was used instead of sulphonylureas. Again, the company found it difficult to credit that the conversation took place in the manner alleged.

The MIRROR tool would provide information on the incidence of such admissions. Clearly, it was likely that a majority of these would be insulin-related, but equally some would result from sulphonylurea use. As noted in a recent review (Barnett *et al*, 2013), one study found that 'the proportion of individuals treated with sulphonylureas or insulin for less than 2 years experiencing at least one severe (requiring external medical assistance) episode of hypoglycaemia was similar: 7% versus 7%'. Likewise: 'Individuals most at risk of hypoglycaemia are those treated with insulin or sulphonylureas'. The authors also summarised the relative risks of Januvia and a sulphonylurea with respect to hypoglycaemia as follows: 'For example, in a study comparing the efficacy and safety of Januvia versus glipizide in people with type 2 diabetes and inadequate glycaemic control on metformin monotherapy, the sulphonylurea was associated with a significantly greater risk of hypoglycaemic events regardless of the most recent HbA_{1c} value'. Finally: 'In a recent UK study, the total costs of severe hypoglycaemia were estimated as … £16.4 million for type 2 diabetes' (which the authors took to be a 'gross underestimate'). Again, while some of this was undoubtedly insulin-related, it was a reasonable inference that a proportion of this figure was related to sulphonylurea administration.

It was well accepted that the class of medicines to which Januvia belonged (the dipeptidyl peptidase

(DPP)-4 inhibitors) was associated with a significantly lower risk of hypoglycaemia than the sulphonylureas (Nauck *et al*, 2007). Noting this in a promotional call was acceptable, as was highlighting the scale of hypoglycaemia-related hospital admissions through tools such as MIRROR. As noted above, employees were briefed that 'We may, where appropriate, suggest that our products might help to address an issue highlighted by the MIRROR tool, but we cannot guarantee what the impact of our products will be and we should not suggest that use of our products will solve an issue completely'. Merck Sharp & Dohme considered that use of Januvia might indeed help to address the issue of sulphonylurea-induced hypoglycaemia, and that noting this would be valid under the Code. However, as per the briefing and training materials, the company expected this to be presented in a balanced way, and without undue emphasis on possible beneficial outcomes. In particular, it would be foolish to deny the role that insulin might play in a proportion of admissions for hypoglycaemia, and there would be no potential benefit to the company if it did so. Merck Sharp & Dohme did not believe that the conversation reported by the complainant took place in the manner alleged.

Summary

Merck Sharp & Dohme noted that it had been asked to consider the requirements of a number of clauses of the Code. As noted above, in the absence of direct evidence other than the complainant's letter as to what was or was not said at the alleged call, the company relied on its internal briefing and training materials.

With regard to Clauses 3.1 and 3.2, there was clear evidence that representatives were instructed and expected to promote only in accordance with the respective marketing authorizations. In particular, they were specifically reminded in training that Ezetrol was not licensed for improvement in cardiovascular outcomes. Merck Sharp & Dohme strongly refuted the allegation that it had breached Clauses 3.1 and 3.2, and had every confidence that its employees would follow the training and briefing.

With regard to Clauses 7.2, 7.4, 7.5 and 7.10, the MIRROR tool itself was based on validated data-sets supplied by the NHS, and could not itself be misleading or require further substantiation. Whether the data had been used to make misleading, inaccurate, unbalanced or non-substantiable verbal statements was the point at issue. In the absence of further information, Merck Sharp & Dohme referred to its briefing and training materials, in which the standards it expected from its representatives who used the tool were explicitly made. The company reiterated that it had great difficulty in accepting the version of events alleged by the complainant. Again, it strongly refuted the allegations, and denied any breach of Clause 7.

It was made abundantly clear to users from the outset that MIRROR was a promotional resource, and therefore the issue of disguised promotion covered by Clause 12.1 did not arise.

Merck Sharp & Dohme submitted that its detailed briefing material complied with Clause 15.9 and that it had maintained the highest standards in the use of the tool. It denied breaches of Clauses 2 or 9.1.

PANEL RULING

The Panel noted that the complainant was anonymous and non-contactable. Such complaints were accepted and like all complaints judged on the evidence provided by the parties. The complainant bore the burden of proof. It was not possible to contact the complainant for further information.

The Panel noted Merck Sharp & Dohme's clear acknowledgement that MIRROR had been designed as a promotional tool. Point 1 of the information which Merck Sharp & Dohme stated representatives had to read through and discuss with customers before they proceeded further with the MIRROR tool stated, 'Merck Sharp & Dohme ("MERCK SHARP & DOHME") has developed this MIRROR tool for the purpose of promoting its products. Prescribing information for relevant MERCK SHARP & DOHME products can be found at the prescribing information tab found at the top of each page'. The Panel noted that it had not been provided with the complete MIRROR tool. Screenshots showed that the pages of MIRROR provided, which Merck Sharp & Dohme submitted were representative of the most recent active version of the tool, all included a link to prescribing information. Merck Sharp & Dohme had further submitted that reports generated at a customer's request would have prescribing information attached. The Panel did not know in what context the meeting in question had been set up but it noted that the complainant had clearly considered that Ezetrol and Januvia had been promoted during the course of the conversation. In that regard the Panel did not consider that the use of MIRROR amounted to disguised promotion. No breach of Clause 12.1 was ruled.

