CASE AUTH/2378/12/10

PRIMARY CARE MEDICAL DIRECTOR v PFIZER

Promotion of Champix

A primary care medical director complained about the conduct of a Pfizer representative who presented at a smoking cessation meeting attended by approximately 60 smoking cessation advisors, who were non-clinical non-prescribers.

A colleague of the complainant attended the meeting. The complainant stated that part of the presentation promoting Champix (varenicline) underplayed the side effects of low mood and suicidal thoughts and attributed the suggested side effects to being similar to someone trying to stop eating chocolate. The complainant's colleague considered that the promotion of Champix had been unbalanced and the warnings attached to Champix had been grossly underplayed. He tried to make the point that chocolate did not come with a warning but that Champix did.

In general the complainant's colleague considered that it was grossly unprofessional to promote the medicine to such an impressionable audience, who did not have the knowledge to question the pharmaceutical representatives.

The complainant considered that the conduct of the representative fell outside the bounds of acceptable professional behaviour.

The detailed response from Pfizer is given below.

The Panel noted that the complainant had not attended the meeting at issue but had complained on behalf of a colleague who had. The purpose of the meeting was to discuss a new patient mental health questionnaire which smoking cessation advisors had to complete before referring smokers for Champix therapy. Not all of the attendees at the meeting were health professionals but they had all been trained to level 2 by the local NHS Stop Smoking Service to provide information on all stop smoking medicines. The Panel considered that in these circumstances it was not unreasonable to give clinical information about Champix. In the Panel's view it could be difficult when presenting to a mixed audience to ensure that no-one was misled. It was particularly important not to mislead with regard to side-effects.

The Panel examined the slides used at the meeting. One slide depicted nicotine binding and stimulation of dopamine and the satisfaction associated with smoking. The next slide referred to the effect of varenicline binding to the receptor and resulting in only a partial stimulation of dopamine release. The partial agonist action of varenicline was stated to provide relief from craving and withdrawal symptoms as the nicotine level declined in a quit attempt and by competing with nicotine to bind to the receptor it also reduced the pleasurable effects of smoking and potentially the risk of full relapse after a 'slip up'.

The next section of slides was entitled 'Varenicline Guidance, Efficacy and Safety Data'. This section included a slide headed 'Considerations for Prescribing Varenicline' which stated:

- **Depressed mood may be a symptom of nicotine withdrawal. Depression, rarely including suicidal ideation and suicide attempt, has been reported in patients undergoing a smoking cessation attempt, including those with varenicline. Treatment should be discontinued if these symptoms occur, or if agitation or changes in behaviour occur that are of concern to the clinician, patient, family or caregivers, or if the patient develops suicidal ideation or suicidal behaviour[1]**
- **The safety and efficacy of varenicline in patients with serious psychiatric illness has not been established[1]**
- **Prescribers should advise their patients with a history of psychiatric illness (e.g. depression) that stopping smoking may exacerbate their condition[1]**
- **No clinically meaningful drug-drug interactions[1]**
- **Stopping smoking can result in physiological changes that may alter the pharmacokinetics or pharmacodynamics of some medicinal products, for which dosage adjustment may be necessary (e.g. theophylline, warfarin and insulin)**

Reference 1 was to the Champix SPC and the slide recommended consulting the SPC before prescribing.

The Panel noted that Section 4.4 of the Champix SPC firstly referred to the emergence of significant depressive symptomatology including suicidal ideation in patients attempting to quit with Champix not all of whom had stopped smoking on the emergence of symptoms. Secondly, it was stated that depressed mood, rarely including suicidal ideation and suicide attempt might be a symptom of nicotine withdrawal and that smoking cessation with or without pharmacotherapy had been associated with exacerbation of underlying psychiatric illness eg depression. The slide

detailed above, however, referred to the general psychological effects of quitting first and then to the effects associated with Champix. In the Panel's view, although the slide clearly referred to the psychological side effects of Champix, by reversing the order of the information from the SPC it had subtly changed the emphasis and increased the importance of side effects associated with quitting in relation to those associated with Champix. The Panel considered that the slide should have presented the information in the same order as the SPC.

