CASE AUTH/2943/3/17

EX-EMPLOYEE OF A SERVICE PROVIDER v BAYER

Conduct of employee and training material

An ex-employee of a service provider to Bayer plc complained about the conduct of a named Bayer employee, at an initial training course for Xarelto held in 2017.

Xarelto 10mg was indicated for the prevention of venous thromboembolism (VTE) in adults undergoing elective hip or knee replacement surgery. The 15mg and 20mg presentations were, *inter alia*, indicated for the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) and for the prevention of recurrent DVT and PE.

The complainant's first concern was that the employee encouraged sales trainees to promote Xarelto for an off-licence indication.

The complainant explained that one of the questions in a revision quiz concerned the licensed indication as per the summary of product characteristics (SPC). The attendees were asked to select from a choice of four, an indication not on the SPC as a licensed indication. The Bayer employee told the class that of the four choices, only 'active cancer' was not licensed. Unfortunately, one of the choices was 'prevention of DVT following hip fracture surgery'. It was brought to the Bayer employee's attention that Xarelto was also not licensed for this indication. This was refuted by the employee who stated that Xarelto was licensed for this indication. The complainant referred to the SPC (Section 4.4, special warnings and precautions for use)' which read: 'Hip fracture surgery Rivaroxaban had not been studied in interventional clinical trials in patients undergoing hip fracture surgery to evaluate efficacy and safety'. The following day, the question was still included in the final examination in the same format. The complainant alleged that it was firmly emphasized to the trainees that Xarelto should be promoted for the use in fracture surgery.

The complainant was further concerned that the employee had encouraged a disrespectful and unprofessional attitude towards clinicians and this would encourage impressionable trainees to also treat clinicians with similar disrespect.

The detailed response from Bayer is given below.

The Panel noted that the parties' accounts differed; it was difficult in such circumstances to determine precisely what had happened. A judgement had to be made on the available evidence whilst noting that the complainant bore the burden of proof and had to establish his/her case on the balance of probabilities.

The Panel considered that the revision quiz was part of the representatives' briefing material. The revision quiz question asked participants to select an indication not on the Xarelto SPC from a selection of four. The complainant gave 'active cancer' as the answer given by the employee who denied stating that only active cancer was not licensed. The complainant noted one of the choices was 'Prevention of DVT following hip fracture surgery' for which Xarelto was not licensed. Bayer stated that this was a verbal quiz and there were no documents to confirm. Nonetheless there was general agreement in the interview transcripts that at the very least this matter had been raised and discussed.

The Panel noted that the complainant was incorrect in stating that the same question in relation to hip fracture surgery was included in the written formal assessment. However a similar answer 'Prevention of VTE following hip fracture surgery' was one of the four possible answers. In that regard the Panel noted the error pointed out by Bayer in that the answer sheet gave 'Treatment of acute DVT in a patient with severe renal impairment' as the answer to the question 'Which of these is not an indication for Xarelto?'. The correct answer should have been 'Prevention of VTE following hip fracture surgery'. In addition, the Panel noted that 'active cancer' was not one of the possible answers to the question about Xarelto's licensed indications.

The Panel did not agree that 'Prevention of VTE following hip fracture surgery was contraindicated as submitted by Bayer. The indications in the SPC for Xarelto 10mg were clear as prevention of VTE in elective hip or knee surgery. Section 4.4 special warnings and precautions for use stated that rivaroxaban had not been studied in interventional trials in patients undergoing hip fracture surgery to evaluate efficacy and safety.

It appeared from the interview transcripts that the attendees understood that products should not be promoted for unlicensed indications. It was questionable whether the licensed indications for Xarelto were made clear. It appeared that the discussion about off-label use added to the confusion. The interview transcripts showed that not all were absolutely clear about whether Xarelto could be promoted for prevention of VTE following hip fracture surgery. In addition the interview transcript of the Bayer employee in question showed a degree of confusion about the treatment of acute DVT in patients with severe renal impairment which was mistakenly recorded as the correct answer in the quiz answer sheet. This was compounded by the marking scheme for the formal assessment which referred to the use of Xarelto in hip fracture surgery as contraindicated rather than unlicensed. The Panel was particularly concerned that of the completed quiz papers provided, not one representative gave prevention of VTE following hip fracture surgery as the correct answer. In the Panel's view, this indicated that the training on the point was unclear.