The Panel noted that both Ezetrol and Januvia had been promoted within the context of a conversation about data held within the MIRROR tool. It appeared that field-based staff used the MIRROR tool to examine data from the local health economy and, within that context, promote a medicine. With regard to Ezetrol, the complainant had submitted that the representatives had shown a number of slides that looked at non-elective admissions for a number of coronary events and had focussed on the number of these events which had occurred in patients with cholesterol levels above the QOF targets. As the complainant was anonymous and non-contactable, Merck Sharp & Dohme could not identify which of its field-based staff were involved but it did submit that the MIRROR tool could conceivably be used to highlight the incidence of hospital admissions for ischaemic heart disease but that it would not be possible to attribute this to hypercholesterolaemia or to assert that the use of Ezetrol would result in fewer hospital admissions. In the Panel's view however, to promote Ezetrol, a lipid lowering agent, following a conversation about non-elective cardiovascular hospital admissions in patients with cholesterol levels above QOF targets,

invited the customer to link the two conversations and assume that Ezetrol had a role in reducing such admissions. Although MIRROR briefing material stated that Merck Sharp & Dohme products must be portrayed accurately, fairly and objectively, and always within their licence, the Panel noted the following statement from the MIRROR briefing document (ref NOND-1034256-0020):

> 'MIRROR can and should also be used with a customer(s) to highlight local performance gaps or disease management issues and to facilitate discussions to progress towards potential solutions.

It is important to ensure that we maintain balance in these discussions. We may, where appropriate, suggest that our products might help to address an issue highlighted by the MIRROR tool but we cannot guarantee what the impact of our products will be and we should not suggest that use of our products will solve an issue completely.'

An earlier briefing document (ref NOND-1034256-0007) stated:

> 'MIRROR can be used in calls with healthcare professionals to raise specific disease management issues and it is acceptable in that same call to then discuss how a treatment/disease management strategy, involving therapy classes that involve 1 or more MSD products, could produce benefits for the patient and local health economy.'

The Panel noted that the summary of product characteristics for Ezetrol stated that 'A beneficial effect of Ezetrol on cardiovascular morbidity and mortality has not yet been demonstrated'. The Panel considered, given the statements above from the briefing documents, that on the balance of probabilities, concurrent use of the MIRROR tool and promotion of Ezetrol had given a misleading impression, which could not be substantiated, that use of the medicine would decrease non-elective hospital admissions due to coronary events. A breach of Clauses 7.2 and 7.4 was ruled. Further, the Panel considered that such an impression, given the statement in the SPC that a beneficial effect on cardiovascular morbidity had not been demonstrated, was inconsistent with the particulars listed in the Ezetrol SPC. A breach of Clause 3.2 was ruled. The Panel considered that Ezetrol had, in effect, been promoted for an unlicensed indication. A breach of Clause 3.1 was ruled. The Panel considered that the representatives had not promoted the rational use of Ezetrol. A breach of Clause 7.10 was ruled.

The Panel noted that although the complainant stated that he/she had asked for outcome data, as the claim for reduced hospital admissions could not be substantiated, none could be provided. In that regard the Panel ruled no breach of Clause 7.5, noting its ruling above of a breach of Clause 7.4.

The Panel noted the complainant's allegation that the representatives had suggested that use of Januvia instead of sulphonylureas would reduce urgent hospital admissions due to hypoglycaemia. The representatives had not been able to produce any data to support this claim. The Panel noted Merck Sharp & Dohme's submission that Januvia belonged to a class of medicines which was associated with a lower incidence of hypoglycaemia than the sulphonylureas and that to highlight this in a promotional call was acceptable, as was highlighting the scale of hypoglycaemia-related hospital admissions through tools such as MIRROR. The Panel noted its comments above and considered that to promote Januvia within the context of a conversation about hypoglycaemia-related hospital admissions would imply that the medicine had a role in reducing such admissions. The Panel considered that such an implication was misleading and could not be substantiated. A breach of Clauses 7.2 and 7.4 was ruled. The Panel did not consider that such an impression was inconsistent with the particulars listed in the Januvia SPC given that the SPC did not refer to hypoglycaemia complications or morbidity. No breach of Clause 3.2 was ruled. The Panel considered, however, that Januvia had, in effect, been promoted for an unlicensed indication. A breach of Clause 3.1 was ruled. The Panel considered that the representatives had not promoted the rational use of Januvia. A breach of Clause 7.10 was ruled.