The Panel noted the representative's account stated that when using the slide described above, she focused on the safety of Champix and suicide ideation, the quotation being taken from the slide and primarily from Gunnell *et al* (2009). The representative showed and offered the audience a copy of Gunnell *et al* and quoted from the paper 'there is no causal link between Champix and suicide ideation, but there is between stopping smoking and suicide ideation'. The representative stated that she made a point of stating that if Champix patients exhibited mood changes or an increase in aggressive behaviour, therapy should be immediately withdrawn.

The Panel noted that it was difficult to be certain about what had been said at the meeting. Clearly it would be unacceptable to liken the side effects of taking Champix with the effects of stopping eating chocolate. It was extremely important that representatives gave clear information particularly when presenting to an audience which included non health professionals. The representative submitted that the analogy used with regard to chocolate was in relation to the reduced dopamine release brought about by Champix and not directly in relation to its side effects of low mood and suicidal ideation. It appeared that the reference to chocolate was the representative's own idea; no such analogy was in any of the slides or briefing material. The Panel noted that the complainant's colleague had linked the reduced dopamine release to the side effects seen with Champix and in that regard had likened the side effects of Champix to the representative's comments about chocolate. When referring directly to side effects the representative had cited Gunnell *et al* and in quoting that paper had stated 'there is no causal link between Champix and suicide ideation'. In the Panel's view this statement was not consistent with the particulars listed in the Champix SPC which stated that suicide ideation had been reported in post-marketing experience.

Overall, the Panel considered that on the balance of probabilities the representative had underplayed the psychological side effects seen with Champix therapy. Although the reference to chocolate was not directly in association with the side effects of the medicine, the link could nonetheless be made. In the Panel's view the reference to chocolate could imply that the severity of psychological side effects was much less than it was in reality. The Panel considered that the representative had been misleading about the side effects of Champix therapy and in that regard it ruled breaches of the Code. The Panel did not consider that the representative had maintained a high standard of ethical conduct. A further breach of the Code was ruled.

Upon appeal by Pfizer the Appeal Board noted the Panel's comments about the Champix SPC. In addition the Appeal Board noted that the SPC stated that in many post-marketing cases, but not all, symptoms of significant depression (agitation, depressed mood, changes in behaviour/thinking that were of concern or the development of suicidal ideation or behaviour) resolved after discontinuation of varenicline.

The Appeal Board noted that the representative had referred to Gunnell *et al* in her presentation and was concerned to note from Pfizer's representatives at the appeal that this paper had not been approved for promotional use. In quoting from the paper the representative had stated that 'there is no causal link between Champix and suicide ideation'. Gunnell *et al*, however, had stated 'There was no evidence that varenicline was associated with an increased risk of … suicidal thoughts …'. The authors found no clear evidence of an increased risk of self harm associated with varenicline compared with other products although the limited study power meant that they could not rule out either a halving or a twofold increase in risk. The Appeal Board was concerned that the representative had thus presented the absence of evidence of a link between Champix and suicidal ideation as evidence of absence of a link. Pfizer's representatives at the appeal submitted that no clinical trial had been designed to establish whether there was a causal link between Champix and suicidal ideation. The Appeal Board was also concerned about the slide headed 'Considerations for prescribing varenicline' (slide eleven of the representative's slide set) (used as the representative referred to Gunnell *et al*) and questioned whether it gave a balanced overview of Section 4.4 of the Champix SPC. In particular the Appeal Board noted the heading to the slide read 'Considerations for prescribing varenicline' whereas Section 4.4 of the SPC was headed 'Special warnings and precautions for use'. Overall, the Appeal Board considered that the representative's interpretation of Gunnell *et al* had underplayed and in that regard misled the audience about a potentially serious adverse effect of Champix. The Appeal Board upheld the Panel's rulings of breaches of the Code.

The Appeal Board noted that the representative said she had referred to chocolate when using the slide showing the mechanism of action of varenicline to illustrate the effect of dopamine levels on mood. The Appeal Board considered that the complainant's comments in relation to

underplaying the warnings about Champix had been addressed in its rulings above.

The Appeal Board noted its rulings but, nonetheless, decided that the representative had not failed to maintain a high standard of ethical conduct. No breach of the Code was ruled in this regard.

A primary care medical director complained about the conduct of one of two representatives from Pfizer Limited who attended a local smoking cessation meeting.