The Panel considered that despite its serious concerns outlined above the complainant had not provided any evidence to show that an unlicensed indication had been promoted to health professionals so the Panel ruled no breach of the Code. The Panel considered that the assessment was not clear with regard to the licensed indications. Bayer acknowledged that there was some confusion regarding the licensed indications. The briefing materials supplied by Bayer used at the training were not clear about the licensed indications, for example data relating to VTE prevention in orthopaedic surgery was described as a licensed indication, and this was compounded by the assessment. The Panel therefore ruled breaches of the Code including that high standards had not been maintained. On balance, the Panel considered that the circumstances brought discredit upon, and reduced confidence in, the pharmaceutical industry. The Panel therefore ruled a breach of Clause 2 which was a sign of particular censure and reserved for such use.

The Panel noted that there was a difference of opinion with regard to whether the employee referred to the clinicians as stupid or the question as stupid. There was no evidence that such language had been used with health professionals or in response to their questions. The Panel considered that the matter of how representatives were to answer questions from health professionals should have been dealt with more professionally at the training as it might impact subsequent behaviours with health professionals etc. The discussions on these points at the company training event did not amount to a disparagement of clinicians, or their views. No breaches of the Code were ruled.

An ex-employee of a third party which provided services to Bayer plc, complained about the conduct of a named employee, at an initial training course for Xarelto held in 2017.

Xarelto 10mg was indicated for the prevention of venous thromboembolism (VTE) in adults undergoing elective hip or knee replacement surgery. The 15mg and 20mg presentations were, *inter alia*, indicated for the treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE) and for the prevention of recurrent DVT and PE.

COMPLAINT

The complainant's first concern was that the employee encouraged sales trainees to promote Xarelto for an off-licence indication.

The complainant explained that at the end of the course a quiz as revision for the final examination had been held. One of the questions concerned the licensed indication as per the summary of product characteristics (SPC). Attendees were asked to select from a choice of four, an indication not on the SPC as a licensed indication. The employee told the class that of the four choices, only 'active cancer' was not licensed. Unfortunately, one of the choices was 'prevention of DVT following hip fracture surgery'. It was brought to the employee's attention that Xarelto was also not licensed for this indication. This was refuted and attendees were informed that Xarelto was licensed for this indication. Although when shown the relevant part of the SPC (Section 4.4, special warnings and precautions for use)' which read: 'Hip fracture surgery Rivaroxaban had not been studied in interventional clinical trials in patients undergoing hip fracture surgery to evaluate efficacy and safety', the employee insisted that Xarelto had been actively promoted for that indication for the last 10 years. The following day, the question was still included in the final examination in the same format. The employee insisted that marks be awarded according to his/her opinion, which firmly emphasized to the trainees that Xarelto should be promoted for the use in fracture surgery.

The complainant alleged a breach of Clauses 3 and 2 of the Code and noted that the examination papers were collected and held by Bayer.

The complainant was further concerned that the employee had encouraged a disrespectful and unprofessional attitude towards clinicians. The complainant explained that during the course, several trainees raised concerns regarding customer enquiries which they found difficult to manage. As they tried to raise the subject (genuine and frequent customer concerns regarding the safety of the product due to its half-life vs other agents in the same class) the employee shouted 'irrelevant' over their voices and even picked up one student's notes and threw them across the class. The class was told that when a clinician asked that question, the employee told them that they were 'stupid'. The complainant was concerned that this behaviour would encourage impressionable trainees to also treat clinicians with similar disrespect.