The Panel noted that although the complainant stated that he/she had asked the representatives to substantiate the claim that Januvia would reduce hospital admissions, as the claim could not be substantiated no data could be provided. In that regard the Panel ruled no breach of Clause 7.5, noting its ruling above of a breach of Clause 7.4.

The Panel was very concerned about the wording of the MIRROR briefing documents quoted above. In the Panel's view, to suggest that a medicine might help to address an issue or could produce benefits usually resulted in the impression that the medicine would definitely do so. MIRROR was used to establish a local health economy need or gap which, when followed by a promotional discussion, invited the customer to link the two and assume that the medicine would address that need or fill the gap. In the Panel's view the briefing material positively encouraged representatives to discuss medicines in relation to the local health economy data provided by MIRROR. The Panel considered that the use of the MIRROR tool to discuss healthcare issues was incompatible with the concurrent promotion of medicines unless those medicines were appropriately licensed or had relevant outcome data (eg reduced hospital admissions). In the Panel's view the MIRROR briefing material advocated a course of action which was likely to breach the Code. A breach of Clause 15.9 was ruled.

The Panel noted its rulings above and considered that high standards had not been maintained. A breach of Clause 9.1 was ruled. The Panel further considered that the use of MIRROR in conjunction with the promotion of medicines, and to brief representatives that it was acceptable to suggest that Merck Sharp & Dohme's products might help to

address an issue highlighted by the tool, was such as to bring discredit upon and reduce confidence in the pharmaceutical industry. A breach of Clause 2 was ruled.

During its consideration of this case, the Panel was concerned to note that in briefing material prepared for the MIRROR launch, (ref NOND-1040876-0005), it was stated that 'Therefore Ezetrol should be an essential part of the management of patients with type 2 diabetes and CVD [cardiovascular disease] to reduce cholesterol and CV risk'. The Panel queried whether describing Ezetrol as an 'essential' part of management met the requirements of the Code. The Panel also queried whether stating that it reduced CV risk was consistent with the particulars listed in the Ezetrol SPC given that the medicine was licensed to reduce cholesterol and that no beneficial effect of the medicine on cardiovascular morbidity or mortality had yet been demonstrated. Similar concerns applied to the statement that Januvia 'improves patient experience by reducing the complications of type 2 diabetes'. The Panel requested that Merck Sharp & Dohme be advised of its concerns.

APPEAL BY MERCK SHARP & DOHME

Merck Sharp & Dohme based its appeal on four key points:

1 There was reason to believe that the complaint which purported to come from a health professional was, in fact, from an ex-employee with a grudge following redundancy. As such, it might be a complete fabrication and could not be taken at face value.
2 The complainant had described a series of interactions that Merck Sharp & Dohme did not recognize as likely to have occurred and could not verify from its records.
3 It was entirely appropriate to use the MIRROR tool in the context of the promotion of medicines.
4 The interactions described in the complaint were inconsistent with everything the company had put in place to ensure appropriate use of the MIRROR tool.

Merck Sharp & Dohme was extremely concerned about the potentially far-reaching implications of the Panel's ruling for the industry as a whole and the manner in which it interacted with the NHS and health professionals. Merck Sharp & Dohme submitted that companies should work with the NHS and NHS health professionals to help them achieve their strategic objectives. One of the NHS's strategic objectives and priorities was to improve the nation's cardiovascular health and the Government had made it clear that key to this was the early diagnosis and management of diabetes and hypercholesterolemia. It was entirely appropriate for a company to help doctors understand the burden of specific diseases within their geographical area, identify unmet needs and inequalities in access to care based on geographical location and identify common risk factors such as type 2 diabetes and elevated cholesterol levels. A company must then be able to explain how its products could help improve glycaemic control in patients with type 2 diabetes (eg Januvia) and address hypercholesterolaemia that was not appropriately controlled with a statin alone (eg Ezetrol).

Merck Sharp & Dohme submitted that if the Panel was correct, companies would not be able to discuss the efficacy of their products for the approved indications in the context of the NHS's strategic priorities and that could not possibly be the right outcome. For the Panel to have found Merck Sharp & Dohme in breach for off-label promotion, it needed to identify an off-label product claim. The Panel had not provided any evidence that Merck Sharp & Dohme had made such a claim. Rather, the Panel had raised a hypothesis that a broad, contextual discussion of cardiovascular health in a doctor's area followed by a discussion of a product's efficacy for its approved indications must constitute off-label promotion.

Merck Sharp & Dohme asked the Appeal Board to identify a single piece of evidence that it had promoted either Januvia or Ezetrol off-label.

