CASE AUTH/2785/8/15

ANONYMOUS, NON-CONTACTABLE CONSULTANT v BAYER

Promotion of Eylea

An anonymous, non-contactable consultant complained about the promotion of Eylea (aflibercept) by Bayer plc. Lucentis (ranibizumab) to which the complainant referred, was marketed by Novartis Pharmaceuticals UK.

Eylea and Lucentis were intravitreal injections indicated, *inter alia*, for the treatment of neovascular (wet) age-related macular degeneration (wAMD) and visual impairment due to diabetic macular oedema (DMO) or due to macular oedema secondary to retinal vein occlusion.

The complainant stated he/she had discussed the treatment of patients with DMO, vein occlusion and wAMD with a Bayer representative and a head office employee several times over the past 18 months. These discussions centred around new trial data and included Protocol T, VIVID, VISTA, RISE and RIDE. The discussions were very informative, however the complainant stated that at a recent Novartis meeting it was explained that the data discussed with Bayer was off-licence in the UK.

The complainant was further concerned to learn that Protocol T was a head-to-head against an unlicensed dose of Lucentis. The complainant stated that the Bayer employees led him/her to believe that Eylea was superior to Lucentis, however they did not explain the dose difference or that it was unlicensed in the UK.

On understanding this difference the complainant raised it with the representative who stated there was no difference between the two doses of Lucentis and referred the complainant to a meeting to be held shortly in the area with a US retinal specialist to discuss Protocol T.

The complainant was concerned that other consultants would be similarly misled and that a forthcoming meeting would promote the unlicensed 0.3mg dose of Lucentis.

The detailed response from Bayer is given below.

The Panel noted that all of the studies cited by the complainant were DMO studies and that he/she appeared to be particularly concerned about the discussion of the Protocol T study as it involved an unlicensed dose of Lucentis.

The Panel was concerned that the complainant had very clearly referred to an 18 month period (ie from February 2014) in which he/she had discussed Eylea/Lucentis data and the treatment of patients with, *inter alia*, DMO with the Bayer representative and/or another employee. The complainant had not stated the context in which those discussions took place and did not refer to any promotional material which might have been used or any claims in particular to which he/she objected. In the Panel's view, it was most unlikely that discussions about DMO had taken place over such an extended period of time; Eylea was not licensed for use in DMO until August 2014 and the sales force was not issued with material until January 2015.

The Panel noted that the complainant also referred to discussions over the last 18 months about vein occlusion and wMAD. The complainant however bore the burden of proof and bearing in mind all the evidence, the Panel considered that the complainant had not established that any meetings or discussions had taken place between February 2014 and January 2015. No breaches of the Code were ruled.

The Panel noted that the e-detailer, available for use from January 2015, discussed the use of Eylea in visual impairment due to DMO and compared data from the RESTORE (Lucentis), VIVID/VISTA (Eylea) and RISE/RIDE (Lucentis), studies. Below tables of data, in small print, was the statement 'The dosing regimen for [Lucentis] used in the RESTORE, RISE and RIDE studies does not represent its current UK posology. For the current UK [Lucentis] posology, please refer to the [Lucentis] Summary of Product Characteristics'. The Panel did not consider that the page detailing the limitations of cross-over comparisons negated the misleading nature of the page in relation to the licensed dose of Lucentis as implied by Bayer. The Panel also noted that a subsequent slide described the design of the RESTORE and RISE/RIDE studies and referred to the unlicensed Lucentis dosing. The Panel noted Bayer's submission that although the 0.3mg dose of Lucentis was referred to on the slide about the study design of RISE/RIDE, the outcome data for this dose was not included. The Panel noted that the fact the results shown only related to the 0.5mg dose of Lucentis only became apparent if the representative 'tapped' on the study to reveal an additional dialogue box ie that information was not otherwise apparent to the reader and it appeared to be optional whether the representative revealed it or not. In addition the Panel noted that pages of the representatives' briefing material which expressed caution about the cross-study nature of the comparisons, were silent on the caution required about the reference to the unlicensed dose of Lucentis and the results. The Panel considered that given the content of the e-detailer and briefing material, the balance of probabilities was that since January 2015 the representative would have referred to the use of unlicensed doses of Lucentis

with customers. The implied comparison of Eylea with an unlicensed dose of Lucentis was misleading as alleged. Breaches of the Code were ruled. The Panel noted that the Lucentis studies cited in the e-detailer did not use the medicine as per the UK marketing authorization, but as Lucentis was marketed by Novartis then Bayer could not promote that product. No breach of the Code was ruled.