When writing to Bayer, the Authority asked it to consider the requirements of Clauses 8.2, 9.1, 15.2 and 15.9 in addition to Clauses 3.2 and 2 as cited by the complainant.

Further information was received from the complainant who stated that he/she was not able to supply documentary evidence of some of the behaviours as these were made verbally and relied on witness statements which he/she was not in a position to gather. However, the complainant stated that one of his/her complaints was the repeated assertion that Xarelto (rivaroxaban) was licensed and should be promoted for prevention of VTE post hip fracture surgery. Despite a challenge to this view, including showing the relevant part of the SPC, (section 4.4), the employee insisted that this was correct and included this indication in the final written examination.

The complainant provided a copy of his/her written examination as proof (question 15), which was marked as correct, but which he/she alleged was in fact incorrect. The complainant also provided a copy of the Xarelto SPC.

The complainant further stated that the employee asserted both verbally and in the written examination, that trainees should promote Xarelto

for prevention of VTE after hip fracture surgery. The complainant believed that this constituted an endorsement to promote off licence.

RESPONSE

Bayer explained that the residential course was organised to train contract sales representatives on Xarelto.

Bayer stated that the complainant in this case also complained via its Compliance Hotline. Bayer stated that this contained exactly the same matters as those cited in the complaint and three additional matters, (details were provided).

Bayer stated that it took the complainant's allegations very seriously and had carried out a detailed investigation including conducting interviews through external lawyers, with the employee and participants.

The training materials used during the course

Certification status of training materials

Bayer stated that it had reviewed the training materials used during the course and it became clear that a PowerPoint presentation entitled 'VTE Training' used for internal training courses, and a quiz used to measure performance at the end of the course, together with the relevant answers attached (copies of all materials provided) were not appropriately certified as required by Bayer's standard operating procedure (SOP) 105 'Certification of Promotional Items, Non-Promotional Items and Activities'.

Bayer explained that the employee was appointed to his/her current role in training in 2016 following the retirement of an independent contractor who was previously an employee of Bayer.

The relevant SOP required that the project owner (the person responsible for the relevant material or activity) should create a job bag for each relevant item in order to ensure that this was assessed for Code compliance. All promotional material must be certified prior to first use and then recertified at least every two years or withdrawn. Material which had been certified was marked with a footer which confirmed its status. The position with respect to the PowerPoint slides and the VTE quiz and answers was as follows:

- The 'VTE Training' slides were certified in March 2013 for external training of health professionals. This slide deck was amended intermittently for internal training of the field force; these changes and the new purpose for which the slides were to be used were, seemingly, not certified. There was, however, substantial overlap between the slides certified in 2013 and the slides used on the course. The slides were certified by Bayer in April 2017, without amendment, following this complaint, confirming that there was no error or deficiency in the information presented by the employee.
- A quiz and answers ('the certified quiz') used for the purposes of course validation following training on VTE and Xarelto was certified in February 2016. The VTE quiz and answers used for the purposes of the course was a variation of the certified quiz (approximately 50% of the questions were the same) however it was not certified as required by the SOP and Clauses 14.1 and 15.9 of the Code. The VTE quiz and answers had now been certified (subject to revision to the answer to Q15, see below).

Bayer stated that it had investigated how non-certified materials came to be used on the course, contrary to the SOP and the Code and despite the extensive training provided to all relevant staff, including the employee (who had undergone some 26 training courses on Bayer SOPs and Code compliance matters over the past three years) and had confirmed that he/she was fully aware of the content of the SOP and the requirements of the Code.

The employee had been briefed by the independent contractor in relation to the role and, during a handover meeting in June 2016, passed on the materials used for various training exercises, including slide decks and quizzes that could be used for validation. The only product related materials passed on which had been subsequently used by the employee, related to internal training on Xarelto and VTE or stroke prevention and atrial fibrillation (SPAF). It was understood at the time of the handover that the material was certified, although it would require recertification in due course in accordance with Bayer's procedures and the Code. While the employee accepted that he/she should have been alerted to the fact that this was not necessarily the case as a result of the absence of 'certification footers' on the materials, this was overlooked as a result of naivety.