COMPLAINT

The complainant stated that a colleague and two representatives from Pfizer were present at a stop smoking training event in November 2010 and the presentation was to approximately 60 smoking cessation advisors, who were non-clinical non-prescribers.

One of the Pfizer representatives promoted Champix (varenicline) but part of the presentation underplayed the side effects of low mood and suicidal thoughts and attributed the suggested side effects to being similar to someone trying to stop eating chocolate. The complainant's colleague considered that the promotion of Champix had been unbalanced and the warnings attached to Champix had been grossly underplayed. He tried to make the point that chocolate did not come with a warning but that Champix did.

In general the complainant's colleague considered that it was grossly unprofessional to promote the medicine to such an impressionable audience, who did not have the knowledge to question the pharmaceutical representatives.

The complainant considered that the conduct of the representative fell outside the bounds of acceptable professional behaviour.

When writing to Pfizer, the Authority asked it to respond in relation to Clauses 2, 7.2, 7.9 and 15.2 of the Code.

RESPONSE

Pfizer stated that the representative was invited to participate in the meeting. The local stop smoking service coordinator and organiser of the meeting told the representative that she could deliver a presentation on Champix to an audience of smoking cessation advisors. This was an audience of health professionals and appropriate administrative staff with specific expertise in smoking cessation including the non-pharmacological and pharmacological management of smokers to support their quit attempts. The purpose of the meeting was to discuss a new patient health questionnaire, the 'PHQ-9 Mental Health questionnaire' which the smoking cessation advisors had to complete before referring patients to receive Champix.

For the meeting, the representative selected and presented 16 slides taken from the master certified slide deck 'Smoking cessation and varenicline' (ref CHA841). The selected slides were considered appropriate for the specific audience and were unchanged from those of the master slide deck. The information contained in the slides presented was accurate and balanced. Copies of the presentation and of the master slide deck were provided.

Relevant to the topic of the meeting, Pfizer provided a copy of a comprehensive safety briefing document for the field force, 'Guidance on promotional activity for Champix (varenicline tartrate) in mental health' (ref CHA743). Pfizer submitted that the briefing document set out clear information for representatives about psychiatric and behavioural disorders and varenicline use. The slides headed 'Considerations for Prescribing Varenicline' dealt with these considerations and also referred the audience to the summary of product characteristics (SPC) before prescribing.

Those attending the meeting were trained smoking cessation advisors and included practice nurses, healthcare assistants, pharmacy technicians, school health workers/nurses and healthcare trainers. Two GPs also attended. An email from the meeting organizer confirmed that the audience had expertise in smoking cessation and had been trained to provide information on all stop smoking medicines. Copies of the emails were provided.

The presentation included slides headed 'The α4β2 Nicotinic Receptor is Key in the Addiction Pathway' and 'Varenicline: A Dual Mode of Action at the α4β2 Nicotinic Receptor' which discussed the mechanism of action of nicotine in the brain, in particular at the α4β2 nicotinic receptor and the physiological and psychological effects associated with the release of dopamine. The latter slide described the effect that varenicline had when it bound to the α4β2 nicotinic receptor and how this might help with symptoms of nicotine withdrawal and also reduce the rewarding effects of nicotine if a patient smoked whilst taking varenicline. In order to illustrate the association of dopamine release with pleasurable sensations, the representative used an analogy with a range of pleasurable external stimuli including eating chocolate. Her use of this analogy was not an attempt to link chocolate and Champix let alone to link any neuropsychiatric side effects of not eating chocolate to those of Champix.

The presentation at issue included a slide detailing the neuropsychiatric warnings and precautions from the Champix SPC and others which discussed the dosing of varenicline and the varenicline treatment course. The final slide was the Champix prescribing information.

Following the presentation, the representative heard that a member of the audience was concerned with the chocolate analogy used to

illustrate the association of dopamine release from nicotine and so she asked the meeting organiser if there was a need for clarification for the audience. In the organiser's view nothing misleading had been presented and there was no need for clarification. Furthermore, no other member of the audience had raised any concern.

In consideration of the above, Pfizer believed that no misleading information, claims or comparisons were made by the representative; the representative conducted herself in a professional and ethical manner and high standards were met. Pfizer thus denied breaches of Clauses 2, 7.2, 7.9 or 15.2. The representative, and her Pfizer colleague who also attended the meeting, had both passed the ABPI Medical Representatives Examination.