The Panel noted its comments above about the representatives' briefing material for the e-detailer. The Panel considered that to cite an unlicensed dose in the e-detailer and not to make the status of that dose clear in the briefing material and further fail to make it clear that the data discussed from RISE/RIDE related solely to the licensed dose was a significant omission which was likely to lead to representatives having discussions which were contrary to the Code. A breach of the Code was ruled.

The Panel noted its ruling of breaches of the Code above with regard to the e-detailer and the representatives' briefing material. In so much as a representative had used the material provided, the Panel ruled a breach of the Code.

With regard to possible discussions of Protocol T (which did not feature in the e-detailer), the Panel noted Bayer's submission that since the publication of the interim results in February 2015 there had been no sales calls recorded in the region in question where the representative and the head office employee had met with customers, nor any calls by the head office employee alone. The company thus could not identify the meetings in question. In any event, representatives had been briefed not to discuss the study proactively and to refer any unsolicited queries to medical information. The Panel did not consider that the complainant had shown that from February 2015, on the balance of probabilities and bearing in mind all of the evidence, that Bayer personnel had discussed and compared Lucentis and Eylea in the context of the Protocol T study as alleged. No breaches of the Code were ruled. There was no evidence that the representative had failed to maintain a high standard of ethical conduct. No breach of the Code was ruled. Whilst in the Panel's view it would have been preferable if the warning not to discuss the results proactively had appeared at the beginning of the briefing material, it did not consider that the Protocol T briefing material had advocated, either directly or indirectly, any course of action that would be likely to lead to a breach of the Code. On balance the Panel ruled no breach of the Code.

The Panel noted that the complainant was further concerned that a planned meeting would promote the unlicensed 0.3mg dose of Lucentis. The Panel presumed this was because the meeting would include discussion of the Protocol T study although the complainant had not been clear in this regard; it was not possible to contact him/her for further details. Bayer submitted that, on the information provided, the meeting appeared to be one of four which Bayer described as non-promotional about the work of a research network group. The Panel noted Bayer's submission that these meetings would discuss several studies including Protocol T. No speakers' slides had yet been submitted for its approval. The Panel noted that the invitation to one of the meetings described it as 'a scientific meet-the-expert session, exploring the latest updates from the [… research network group]'. The Panel noted Bayer's general submission about the likely considerable interest from UK ophthalmologists in the Protocol T data. In these circumstances and given Bayer's role and commercial interest, the Panel queried whether such meetings would be considered promotional. However, the complainant had made a very broad allegation about 'a forthcoming meeting' and no further details had been provided. In any event and as noted above, Lucentis was marketed by Novartis and in that regard a pharmaceutical company could not promote another company's medicine. No breach of the Code was ruled.

The Panel noted its rulings of breaches of the Code above with regard to the e-detailer and considered that Bayer had not maintained high standards. A breach of the Code was ruled. However the Panel did not consider that the rulings were such as to merit particular censure and in that regard no breach of Clause 2 was ruled.

An anonymous, non-contactable complainant who described themselves as a 'concerned consultant' complained about the promotion of Eylea (aflibercept) by Bayer plc. Lucentis (ranibizumab) to which the complainant referred, was marketed by Novartis Pharmaceuticals UK.

Eylea and Lucentis were intravitreal injections (ie into the eye). Both medicines were indicated, *inter alia*, for the treatment of neovascular (wet) age-related macular degeneration (wAMD) and visual impairment due to diabetic macular oedema (DMO) or due to macular oedema secondary to retinal vein occlusion.