The independent contractor had provided Bayer with a set of the training material provided to the employee in relation to VTE and SPAF. In addition to the PowerPoint slides and the VTE quiz and answers and the certified quiz referenced above, Bayer had identified the following:

i) Internal training course slides entitled 'SPAF Training' (copy provided) prepared by the independent contractor and originally certified in February 2014 for both training of health professionals and of the field force. Bayer now understood that the independent contractor amended the SPAF slide deck intermittently and these changes were, seemingly, not certified. There was, however, substantial overlap between the slides certified in 2014 and the 'SPAF Training' slide deck as provided by the independent contractor which was currently undergoing certification by Bayer.
ii) Six SPAF internal training course final quizzes and answers; two of these had been certified in 2013, one had been certified in 2016 and four had not been certified. The format of these documents was the same. All of the SPAF quizzes and answers which had not previously been certified, had been certified in April 2017: For all of the quizzes and answers, which had undergone certification, minor updates were required, to reflect changes in the price of Xarelto

over time and in relation to the quizzes and answers, some of the questions listed in the quiz document were different from the equivalent questions and answers in the answer sheet or the questions were presented in a different order or other minor changes were needed. Most of the changes reflected the fact that some amendment of the document had been made that had not been fully incorporated. These matters had now been addressed. The quizzes and answers which were previously certified in 2013 were currently undergoing recertification; the quiz and answers certified in February 2016 did not require recertification until February 2018.

iii) Five further VTE internal training course final quizzes and answers which all represented variations on the certified quiz but contained additional questions. Two of these had been certified in 2013 and three had not been certified. The format of these documents was the same as that for the SPAF quizzes and answers. All of the quizzes and answers which had not previously been certified, had been certified in April 2017. For all of these quizzes and answers, minor updates were needed on certification to reflect changes in price of Xarelto over time; As with the SPAF quizzes and answers, for certain of the quizzes and answers, some of the questions listed in the quiz document were different from the equivalent questions and answers in the answer sheet or the questions were presented in a different order or other minor changes were needed. Most of the changes reflected the fact that some amendment of the document had been made that had not been fully incorporated. These matters had now been addressed. The quizzes and answers which were previously certified in 2013 were currently undergoing recertification.

Actions taken by Bayer to reinforce certification requirements for internal training materials and to address the situation following its investigation of the materials used

Bayer stated that it had taken the following actions in relation to the complaint and, in particular, the failures noted above to certify certain materials used for internal training courses:

- As well as interviews with participants on the course, Bayer's investigation confirmed that no member of its training team, other than the employee, had used non-certified materials for training.
- No amendment to the PowerPoint slides used had been required as a result of the certification in April 2017; this confirmed that the internal training provided in accordance with this material was correct.
- Out of an abundance of caution, Bayer would introduce online validation tests for the full field force, to confirm that they all had correct and up-to-date knowledge about Xarelto; those who did not obtain a satisfactory validation score would have further training.
- Details of actions taken regarding the employee were provided which included reinforcing knowledge and understanding of the requirements of the Code and Bayer's SOPs.
- A training log had been created to capture every training intervention (dates, materials used, trainer) and all training materials (owner, date of certification, date due for recertification) as a way to ensure that all training materials were appropriately certified in the future. A copy of the log was provided.

Members of the training team were reminded by email on 12 and 19 April 2017 of the need to ensure that they were up-to-date with all Bayer SOPs and they were asked to reread the SOP which dealt with the Code and training; each had to confirm that they had read the email. The head of sales and marketing training had also met with the Bayer training team to reinforce, in person, the email of 12 April 2017 and the requirement to comply with Bayer SOPs and the Code. Attendance at this meeting was recorded and all non-attendees had been followed up on an individual basis.