In response to a request for further information Pfizer stated that the presentation at issue was also the training presentation for representatives. There was no separate briefing document covering the training slide set.

PANEL RULING

The Panel noted that the complainant had not attended the meeting at issue but had complained on behalf of a colleague who had. The purpose of the meeting was to discuss a new patient mental health questionnaire which smoking cessation advisors had to complete before referring smokers for Champix therapy. Not all of the attendees at the meeting were health professionals but they had all been trained to level 2 by the local NHS Stop Smoking Service to provide information on all stop smoking medicines. The Panel considered that in these circumstances it was not unreasonable to give clinical information about Champix. The information had to be tailored towards the audience and otherwise comply with the Code. The representative had selected 16 slides which she considered were appropriate for the audience. In the Panel's view it could be difficult when presenting to a mixed audience to ensure that no-one was misled. It was particularly important not to mislead with regard to side-effects.

The Panel examined the slides used at the meeting. One slide depicted nicotine binding to the α4β2 nicotinic receptor and thus stimulating dopamine release which resulted in the satisfaction associated with smoking. The next slide referred to the effect of varenicline binding to the receptor and resulting in only a partial stimulation of dopamine release. The partial agonist action of varenicline was stated to provide relief from craving and withdrawal symptoms as the nicotine level declined in a quit attempt and by competing with nicotine to bind to the receptor it also reduced the pleasurable effects of smoking and potentially the risk of full relapse after a 'slip up'.

The next section of slides was entitled 'Varenicline Guidance, Efficacy and Safety Data'. This section included a slide headed 'Considerations for Prescribing Varenicline' which stated:

- Depressed mood may be a symptom of nicotine withdrawal. Depression, rarely including suicidal ideation and suicide attempt, has been reported in patients undergoing a smoking cessation attempt, including those with varenicline. Treatment should be discontinued if these symptoms occur, or if agitation or changes in behaviour occur that are of concern to the clinician, patient, family or caregivers, or if the patient develops suicidal ideation or suicidal behaviour[1]

- The safety and efficacy of varenicline in patients with serious psychiatric illness has not been established[1]

- Prescribers should advise their patients with a history of psychiatric illness (e.g. depression) that stopping smoking may exacerbate their condition[1]

- No clinically meaningful drug-drug interactions[1]

- Stopping smoking can result in physiological changes that may alter the pharmacokinetics or pharmacodynamics of some medicinal products, for which dosage adjustment may be necessary (e.g. theophylline, warfarin and insulin)

Reference 1 was to the Champix SPC and the slide recommended consulting the SPC before prescribing.

The Panel noted that Section 4.4 of the SPC firstly referred to the emergence of significant depressive symptomatology including suicidal ideation in patients attempting to quit with Champix not all of whom had stopped smoking on the emergence of symptoms. Secondly, it was stated that depressed mood, rarely including suicidal ideation and suicide attempt might be a symptom of nicotine withdrawal and that smoking cessation with or without pharmacotherapy had been associated with exacerbation of underlying psychiatric illness eg depression. The slide detailed above, however, referred to the general psychological effects of quitting first and then to the effects associated with Champix. In the Panel's view, although the slide clearly referred to the psychological side effects of Champix, by reversing the order of the information from the SPC it had subtly changed the emphasis and increased the importance of side effects associated with quitting in relation to those associated with Champix. The Panel considered that the slide should have presented the information in the same order as the SPC.

The Panel noted that in the representative's account of the meeting, she had stated that when she used the slide described above, she focused on the safety of Champix and suicide ideation, the quotation being taken from the slide and primarily from Gunnell *et al* (2009). The representative

showed and offered the audience a copy of Gunnell *et al* and quoted from the paper 'there is no causal link between Champix and suicide ideation, but there is between stopping smoking and suicide ideation'. The representative stated that she made a point of stating that if Champix patients exhibited mood changes or an increase in aggressive behaviour, therapy should be immediately withdrawn.

The complainant had alleged that part of the presentation underplayed the side effects of low mood and suicidal thoughts attributing the suggested side effect to being similar to someone trying to stop eating chocolate. It was alleged that the promotion of Champix had been unbalanced and the associated warnings grossly underplayed. The colleague attending the meeting had tried to make the point that chocolate did not come with a warning whereas Champix did.