COMPLAINT

The complainant stated that he/she had discussed the treatment of patients with DMO, vein occlusion and wAMD with a Bayer representative and a head office employee several times over the past 18 months. These discussions largely centred around new trials data from the diabetic retinopathy clinical research network group and included Protocol T, VIVID, VISTA, RISE and RIDE. The discussions were very informative, however the complainant stated that at a recent Novartis meeting, the chair, a well known professor in the complainant's region, explained that the data that he/she (the complainant) had been discussing with the Bayer representative was off-licence and off-label in the UK.

The complainant was further concerned to learn that Protocol T was a head-to-head against an unlicensed dose of Lucentis. The complainant stated that the Bayer employees led him/her to believe that Eylea was superior to Lucentis, however they did not explain the dose difference or that it was unlicensed in the UK.

On understanding this difference the complainant raised it with the representative who stated there was no difference between the two doses of Lucentis and referred the complainant to a meeting to be held shortly in the area with a US retinal specialist to discuss ProtocolT.

The complainant stated that he/she had always maintained a good relationship with the local representative and so preferred to remain anonymous, but was concerned that other consultants would also be misled in this way at the expense of patient care. The complainant was further concerned that a forthcoming meeting would promote the unlicensed 0.3mg dose of Lucentis.

When writing to Bayer, the Authority asked it to respond in relation to Clauses 2, 3.2, 7.2, 7.3, 9.1, 15.2 and 15.9 of the Code.

RESPONSE

Bayer stated that it took its responsibilities under the Code very seriously and as such, it undertook to ensure that all promotion in relation to Eylea was in line with its marketing authorization and those of any competitor products, comprised only accurate, fair and balanced communication of the scientific data and did not contain any misleading comparisons with other treatments. All personnel, including representatives, were regularly trained on the Code and were carefully briefed on how to manage unsolicited enquiries regarding unlicensed products. All off-label enquiries received by sales or marketing personnel were recorded on a request card and directed to the medical department for response. This procedure applied to all off-label enquires about prescription-only products in all indications.

Allegations of promotional activities relating to ProtocolT

Bayer submitted that ProtocolT was a randomised, controlled, US trial which compared Eylea, Lucentis and bevacizumab (Avastin) for the treatment of visual impairment due to DMO. The study was sponsored by the diabetic retinopathy clinical research network group, an independent, government-funded US research network which conducted research into a wide variety of treatments for diabetic eye disease. Bayer was not involved in the design or conduct of the study. ProtocolT used a 0.3mg dose of Lucentis which was approved in the US for the treatment of visual impairment due to DMO but was not the dose approved in the European marketing authorization (0.5mg); a posology of Eylea which differed from the exact wording of the summary of product characteristics (SPC) [2mg every four weeks vs 2mg every month]; and an intravitreal reformulation of Avastin which was not licensed for use anywhere in the world. The study was therefore inconsistent with the marketing authorizations of all three study medicines and so could not be included in any promotional material for Eylea nor discussed proactively by Bayer representatives. Unsolicited enquiries about ProtocolT were therefore handled exclusively by Bayer's medical department, as with all off-label enquiries.

The anonymous complainant referred to meetings with Bayer staff 'over the past 18 months' at which Eylea use in DMO and specific DMO studies were discussed, amongst other indications. This statement could not be correct as no Bayer representatives or other relevant personnel discussed any aspect of Eylea's use in visual impairment due to DMO in field-based customer visits before January 2015 – which was when sales materials for promotion in visual impairment due to DMO were first made available for use in the field – and no promotion of Eylea in DMO by any means occurred in the UK before September 2014. The marketing authorization for Eylea in visual impairment secondary to DMO was granted in August 2014, and although Bayer's sales team were trained and validated in this new indication by September 2014 in order to permit their presence on promotional stands carrying details of the new indication, Bayer did not release the DMO sales e-detailer to the team until January 2015.

In addition, the first full publication of interim 1 year results from ProtocolT only appeared online in February 2015 (Wells *et al* 2015), ie within 6 months of this complaint being received by the PMCPA. It was therefore not possible that the alleged ProtocolT discussions could have occurred with any Bayer staff over 18 months as claimed.