Conclusion

The failure to use only currently certified material during the course was not consistent with the SOP and the associated training provided by Bayer to the relevant staff. In addition, Bayer accepted that use of the PowerPoint slides and the VTE quiz and answers at the course did not comply with Clauses 15.9 or 14.1 of the Code.

Bayer submitted that its thorough investigation had confirmed the source and extent of these omissions and that it had acted quickly to address the errors by the three individuals concerned and to reinforce its SOPs and the requirements of the Code with all of the training team.

Response to the specific issues raised by the complainant

Bayer stated that its response to the matters raised by the complainant were based on its review of the limited documentation available (the training materials used for the course), the interviews including with some of course participants, selected because they were involved in the incidents mentioned in the complaint. Bayer had additionally tried, without success, to speak to staff at the venue. Bayer further stated that its ability to investigate these matters had been prejudiced by the delay of over about a month, between the conclusion of the course and the complaint to PMCPA.

1 Alleged promotion of an off-licence indication for Xarelto

Bayer stated that its investigation did not indicate that the employee advised trainees that Xarelto should be promoted for an off-label indication.

Revision session

The practice questions used during the revision session and referenced by the complainant were verbal and there were no documents to confirm the questions or the answers proposed to the course participants. However investigations indicated that the content of the session included the following:

- The quiz included a question on the licensed indications for Xarelto with four possible answers. One of the possible answers was 'active cancer'.
- The employee explained that some clinicians would use the product off-label and representatives needed to be aware of this. In addition there seemed to have been discussion regarding different licensed indications in other countries.
- There were several discussions between the employee and the complainant about the licensed indications for Xarelto. These appear to have taken place while course participants were considering the questions in teams; the employee and some trainees stated that the discussions did not involve the class whereas others stated that the wider group did participate. The precise nature of these discussions was unclear, however it seemed that they involved the complainant and the employee reviewing the Xarelto SPC.
- There was no support from course participants for the allegation that the employee advised the class during the revision session that Xarelto had been actively promoted for 'prevention of DVT following hip fracture surgery' for 10 years and this was denied by the employee.
- All course participants confirmed that the employee stated unequivocally that off-label promotion was not permitted.
- The employee was quite clear as to the correct licensed indications for Xarelto.

Final quiz

Question 15 of the quiz used during the validation session at the end of the course addressed the licensed indications for Xarelto:

> 'Which of these is NOT an indication for Xarelto? (1)
> (a) prevention of VTE following total hip replacement:
> (b) secondary prevention of VTE after a PE
> (c) Prevention of VTE following hip fracture surgery
> (d) Treatment of acute DVT in a patient with severe renal impairment.'

The employee did not remain in the classroom throughout the quiz, but came in intermittently to confirm that there were no issues. The quiz was then marked by course participants (each one marking the quiz completed by another trainee) using the answers displayed on the screen.

The answer for question 15, noted that (c) Prevention of VTE following hip fracture surgery was 'contraindicated', but highlighted answer (d) as being correct.

- There was no evidence from the interviews conducted by Bayer that there was any discussion before the quiz regarding use of Xarelto for 'prevention of DVT following hip fracture surgery'.
- The questions administered during the quiz were not the same as those used during the revision session. In particular question 15 did not refer to 'active cancer' (an option given during the practice questions).
- The answer given to question 15 was incorrect. The correct answer should have been (c) consistent with the wording 'contraindicated' marked on the answer sheet. Xarelto was not indicated for the prevention of VTE following hip fracture surgery, but was indicated (with caution) for the treatment of acute DVT in patients with severe renal impairment, as long as creatinine clearance was ≥ 15 ml/min. During the course of the investigation the employee agreed that the original answer was incorrect.
- Bayer had identified completed quiz papers from the majority of attendees but had been unable to locate the remaining 7 quiz papers; it was unclear why these were not retained with the others. 14 of the quiz papers available to Bayer answered (d) to question 15 (ie an incorrect answer, but marked correct in accordance with the answers displayed on the screen). The final quiz paper did not include an answer to question 15. These answers showed confusion among course participants as to the licensed indication for Xarelto. This might have been a consequence of the previous day's discussion regarding the fact that some clinicians used Xarelto off-label for prevention of VTE in patients undergoing hip fracture surgery.