1 The complaint

Merck Sharp & Dohme appreciated the need for the PMCPA to be able to consider anonymous complaints as there would undoubtedly be cases where a genuine 'whistle blower' felt unable to identify him/herself when he/she nonetheless raised important matters. However, the acceptance of anonymous complaints at face value, as seemed to have taken place here, without a critical appraisal of the veracity of the allegations, left open the possibility that vindictive allegations were assumed to be true and Merck Sharp & Dohme was left to defend itself against an unverifiable 'he said, she said' situation. Historically in such situations, where versions of events differed between complainant and respondent, the PMCPA had generally concluded that the level of proof required to rule a breach had not been reached. This was also reflected in fundamental concepts of procedural fairness and the right to a fair hearing. On this occasion, however, the unverified accusations of the complainant seemed to have been taken as true, despite extensive evidence from Merck Sharp & Dohme that the described events were unlikely to have occurred.

Merck Sharp & Dohme noted that over the past few months, it had been the subject of three complaints from anonymous, non-contactable complainants – the current case (Case AUTH/2699/2/14), and Cases AUTH/2651/11/13 and AUTH/2646/10/13. Historically, this was very much out of character. The timing fitted with a significant downsizing and restructuring of the company's primary care division.

Merck Sharp & Dohme had examined the complaint submitted in the current case alongside that of Case AUTH/2646/10/13, which purported to come from a health professional, and noted unusual structure (eg subject matter line being placed above the salutation line) and phraseology ('the drug firm Merck Sharp & Dohme') which raised significant doubt about whether they truly came from two independent health professionals. If there was doubt about the

complaint's true provenance, then there must be doubt about the truthfulness of the content.

2 The described interaction

Merck Sharp & Dohme submitted that since the complainant was anonymous and non-contactable, it was not possible to be certain of some information, eg the location of alleged activities. The complainant had alleged that he/she had met two Merck Sharp & Dohme representatives. Merck Sharp & Dohme representatives did not usually call on health professionals in pairs. A manager sometimes accompanied a more junior representative, but the MIRROR tool was used only by more experienced representatives, so this was unlikely to have occurred in this case. In any event, had two representatives visited a single health professional together, this would have been documented in Merck Sharp & Dohme's customer relationship management (CRM) tool in which representatives had to record details of all interactions with health professionals, including the names of other representatives present. Merck Sharp & Dohme had not found any record that a meeting involving two representatives using the MIRROR tool had taken place.

Merck Sharp & Dohme submitted the complainant had provided no evidence to show that this meeting took place (representative names, for example, or copies of print-outs that might have been left) and no evidence to support that the alleged claims were made by its representatives. This was not a description of an event that Merck Sharp & Dohme recognised, and it submitted that this was unlikely to be a true record of a meeting between Merck Sharp & Dohme and a health professional.

Merck Sharp & Dohme submitted that even if the Appeal Board concluded that the interaction did take place as described, it did not accept that there was any clear evidence that the alleged claims were made by its representatives.

3 Use of the MIRROR tool

Merck Sharp & Dohme submitted that the MIRROR tool was essentially a 'front end' computer programme that displayed data from NHS databases, specifically hospital episode statistics. As such, it allowed prescribers and purchasers to understand the burden of illness in their own locality, and by implication draw conclusions about the relative position with neighbouring areas, national averages, achievement of NHS targets, strategies and outcomes, volume of events, etc.

Merck Sharp & Dohme submitted that the MIRROR tool was used to help health professionals understand the burden of specific diseases within their geographical area and to identify unmet needs. In particular, the MIRROR tool could highlight the real world implications of particular conditions or health risks, such as cardiovascular risk, and the size of the problem in the health professional's locality. Educating health professionals about this was entirely appropriate and consistent with the Government's health strategy. The UK had a high rate of cardiovascular disease with significant cost implications that placed a huge financial burden on the NHS. As a result, in 2013 the Department of Health (DoH) developed a specific cardiovascular disease outcomes strategy for the prevention, diagnosis and treatment of cardiovascular disease to improve outcomes ('Cardiovascular Disease Outcomes Strategy: Improving outcomes for people with or at risk of cardiovascular disease'). This document specifically recognized inequalities in access to care, including inequalities based on geographical location, and identified common risk factors, such as diabetes and elevated cholesterol levels. The MIRROR tool allowed Merck Sharp & Dohme representatives to establish a context, namely that it was important for health professionals to identify, and where appropriate treat, patients with a particular condition or health risk. Merck Sharp & Dohme representatives could then discuss the use of the company's products, within their licensed indications, as part of the NHS's overall treatment strategies.

Merck Sharp & Dohme submitted that this did not involve off-label product claims. Nor did it explore the 'what if….' type of question – 'What if I prescribed more Ezetrol?' or 'What if I prescribed more Januvia?'. These questions could not be addressed because the impact of Ezetrol on cardiovascular-related hospital admissions, or Januvia on diabetes-related hospital admissions, was unknown. Whilst the software was clever and attractive, there was nothing unique about the data, only about how they were presented.