The Panel noted that it was very difficult to be certain about precisely what had been said at the meeting. Clearly it would be unacceptable to liken the side effects of taking Champix with the effects of stopping eating chocolate. It was extremely important that representatives gave clear information particularly when presenting to an audience which included non health professionals. The representative submitted that the analogy used with regard to chocolate was in relation to the reduced dopamine release brought about by Champix and not directly in relation to its side effects of low mood and suicidal ideation. It appeared that the reference to chocolate was the representative's own idea; no such analogy was in any of the slides or briefing material. The Panel noted that the complainant's colleague had linked the reduced dopamine release to the side effects seen with Champix and in that regard had likened the side effects of Champix to the representative's comments about chocolate. When referring directly to side effects the representative had cited Gunnell *et al* and in quoting that paper had stated 'there is no causal link between Champix and suicide ideation'. In the Panel's view this statement was not consistent with the particulars listed in the Champix SPC which stated that suicide ideation had been reported in post-marketing experience.

Overall, the Panel considered that on the balance of probabilities the representative had underplayed the psychological side effects seen with Champix therapy. Although the reference to chocolate was not directly in association with the side effects of the medicine, the link could nonetheless be made. In the Panel's view the reference to chocolate could imply that the severity of psychological side effects was much less than it was in reality. The Panel considered that the representative had been misleading about the side effects of Champix therapy and in that regard it ruled breaches of Clauses 7.2 and 7.9. The Panel did not consider that the representative had maintained a high standard of ethical conduct. A breach of Clause 15.2 was ruled.

The Panel noted its rulings above and considered that the representative's conduct was not such as to reduce confidence in, or bring disrepute upon, the industry. No breach of Clause 2 was ruled.

APPEAL BY PFIZER

Pfizer noted that this case arose from a meeting of a local smoking cessation service. The purpose of the meeting was to discuss the new PHQ-9 mental health questionnaire which smoking cessation advisors had to complete before they referred patients to receive Champix. The representative was invited to speak about Champix; other companies were also invited to participate and discuss their own products. Those attending the meeting were trained smoking cessation advisors including practice nurses, health assistants, pharmacy technicians, school health workers/nurses and health trainers. Two GPs also attended.

Pfizer submitted that at the meeting, the representative presented from the certified slide deck 'Smoking cessation and varenicline'. The representative presented sixteen slides which were taken from the master slide deck and these were considered appropriate for the specific audience. The focus of this presentation was the importance of smoking cessation, the mode of action of varenicline, how to prescribe varenicline and safety considerations, including warnings, precautions and drug interactions.

The slides discussed the mechanism of action of nicotine in the brain and the physiological and psychological effects associated with dopamine release. To help explain to the audience the pleasurable sensation created by dopamine release from smoking, an analogy was used to compare smoking with shopping, sex and eating chocolate. No link was made between chocolate and any medicine. The presentation went on to describe the dual mode of action of varenicline at the nicotinic receptor, and how this might help with symptoms of nicotine withdrawal (such as cravings) and also reduce the rewarding effects of nicotine if a cigarette was smoked during varenicline use.

The representative then presented 'Considerations for Prescribing Varenicline'; the slide included details of the Champix indication and contraindications and the statement 'Refer to the full Summary of Product Characteristics before prescribing'. The following slide detailed relevant safety information, warnings and precautions and interactions with other medicinal products. It stated 'Depressed mood may be a symptom of nicotine withdrawal. Depression, rarely including suicidal ideation and suicide attempt, has been reported in patients undergoing a smoking cessation attempt, including those with varenicline. Treatment should be discontinued if these symptoms occur, or if agitation or changes in behaviour occur that are of concern to the

clinician, patient, family or caregivers, or if the patient develops suicidal ideation or suicidal behaviour. The safety and efficacy of varenicline in patients with serious psychiatric illness has not been established. Prescribers should advise their patients with a history of psychiatric illness (eg depression) that stopping smoking may exacerbate their condition'. This slide also had the statement 'Refer to the full Summary of Product Characteristics before prescribing'. The representative went on to discuss dosing guidance for Champix and the treatment course. The final slide was of the prescribing information.