Overall conclusion

While there was clearly some confusion among course participants regarding the licensed indications for Xarelto, as demonstrated by the incorrect answers given to question 15 on the VTE quiz (not assisted by the error in the answers provided for marking purposes), this was likely to have resulted from the discussion the previous day on circumstances in which off-label use might be initiated by clinicians; there was no evidence that the employee advised trainees to promote an off-label indication contrary to Clause 3 of the Code. All course participants who were interviewed were clear that, while off-label use might occur, promotion of an unlicensed indication was prohibited.

Following notification of the complaint, the VTE quiz and answers had been certified as described above. No revision to the VTE quiz and answers was required as a result of certification save for question 15.

Xarelto was not actively promoted in orthopaedic surgery, however following certification of the VTE quiz and answers and in light of the answers given to question 15 following the course, Bayer had contacted the entire field force to ensure that it knew that Xarelto was not authorised for the prevention of VTE following hip fracture surgery.

2 Encouragement of a disrespectful and unprofessional attitude towards clinicians.

Bayer stated that based on its investigation, it believed that the complainant had misrepresented the employee's remarks and that a disrespectful or unprofessional attitude towards clinicians was not encouraged.

- This large group of 22 trainees included a range of experience levels. Trainees asked many questions

during the course and some of those asked by more junior participants were not relevant to the issues. While Bayer would support an interactive approach, there was a substantial amount of material to be covered during the time available and, in order to complete this, some discipline was required.
- Therefore the employee did characterise some of the more unlikely questions as 'irrelevant' in order to bring the class back to the point of the session and the employee did flick the papers of one trainee who asked such a question on the floor. These comments and actions were all undertaken in good humour and in a joking manner and, so far as Bayer was aware, no course participant took offence.
- The source and context of the 'stupid' comment was unclear. The course participants were generally unable to remember such a statement or denied that any such statement has been made. One participant stated that the employee had advised trainees in the context of 'how much' food should be taken with Xarelto, that if a clinician kept on asking a question after they had answered it, they should not 'dwell on it'. The participant did not understand that the employee had stated that doctors were 'stupid' and did not consider that trainees were being advised to treat clinicians disrespectfully.

In summary, therefore, the interviews with course participants provided no evidence that the employee encouraged a disrespectful or unprofessional attitude towards clinicians. There was no disparagement of clinicians or of their views contrary to Clause 8.2 of the Code. There was, in any event, no evidence that the employee's attitude towards clinicians failed to maintain high standards as required by Clause 9.1.

Overall conclusion

Bayer stated that its investigation of this complaint had revealed that the PowerPoint slides and VTE quiz and answers used for the training and validation of representatives, had not been certified in accordance with the Code, even though a substantially similar version of the quiz had been certified. The fact that this occurred, contrary to the SOP and the training provided to the individual responsible, was deeply regrettable. Subsequent investigation by Bayer had revealed use of PowerPoint slides and quizzes and answers used for internal training on SPAF that had also not been certified/recertified. All such non-certified material originated from the same source. No substantive errors in any of this material had yet been identified save for question 15 in the VTE quiz and answers and Bayer would shortly complete its certification/recertification of the 'SPAF Training' slide deck and the previously certified quizzes and answers (and would inform the PMCPA of the results of this certification/recertification - see below).

A detailed review of all other training material used by the Bayer training team for all other products had revealed no other deficiencies.

Bayer stated that it had acted promptly to address this issue. Further training on Code and Bayer SOP compliance had been instituted for the employee whose activities would be subject to close supervision to ensure that the requirements of the Code and Bayer's procedures were being implemented. A training log had been introduced to support existing arrangements for Code and Bayer SOP compliance by the Bayer training team.

In other respects, Bayer did not consider that the complaint had any foundation.