Merck Sharp & Dohme was confident that its comprehensive and thorough training programme, which it discussed below, meant that no Merck Sharp & Dohme representative would make inappropriate claims as alleged.

Merck Sharp & Dohme submitted that during the development of the MIRROR tool there were extensive discussions about whether or not to use it for promotional purposes, because the data contained within it – effectively local demographics and health resource data – were unrelated to specific products. The data did not represent or purport to represent the impact of any particular medicine. It was also anticipated that in demonstrating the tool, the customer might ask for a 'cut' of the data that identified patients who were outside the licensed indication for Merck Sharp & Dohme's products. Unlike a printed detail aid, where epidemiological data could be presented that matched the licensed patient population, with an interactive system it was not possible to prescribe what data were explored.

On balance, Merck Sharp & Dohme submitted that given the value of the data and the surrounding discussions, it decided that the tool could be used in association with a promotional call, to establish the size of the problem in the locality, before detailing Ezetrol and/or Januvia.

Merck Sharp & Dohme noted that the Panel, however, had concluded that '… to suggest

a medicine might help to address an issue or could produce benefits usually resulted in the impression that the medicine would definitely do so'. It stated that using MIRROR to identify a local health economy need or gap followed by a promotional discussion '... invited the customer to link the two and assume that the medicine would address that need or fill the gap'. Finally, the Panel considered that 'the use of the MIRROR tool to discuss healthcare issues was incompatible with the concurrent promotion of medicines unless those medicines were appropriately licensed or had relevant outcome data (eg reduced hospital admissions)'.

Merck Sharp & Dohme strongly disagreed with the Panel's unfounded conclusions. Indeed, if the Panel's ruling was maintained, it would negatively impact not just Merck Sharp & Dohme but the entire British pharmaceutical industry. The Panel's position meant that representatives could never draw attention to the burden of specific diseases on the NHS, educate health professionals about DoH strategy or clinical guidelines from the National Institute for Health and Care Excellence (NICE) or even discuss general disease areas. In particular, pharmaceutical companies could not explain how their products fitted into the overall treatment priorities of the NHS. Essentially, the Panel's position would prohibit pharmaceutical companies from giving any sort of context to their discussions about the licensed uses of their medicines. This could not be a correct interpretation of the Code.

Further, Merck Sharp & Dohme submitted that there was no justification for the Panel's assertion that to suggest a medicine might play a distinct role in addressing a broader public health issue usually resulted in the impression that the medicine would definitely do so. If that assertion were true, any claim that a medicine could treat a particular condition that played a role in a wider public health concern, in this case cardiovascular health and/or diabetic complications, would be interpreted as a guarantee of its efficacy in the broader context. Such a conclusion was illogical and did not reflect the many years of experience of promotional interactions between pharmaceutical representatives and sophisticated prescribers.

To illustrate this, Merck Sharp & Dohme noted the following quotation from the DoH's 2013 'Cardiovascular Disease Outcomes Strategy: Improving outcomes for people with or at risk of cardiovascular disease.'

Excerpt from executive summary, page 5:

> '... CVD [cardiovascular disease] in practice represents a single family of diseases and conditions linked by common risk factors and the direct effect they have on CVD mortality and morbidity. These include coronary heart disease, stroke, hypertension, hypercholesterolemia, diabetes, chronic kidney disease, peripheral arterial disease and vascular dementia. Many people who have one CVD condition commonly suffer from another and yet opportunities to identify and manage these are often missed. Patients often receive care from multiple different teams in a disjointed way. This results in uncoordinated care, multiple different hospital visits and, in some cases, confusing or contradictory information. This happens both in hospitals and in the community. A more co-ordinated and integrated approach is needed to assessment, treatment and care to improve outcomes, including patient experience and patient safety.'

Paragraph 1.3-1.4:

> 'CVD is an overarching term that describes a family of diseases sharing a common set of risk factors. This outcomes strategy largely focuses on conditions causing, or resulting from, atherosclerosis (furring or stiffening of the walls of arteries), particularly coronary heart disease, stroke and peripheral arterial disease (PAD).
>
> It also covers other conditions such as vascular dementia, chronic kidney disease (CKD), arrhythmias, sudden cardiac death and heart failure, because they share common risk factors or have a significant impact on CVD mortality or morbidity. The complications of diabetes also share the same modifiable risk factors as CVD and having diabetes increases individuals' risk of CVD. This strategy considers the implications of diabetes on CVD risk rather than its detailed management.'

Paragraph 1.6

'A number of common risk factors are recognised as increasing the likelihood of individuals developing atherosclerosis. [...]

- hypertension/raised blood pressure;
- raised cholesterol/disordered lipids;
- impaired glucose tolerance/diabetes; and
- chronic kidney disease (CKD).'