Pfizer submitted that following the presentation, the representative became aware that a member of the audience was concerned with the chocolate analogy used to illustrate the association of dopamine release with pleasurable sensation. In response to this the representative asked the meeting organizer if there was a need for clarification for the audience. However, the organiser's view was that nothing misleading had been presented and therefore there was no need for clarification. Furthermore, no other member of the audience had raised any concern.

Pfizer noted that the complainant had not been at the meeting in question, but was writing on behalf of a colleague who had. The complaint was therefore not a first-hand account of what was presented at the meeting. The colleague who attended the meeting had not submitted a written complaint.

Pfizer noted that the Panel had noted that Section 4.4 of the SPC firstly referred to neuropsychiatric symptoms reported in post-marketing experience and secondly, symptoms associated with nicotine withdrawal with or without pharmacotherapy. The Panel also noted that the presentation referred to the general psychological effects of nicotine withdrawal first and then to the events reported in the post-marketing experience and considered that by reversing the order of this, it changed the emphasis and increased the importance of side effects associated with smoking cessation compared with those associated with varenicline. The Panel considered that the presentation should have discussed the information in the same order as the SPC.

Pfizer submitted that Section 4.4 of the SPC should be considered in its entirety and that the order of presenting the information did not emphasise one part over another. It was unreasonable to expect that, in a presentation about smoking cessation and the role of varenicline, the neuropsychiatric adverse events and varenicline should be discussed before the neuropsychiatric effects associated with smoking cessation overall. A significant body of evidence showed that smokers generally had a higher incidence of neuropsychiatric symptoms compared with non smokers and that smoking cessation itself, regardless of pharmacological intervention, could be associated with such symptoms. It seemed reasonable to present this context before discussing the safety profile of varenicline. In addition Pfizer noted that post-marketing experience of adverse events did not imply causality. Importantly no causal relationship had been established between varenicline and neuropsychiatric events. The representative very clearly presented and emphasised the warnings and precautions associated with Champix in Section 4.4 of the SPC, and the conditions under which treatment should be discontinued. Therefore it was not the case that greater importance was placed on any particular section of the SPC. The information was presented in its entirety, was accurate, balanced, and was not misleading.

Pfizer noted that the allegation that part of the presentation underplayed the side effects of varenicline, attributing the side effects to being similar to those that might occur when stopping eating chocolate. The Panel noted that it was difficult to be certain about precisely what had been said in the meeting. Pfizer submitted that it was difficult for the complainant as they were not at the meeting. However, Pfizer was clear that no comparison was made between the side effects of varenicline and stopping eating chocolate. In fact there was no link between chocolate and any pharmacological treatment. The analogy with chocolate (as another addictive substance) was simply to help explain the pleasurable sensation caused by dopamine release.

Pfizer submitted that this was an individual misunderstanding on the part of the complainant's colleague regarding the representative's presentation. Pfizer emphasised that the presentation contained a large amount of clear and detailed safety information from the Champix SPC. Furthermore, once the representative knew that one of the attendees might have misinterpreted what she had said, she offered to provide immediate clarification but was advised by the meeting organiser that her presentation was not misleading and therefore further clarification was not required. Confirmation of Pfizer's view could be sought from the meeting organiser and any of the other attendees at the meeting.

Pfizer noted that, in the Panel's view, reference to Gunnell *et al*, which analysed safety data from the UK General Practice Research Database (GPRD) database and could not demonstrate a causal link between varenicline and neuropsychiatric events, was not consistent with the particulars listed in the SPC. Pfizer emphasised that no causal link between the use of varenicline and neuropsychiatric events had been established, therefore the findings from Gunnell *et al* were consistent with the particulars of the SPC, which itself did not attribute any causal relationship with varenicline. As previously stated, post-marketing experience did not imply causality.

Pfizer submitted that in addition to Gunnell *et al*, no clinical trials or meta-analyses in the varenicline clinical programme had demonstrated a causal link between varenicline and neuropsychiatric events, and yet it would not be logical to dis-allow presentation of the safety information from this clinical data in promotional material on the basis that it did not demonstrate causality. The representative gave a balanced presentation. She discussed Gunnell *et al* and she presented the warnings and precautions from the SPC. She did not do one without the other. As there was no causal link within the SPC, the clinical data she presented was consistent with the SPC.