- Bayer respectfully requested the Panel to take into account its detailed investigation of the certification issue, the extensive corrective measures which had been instituted, which demonstrated that the deficiencies identified as a result of this complaint were not typical and that the company's procedures routinely worked well.
- In relation to the incidents, allegations made by the complainant had not been established and Bayer acted entirely properly to manage a situation that was not caused by any inappropriate action by any Bayer employee.

Finally, Bayer had experienced some difficulty in conducting its investigation of this complaint in circumstances where there was a delay of some four weeks after the training course in question before the complaint was made and where there was no documentary record in relation to most of the allegations. The recollections of the trainees who attended the course had undoubtedly been affected by this delay and it seemed likely that this was also the position with the complainant.

FURTHER RESPONSE

Bayer stated that in its response it referred to the certification of certain material used for internal training on Xarelto VTE and SPAF. One of these items was a set of internal training course power point slides entitled 'SPAF Training'. Unfortunately, on review Bayer had discovered that 17 slides were omitted in error, during the photocopying process. These were now provided.

The 'SPAF Training' slide deck was now certified, the changes included:

- Citations had been added to some of the slides to support product claims and, where posters were previously used as references, but data had now been published in peer reviewed journals, the citation had been revised;
- Some minor inaccuracies on graphs and artwork had been corrected (eg a reference to use of CT scans when in fact an MRI had been conducted);
- The slides referred to Clinical Guidelines on management of Atrial Fibrillation issued by NICE, which have now been superseded; the references and content of the slides have therefore been updated to reflect the current Guidelines.

A copy of the certified SPAF Training slide deck was provided.

PANEL RULING

The Panel noted that the parties' accounts differed; it was difficult in such circumstances to determine precisely what had happened. A judgement had to be made on the available evidence whilst noting that the complainant bore the burden of proof and had to establish his/her case on the balance of probabilities.

The Panel noted the response from Bayer that a broader complaint had been made to Bayer's compliance hotline. The three additional matters referred to by Bayer were not the subject of the complaint to the PMCPA and were not considered. The Panel noted that the complainant's identity had not been disclosed or confirmed by the Authority to Bayer.

In relation to the complaint made to the PMCPA, the Panel was only able to consider matters within the scope of the Code. It considered the complaint as follows.

1 Alleged promotion for an unlicensed indication

The Panel considered that the revision quiz was part of the representatives' briefing material as referred to in Clause 15.9 of the Code. The revision quiz question asked participants to select an indication not on the Xarelto SPC from a selection of four. The complainant gave 'active cancer' as the answer given by the employee who denied stating that only active cancer was not licensed. The complainant noted one of the choices was 'Prevention of DVT following hip fracture surgery' for which Xarelto was not licensed. The complainant stated that he/she highlighted that Xarelto was not so licensed. Bayer stated that this was a verbal quiz and there were no documents to confirm. Nonetheless there was general agreement in the interview transcripts that at the very least this matter had been raised and discussed. The complainant stated that a similar question was included in the formal assessment which took place the following day.

The Panel noted that the complainant was incorrect in stating that the same question was included in the written formal assessment. However a similar answer 'Prevention of VTE following hip fracture surgery' was one of the four possible answers. In that regard the Panel noted the error pointed out by Bayer in that the answer sheet gave 'Treatment of acute DVT in a patient with severe renal impairment' as the answer to the question 'Which of these is not an indication for Xarelto?'. The correct answer should have been 'Prevention of VTE following hip fracture surgery'. In addition, the Panel noted that 'active cancer' was not one of the possible answers to the question about Xarelto's licensed indications.

The Panel did not agree that 'Prevention of VTE following hip fracture surgery was contraindicated as submitted by Bayer. The indications in the SPC for Xarelto 10mg were clear as prevention of VTE in elective hip or knee surgery. Section 4.4 special warnings and precautions for use stated that rivaroxaban had not been studied in interventional trials in patients undergoing hip fracture surgery to evaluate efficacy and safety.