Merck Sharp & Dohme submitted that if the Panel was correct, no representative would be able to discuss the importance of managing diabetes and elevated cholesterol levels using products approved for those purposes, given their importance as common risk factors linked to cardiovascular disease (CVD). In the Panel's view, to 'suggest a medicine might help to address [CVD] or could produce benefits usually resulted in the impression that the medicine would definitely do so'.

Merck Sharp & Dohme submitted that that was simply not what MIRROR or its representatives did and the Panel had produced no evidence that this had occurred. Merck Sharp & Dohme and its representatives had helped doctors understand cardiovascular health issues and inequalities in treatment between areas, before discussing use of Ezetrol and Januvia for their approved indications. There was no claim that the products were efficacious against CVD. If clinicians stated that 'patients with elevated cholesterol levels and type 2 diabetes have a higher risk of CVD, so it was important that we do something about blood sugar

and LDL cholesterol levels', they were not stating medicines they prescribed for that purpose were efficacious against, for example, coronary heart disease, stroke and peripheral arterial disease; they were merely stating that the patients needed to lower their blood sugar and cholesterol levels because elevated levels put them at risk of heart disease. There was no claim of efficacy against CVD. Nor did it follow that just because MIRROR allowed the presentation of data relating to the significance of cardiovascular health issues in a particular locality, that any subsequent discussion of the efficacy of Merck Sharp & Dohme's products must necessarily be off-label.

4 Training and briefing materials

Merck Sharp & Dohme submitted that its representatives had been rigorously trained on the use of the MIRROR tool and the types of statements that were acceptable. This training was delivered at a full day, face-to-face, training session attended by the medical and compliance teams. A significant part of the training was role play scenarios where the representatives were thoroughly trained on how to present the MIRROR data, and to make sure that they discussed only the licensed indications for both Ezetrol and Januvia.

Merck Sharp & Dohme submitted that representatives were made fully aware of the source of the data in MIRROR and what the data represented (and what they did not represent). The representatives were clearly instructed that the data should not be used to make product-related claims that either could not be substantiated, or that might recommend, directly or indirectly, the use of either Ezetrol and/or Januvia in patients outside the respective licensed indications.

Merck Sharp & Dohme submitted that with a comprehensive and thorough training programme in place, it was confident that none of its representatives would make inappropriate claims as alleged.

Merck Sharp & Dohme noted that the Panel appeared to have focused on three paragraphs from MIRROR briefing documents. Two of these, from briefing document (ref NOND-1034256-0020) were:

> 'MIRROR can and should also be used with a customer(s) to highlight local performance gaps or disease management issues and to facilitate discussions to progress towards potential solutions.
>
> It is important to ensure that we maintain balance in these discussions. We may, where appropriate, suggest that our products might help to address an issue highlighted by the MIRROR tool but we cannot guarantee what the impact of our products will be and we should not suggest that use of our products will solve an issue completely.'

The third paragraph, from briefing document (ref NOND-1034256-0007), stated:

> 'MIRROR can be used in calls with healthcare professionals to raise specific disease management issues and it is acceptable in that same call to then discuss how a treatment/disease management strategy, involving therapy classes that involve 1 or more MSD products, could produce benefits for the patient and local health economy.'

Merck Sharp & Dohme noted an additional statement from the briefing document ref NOND-1034256-0007, which the Panel appeared to have overlooked or ignored:

> 'MIRROR is a flexible and interactive tool and it is extremely important that you ensure it is used in line with the core principles of the Code i.e. it must be used in a manner that portrays MSD products accurately, fairly and objectively. **As always we must also ensure that discussions of MSD products are always within their licence** indications' (emphasis added by Merck Sharp & Dohme).

Contrary to the Panel's views, Merck Sharp & Dohme submitted that, in conjunction with the face-to-face training, the three paragraphs from the briefing material quoted by the Panel and the additional paragraph highlighted above, made it clear to representatives that they must be very careful not to claim, suggest or infer use of any Merck Sharp & Dohme product outside of their licensed indications, ie for a beneficial effect on health outcomes.

5 Appeal

Merck Sharp & Dohme did not accept that there was any reliable evidence that its representatives had claimed a reduction in cardiovascular hospital admissions in patients treated with Ezetrol, or diabetes-related admissions in patients treated with Januvia. Consequently, Merck Sharp & Dohme appealed the Panel's rulings of breaches of Clauses 7.2, 7.4 and 7.10.

Merck Sharp & Dohme noted that the Panel had ruled breaches of Clause 3.1, which stated that a medicine must not be promoted prior to the grant of a marketing authorization. Merck Sharp & Dohme did not agree that this had occurred, nor was there evidence to suggest so. Both Ezetrol and Januvia had marketing authorizations. Consequently, Merck Sharp & Dohme appealed the Panel's ruling that there had been breaches of Clause 3.1.