As ProtocolT was the first, and to date, only large, randomised, head-to-head comparison of the three anti-vascular endothelial growth factor (anti-VEGF) medicines used to treat DMO worldwide – Eylea, Lucentis and Avastin – Bayer knew that there would be considerable interest from UK ophthalmologists in these data when published and that it was highly likely that Bayer would receive unsolicited enquiries about the study and the outcomes for Eylea. For this reason, a comprehensive sales briefing document on ProtocolT covering its limitations and where the protocol deviated from the UK marketing authorizations of the study medicines, was certified and distributed to the sales and brand management team immediately after the paper was published in February 2015. The messages contained within were also reinforced through a conference call with the sales and marketing team. A copy of the briefing document was provided. Bayer submitted that this briefing gave clear instruction that the Lucentis 0.3mg dose was unlicensed and stated that Protocol T must therefore not be discussed proactively. All requests for reprints or further questions about ProtocolT must be documented and referred to medical information, which would respond to the customer and/or pass the request to the medical science liaison (MSL) team if more detailed discussion was required.

Bayer submitted that senior managers had interviewed the representative responsible for the region mentioned, and reviewed call records, which detailed any colleagues who had accompanied them on a call. All relevant head office staff had also been questioned by their senior manager about any meetings involving Bayer's representative in the area and/or customers in that area. Since the publication of ProtocolT, there had been no sales call recorded where the representative and the head office employee met with a customer in this region, and

also no calls made by the head office employee on customers where the representative was not present. Bayer had thus been unable to identify any meeting in the area where the alleged discussion between the complainant and the two Bayer employees might have occurred. Furthermore, Bayer's representative confirmed that he/she had always adhered to the briefing document and referred all unsolicited enquiries about ProtocolT to the medical department. Relevant head office staff likewise had confirmed that they did not engage in off-label discussion under any circumstances but always documented and then referred any unsolicited ProtocolT enquiries to the medical department for response. Sales/commercial personnel were not permitted to be present in the room when the MSL responded to customers' unsolicited off-label enquiries, and Bayer's medical director for ophthalmology confirmed with the MSL responsible for the region that there had been no deviations from this procedure.

Bayer was unable to comment on the Novartis-sponsored meeting reportedly attended by the complainant, at which ProtocolT appeared to have been discussed.

Alleged off-label promotional comparisons between Eylea and Lucentis

Copies of promotional material used by Bayer's sales team which compared Eylea and Lucentis in visual impairment secondary to DMO and/or was based upon the data/studies mentioned in the complaint were provided.

Bayer confirmed that the ProtocolT study was not mentioned in any promotional material for Eylea, for the reasons stated above, nor were there any comparisons of Eylea and Lucentis which quoted or otherwise referred to unlicensed doses of either medicine.

Bayer noted that the complainant had also referred to VIVID/VISTA and RISE/RIDE. VIVID and VISTA were the pivotal phase III studies for Eylea in DMO, where the sole comparator was macular laser photocoagulation, and RISE/RIDE were the equivalent studies for 0.3mg and 0.5mg Lucentis given monthly for two years vs placebo injection. For clarity, Bayer noted that the complainant implied that VIVID/VISTA and RISE/RIDE were also studies from the diabetic retinopathy clinical research network – this was not so. VIVID/VISTA (Eylea) and RISE/RIDE (Lucentis) were sponsored by the respective marketing authorization holders, whereas the diabetic retinopathy clinical research network was an independent, government-funded US research network.

The only promotional material which compared Eylea with Lucentis in DMO was a section of a DMO e-detailer, released to the sales team in January 2015. It contained only limited, qualitative cross-study comparisons of Eylea in the treatment of visual impairment due to DMO with trials of Lucentis, as in this indication there were no head-to-head data involving the licensed doses of both products. Certified briefing material for the sales team, which accompanied the e-detailer, made the limitations of such cross-study comparisons clear and required representatives to present the page describing these limitations to the health professional. Furthermore, the e-detailer was designed such that the slide presenting the limitations of the indirect comparison must be viewed before proceeding to any other part of the presentation.