As explained above, Pfizer submitted that all information, claims and comparisons were accurate, balanced, fair, objective and unambiguous, based on an up-to-date evaluation of all evidence and reflected that evidence clearly. The representative had not misled the audience about the side effects of Champix and indeed reflected the particulars of the SPC throughout the meeting. Pfizer denied breaches of Clauses 7.2 and 7.9.

As evident from the accounts provided, Pfizer submitted that the representative conducted herself in a professional and ethical manner and that high standards were maintained before, during and after the meeting. Pfizer denied a breach of Clause 15.2.

In summary, Pfizer submitted that the Panel's rulings appeared to be based on comments made by an individual who was not at the meeting and the actual attendee had not submitted a written complaint. Pfizer provided the Panel with evidence of the slides presented and the representative's account of the discussions that took place. No link was made by the representative between eating chocolate and Champix. The presentation clearly discussed the safety profile, warnings and precautions for Champix as described in the SPC and was consistent with the SPC. The representative offered, at the time, to clarify any points that might have been misinterpreted by an individual attendee but this was not considered necessary. For the reasons stated above Pfizer submitted that the rulings of breaches of Clauses 7.2, 7.9 and 15.2 were unwarranted.

COMMENTS FROM THE COMPLAINANT

The complainant accepted Pfizer's assertion that he was not present at the meeting in question, however this matter was brought to his area prescribing committee as there were concerns about the way the presentation had represented Champix.

The complainant noted that the audience had two GPs who were the only prescribers. The rest were a mixture of non-clinical and nursing advisors, all of whom guided patients through the process of stopping smoking. The area prescribing committee considered that to mention chocolate that had no licence for prescribing, and Champix, a licensed medicine, in the same presentation seemed inappropriate. It potentially gave non-prescribers a false impression.

The complainant noted that the sole intention of the area prescribing committee was to draw this to the attention of the industry, to prevent this possible conflict occurring in other areas, and not to impune the reputation of Pfizer.

APPEAL BOARD RULING

The Appeal Board noted the Panel's comments about the Champix SPC. In addition the Appeal Board noted that the SPC stated that in many post-marketing cases, but not all, symptoms of significant depression (agitation, depressed mood, changes in behaviour/thinking that were of concern or the development of suicidal ideation or behaviour) resolved after discontinuation of varenicline.

The Appeal Board noted that the representative had referred to Gunnell *et al* in her presentation and was concerned to note from Pfizer's representatives at the appeal that this paper had not been approved for promotional use. In quoting from the paper the representative had stated that 'there is no causal link between Champix and suicide ideation'. Gunnell *et al*, however, had stated 'There was no evidence that varenicline was associated with an increased risk of … suicidal thoughts …'. The authors found no clear evidence of an increased risk of self harm associated with varenicline compared with other products although the limited study power meant that they could not rule out either a halving or a twofold increase in risk. The Appeal Board was concerned that the representative had thus presented the absence of evidence of a link between Champix and suicidal ideation as evidence of absence of a link. Pfizer's representatives at the appeal submitted that no clinical trial had been designed to establish whether there was a causal link between Champix and suicidal ideation. The Appeal Board was also concerned about the slide headed 'Considerations for prescribing varenicline' (slide eleven of the representative's slide set) (used as the representative referred to Gunnell *et al*) and questioned whether it gave a balanced overview of Section 4.4 of the Champix SPC. In particular the Appeal Board noted the heading to the slide read 'Considerations for prescribing varenicline' whereas Section 4.4 of the SPC was headed 'Special warnings and precautions for use'. Overall, the Appeal Board considered that the representative's interpretation of Gunnell *et al* had underplayed and in that regard misled the audience about a potentially serious adverse effect of Champix. The Appeal Board upheld the Panel's rulings of breaches of Clauses 7.2 and 7.9. The appeal on these points was unsuccessful.

The Appeal Board noted that the representative said she had referred to chocolate when using the slide showing the mechanism of action of varenicline to illustrate the effect of dopamine levels on mood. The Appeal Board considered that the complainant's comments in relation to underplaying the warnings about Champix had been addressed in its rulings above.

The Appeal Board noted its rulings but, nonetheless, decided that the representative had not failed to maintain a high standard of ethical conduct. No breach of Clause 15.2 was ruled. The appeal on this point was successful.

Complaint received	**23 December 2010**
Case completed	**16 May 2011**