Similarly, Clause 3.2 stated that the promotion of a medicine must not be inconsistent with the particulars listed in the SPC. Merck Sharp & Dohme submitted that as its representatives had only promoted Ezetrol to reduce cholesterol in patients with hypercholesterolaemia, and Januvia to improve glycaemic control, there had been no breach of Clause 3.2 and it appealed the Panel's ruling.

Contrary to the Panel's view, Merck Sharp & Dohme submitted that the representative's briefing materials and associated training made it clear when and where it was acceptable to suggest the use

of Ezetrol and/or Januvia. Merck Sharp & Dohme was confident that its representatives had not been inappropriately briefed to suggest, imply or claim that Merck Sharp & Dohme products reduced hospital admissions. As a result Merck Sharp & Dohme denied a breach of Clause 15.9 and it appealed the Panel's ruling.

Merck Sharp & Dohme strongly believed that high standards had been maintained at all times and that the reputation of, and confidence in, the pharmaceutical industry had not been compromised. Merck Sharp & Dohme therefore submitted that there had been no breach of either Clauses 9.1 or 2, and it appealed the Panel's rulings in this regard.

6 Summary

In summary, Merck Sharp & Dohme submitted that there was considerable doubt whether the meeting described by the anonymous, non-contactable complainant actually occurred. In Merck Sharp & Dohme's view, the meeting was highly unlikely to have taken place due to the robust, face-to-face, detailed training and briefing documents provided for representatives and the fact that it had been unable to find any evidence in the CRM system of a meeting between two Merck Sharp & Dohme representatives and a health professional involving the use of the MIRROR tool. Merck Sharp & Dohme suspected that the alleged incident had been fabricated.

Merck Sharp & Dohme was certain that, as a result of extensive training, its representatives who used MIRROR understood the difference between describing the local epidemiology, incidence, prevalence etc, and making a claim for Ezetrol and Januvia.

Merck Sharp & Dohme submitted that Code and compliance-related training provided to representatives had created a strong culture of Code awareness and compliance within the company. Merck Sharp & Dohme was confident and proud that all of its representatives were fully conversant with relevant areas of the Code and would never make claims that were misleading, incapable of substantiation, or outside the licensed indications for any of its products.

Merck Sharp & Dohme was greatly concerned that in the absence of any proof offered by the complainant, the Panel appeared to have taken the complaint at face value. The Panel's rulings also appeared to have been based on an interpretation that the representative's briefing and training material, as well as some content of the MIRROR tool, encouraged representatives to promote products outside their licensed indications, when in fact the briefing materials and the training made it absolutely clear that they must not do that. Further, the Panel seemed to have assumed that representatives would use the data displayed within MIRROR to promote Ezetrol and Januvia outside their licensed indications, contrary to the clear instructions given to them. There was no evidence that any of the alleged breaches actually occurred and Merck Sharp & Dohme asked the Appeal Board to overturn all breaches ruled.

Merck Sharp & Dohme submitted that while it understood the importance of complying with its obligations under the Code, and it took any alleged breach very seriously indeed, it was particularly disappointed by the Panel's ruling of a breach of Clause 2. Rulings of breaches of Clause 2 were a sign of particular censure and were reserved for circumstances that brought discredit on the pharmaceutical industry. Merck Sharp & Dohme considered it was unjust and distinctly unfair to rule a breach of Clause 2 where the only 'evidence' was an unreliable complaint from an anonymous and non-contactable individual who claimed to be a health professional and for the Panel to take that complaint at face value, without questioning its accuracy or veracity.

Indeed, Merck Sharp & Dohme submitted that the Panel seemed to have ignored its own procedures, as it had described them in the ruling. The first paragraph of the Panel ruling stated:

> 'The Panel noted that the complainant was anonymous and non-contactable. Such complaints were accepted and like all complaints **judged on the evidence** provided by the parties. **The complainant bore the burden of proof** (emphasis added by Merck Sharp & Dohme).'

Merck Sharp & Dohme submitted that the anonymous complainant had not provided any evidence and as such it could not understand how, when the complaint was 'judged on the evidence' and that 'the complainant bore the burden of proof' the Panel could make any ruling against Merck Sharp & Dohme, and certainly not a ruling of a breach of Clause 2.

APPEAL BOARD RULING

The Appeal Board noted that the Merck Sharp & Dohme had raised points about the veracity of the complaint, conduct of the meeting and use of the MIRROR tool that had not previously been submitted to the Panel.

Firstly the Appeal Board considered whether the meeting as described took place and consequently whether the alleged claims were made, bearing in mind that the complainant had to establish his/her case on the balance of probabilities.