It appeared from the interview transcripts that the representatives understood that products should not be promoted for unlicensed indications. It was essential that representatives were clear about the licensed indications of the products they promoted. Training in this regard should be unambiguous. It was questionable whether the licensed indications for Xarelto were made clear to the representatives. It appeared that the discussion about off-label use added to the confusion. The interview transcripts showed that not all were absolutely clear about whether Xarelto could be promoted for prevention of VTE following hip fracture surgery. In addition the interview transcript of the employee showed a degree of confusion about the treatment of acute DVT in patients with severe renal impairment which was mistakenly recorded as the correct answer in the quiz answer sheet. This was compounded by the marking scheme for the formal assessment which referred to the use of Xarelto in hip fracture surgery as contraindicated rather than unlicensed. The Panel was particularly concerned that of the completed quiz papers provided, not one representative gave prevention of VTE following hip fracture surgery as the correct answer. In the Panel's view, this indicated that the training on the point was unclear.

The Panel considered that despite its serious concerns outlined above the complainant had not provided any evidence to show that an unlicensed indication had been promoted to health professionals so the Panel ruled no breach of Clause 3.2 of the Code. The Panel considered that the representatives' assessment was not clear with regard to the licensed indications. Bayer acknowledged that there was some confusion regarding the licensed indications. The briefing materials supplied by Bayer used at the training were not clear about the licensed indications, for example data relating to VTE prevention in orthopaedic surgery was described as a licensed indication, and this was compounded by the representatives' assessment. The Panel therefore ruled a breach of Clause 15.9.

The Panel was concerned that training materials for VTE had not been certified prior to use. These had been certified in April 2017 without amendment. This was of concern to the Panel given its comments about the training material above. The quiz and answers were certified in 2016 but the variation of the certified quiz had not been certified. It appeared that the marking sheet which contained the error had been certified.

The Panel noted Bayer's submission that the failure to certify was contrary to the Code and its SOPs. The complainant had not alleged any breach of the Code in relation to certification, but the failure to certify was in the Panel's view relevant. The Panel was concerned about the quality of the certification.

The Panel noted its ruling of a breach of Clause 15.9 above. It decided that high standards had not been maintained and a breach of Clause 9.1 was ruled. The Panel noted that it was essential to be clear about a medicine's licensed indications. It was apparent that Bayer had failed in that regard as evidenced by the training and validation materials. The employee appeared to be unclear about certain aspects of the product's licence. It was of particular concern that given the marking sheet containing the error had been certified and the variation of the certified quiz had never been certified, representatives beyond those on the training course at issue had, on the balance of probabilities, been exposed to such material. The Panel noted that in consequence Bayer had contacted its entire field force to ensure that they were clear that Xarelto was not licensed for the prevention of VTE following hip fracture surgery. On balance, the Panel considered that the circumstances brought discredit upon, and reduced confidence in, the pharmaceutical industry. The Panel therefore ruled a breach of Clause 2 which was a sign of particular censure and reserved for such use.

2 Alleged encouragement of a disrespectful and unprofessional attitude towards clinicians.

The Panel noted that there was a difference of opinion with regard to whether the employee referred to the clinicians as stupid or the question as stupid. There was no evidence that the representatives had used such language with health professionals or in response to their questions. The Panel considered that the matter of how representatives were to answer questions from health professionals should have been dealt with more professionally at the training as it might impact representatives' subsequent behaviours with health professionals etc. The discussions on these points at the company training event did not amount to a disparagement of clinicians, or their views. No breach of Clause 8.2 was ruled. Given there were different opinions about what the employee said, the Panel considered that it was not possible to establish, on the balance of probabilities, whether a disrespectful attitude had been encouraged. No breach of Clause 9.1 was ruled. It did not consider that the employee was a representative as such and therefore Clause 15.2 did not apply and no breach was ruled.

Complaint received **10 March 2017**

Case completed **21 July 2017**