The Appeal Board noted from the Merck Sharp & Dohme representatives at the appeal that the company's field based area access leads (AALs) who used the MIRROR tool were separate from its sales representatives. The AALs had a promotional and non promotional role. Each AAL was experienced and had received specialist training. A call by an AAL to use the MIRROR tool would only be in response to a request from a health professional (payers, commissioners etc) usually elicited by a sales representative at a prior call. The way in which the AAL would use the MIRROR tool in each meeting was led by the health professional choosing

which information he/she wanted to view in a chosen disease area and region. The discussion and extraction of data in just one disease area could take up to 2 hours. The Appeal Board noted from the Merck Sharp & Dohme representatives at the appeal that the MIRROR tool examined the burden of illness and despite its description as a promotional tool, it was not designed to funnel down to a product discussion although this might happen.

The Appeal Board noted that the complainant had alleged that two representatives had detailed the MIRROR tool for both Ezetrol and its effect on coronary events and Januvia and its effect on hypoglycaemic events. The Appeal Board noted from the Merck Sharp & Dohme representatives at the appeal that a call detailing the MIRROR tool concerning two different disease areas did not occur but if it had, it would take up to 4 hours to complete which would be impractical for most health professionals. The Appeal Board noted from the Merck Sharp & Dohme representatives at the appeal that it was standard practice for AALs to work alone and in that regard Merck Sharp & Dohme had checked previous AAL visits and it could find no record of an AAL detailing the MIRROR tool with another Merck Sharp & Dohme employee as described by the complainant. The company's CRM database required a dual call to be recorded.

The Appeal Board noted from the Merck Sharp & Dohme representatives at the appeal that at the end of detailing the MIRROR tool a report was generated for the health professional to keep. The Appeal Board noted that the complainant had not provided any additional evidence such as this report to support his/her allegations.

The Appeal Board noted that all complaints were judged on the evidence provided by the parties with the burden on the complainant to prove his/her case on the balance of probabilities. The Appeal Board noted its comments above and considered that, on the balance of probabilities, it was not satisfied that the alleged meeting took place. Consequently the Appeal Board ruled no breaches of Clauses 3.1, 3.2, 7.2, 7.4 and 7.10 in relation to the claims about Ezetrol allegedly made by Merck Sharp & Dohme's representatives. Similarly the Appeal Board also ruled no breaches of Clauses 3.1, 7.2, 7.4 and 7.10 in relation to the claims about Januvia allegedly made by Merck Sharp & Dohme's representatives. The appeal on these points was successful.

The Appeal Board noted that in the information which preceded the MIRROR tool, it was clearly stated that Merck Sharp & Dohme had developed the tool for the purpose of promoting its medicines. The company representatives at the appeal stated, however, that it was for use in a non promotional/ health inequality/service improvement discussion but that if that discussion led into a promotional discussion the tool would nonetheless meet the requirements of the Code. The Appeal Board was concerned that the MIRROR tool thus appeared to have both a non promotional and a promotional purpose and in that regard it queried whether all of the Code requirements for each could truly be met.

The Appeal Board noted that the MIRROR tool launch materials (ref NOND-1040876-0005), part of the briefing material provided by Merck Sharp & Dohme, referred to the core campaigns for both Januvia and Ezetrol. In the Appeal Board's view some of the slides appeared to positively encourage AALs to take opportunities to promote Merck Sharp & Dohme's products (eg the slide headed 'Value Proposition for key stakeholders'). This slide stated that Ezetrol should be an *essential* part of the management of patients with type 2 diabetes and CVD to reduce cholesterol and CV risk' (emphasis added). In the Appeal Board's view to describe Ezetrol as essential was exaggerated; it was indicated only as add-on therapy when patients had been inadequately controlled with a statin alone. A slide which detailed the payer proposition for Januvia stated that '... sitagliptin improves patient experience by reducing the complications of type 2 diabetes'. In that regard the Appeal Board noted from the Merck Sharp & Dohme representatives that there was no outcome data to show that Januvia reduced cardiovascular disease, skin conditions etc (ie the 'complications' of diabetes) and although it had a low incidence of hypoglycaemia, hypoglycaemic episodes were acute events/side effects of therapy, not complications of the disease.

The Appeal Board considered that the MIRROR tool briefing materials were likely to encourage AALs to discuss Merck Sharp & Dohme products in relation to data generated by the MIRROR tool. It noted its comments above about the briefing material and the absence of patient outcome data. The Appeal Board considered that the briefing materials advocated a course of action that was likely to lead to a breach of the Code and consequently it upheld the Panel's ruling of a breach of Clause 15.9. High standards had not been maintained and the Appeal Board upheld the Panel's ruling of a breach of Clause 9.1. The appeal on these points was unsuccessful. The Appeal Board did not consider that the circumstances warranted a ruling of a breach of Clause 2 and no breach was ruled. The appeal on that point was successful.

Complaint received **3 February 2014**

Case completed **8 July 2014**