In addition, the pivotal studies of Lucentis (RISE/RIDE) used a monthly dosing regimen of 0.5mg over 2 years. Monthly dosing was not inconsistent with the licensed posology of Lucentis (where monthly injection was mandated until maximum visual acuity was achieved and/or there were no signs of disease activity, with no maximum period of monthly dosing specified), but prolonged monthly dosing was not typical of the clinical use of Lucentis in the UK, where an 'as required' regimen with regular monitoring was more usual, nor did the regimen in RISE/RIDE reflect the full range of dosing options possible within the current Lucentis SPC. Advice to this effect, and a recommendation to consult the current Lucentis SPC, was therefore always included in promotional materials which quoted RISE and RIDE.

For completeness and accuracy, Bayer highlighted that the 0.3mg dose of Lucentis was briefly mentioned on the slide about the study design of RISE/RIDE, but the outcome data for this dose were not included and there was no attempt to compare this dose with Eylea. Most of the qualitative comparison pages in the e-detailer related to RESTORE, a study not mentioned by the complainant, which used an 'as required' posology of 0.5mg Lucentis corresponding most closely of all published Lucentis studies to real-life UK clinical usage; this study was also referenced by the National Institute for Health and Care Excellence (NICE) for the same purpose, in the single technology appraisal of Eylea in DMO.

In addition, there was a leavepiece, promotional stand video and a supplement all of which referred to studies mentioned by the complainant, excepting ProtocolT. These did not include any mention of off-label doses or any comparison between products.

Planned Bayer-sponsored meetings

Bayer submitted that the meeting referenced in the complaint was one in a series of four non-promotional, scientific meetings due to be held in late September 2015 at different geographic locations. Bayer could not be certain from the complaint of the specific meeting at issue, but all four were similar in scope. These meetings were not 'ProtocolT' meetings nor Eylea promotional meetings, but were scientific, non-promotional meetings about the work of the diabetic retinopathy clinical research network group, and topics would include discussion of several different studies, for example, Protocol S which compared Lucentis to prompt or deferred pan-retinal photocoagulation. As previously stated, the diabetic retinopathy clinical research network group was a highly regarded,

independent, government-funded US research network which conducted research into a wide variety of medical and non-medical treatments for diabetic eye disease. The two speakers were recognised as world-class researchers in this field. UK clinicians were genuinely interested in the breadth of the research sponsored by the group and enthusiastic to learn how the network was organised to maximise the efficiency of study conduct and how these learnings might be applied within the UK.

These non-promotional, scientific meetings were managed by the medical team. The sales team would not attend them, would not distribute invitations (which would be done via the medical department and/or the local meeting chair) and there would be no promotional stand or other promotional activities linked to the meetings. The only external materials available at present were the invitations and template covering emails for delegates and chairs of the meetings, all of which had been approved and certified. There was also an internal concept document, which provided more information about the objectives and proposed content of the meetings.

There were currently no slides available for the meetings, as these were still being prepared by the speakers. The meeting content, any further external materials relating to the meetings and all other relevant arrangements would, in due course, be certified as required by the Code before the first meeting was held.

Summary

In summary, with regard to Clause 3.2, Bayer submitted that it had taken every step necessary to ensure Eylea was promoted only within its marketing authorization and in line with its SPC. The company recognised that ProtocolT used products with dosage/posology/formulation outside their marketing authorizations, the representatives had been briefed accordingly to document and refer all unsolicited enquiries to the medical department. Bayer had never used data from ProtocolT promotionally. The meetings planned for late September were non-promotional, scientific exchange meetings with a balanced, educational agenda that had wide relevance for clinicians interested in research and treatment in diabetic eye disease; the meetings were neither focussed on studies involving Eylea nor designed to promote Eylea, and the sales team was not involved in them in any way. Bayer thus denied a breach of Clause 3.2.

With regard to Clauses 7.2 and 7.3, no promotional material, about the use of Lucentis vs Eylea in visual impairment secondary to DMO, included comparisons based on, or referred to, ProtocolT; nor had any other comparisons been made which involved unlicensed doses of either medicine. Bayer therefore denied any breach of the Code in relation to inappropriate or off-licence promotional claims and/or comparisons.

With regard to Clauses 15.2 and 15.9, Bayer submitted its sales team was always fully briefed on any relevant new data, and such briefings were certified under the Code. For ProtocolT, the briefings clearly stated that the dose of Lucentis used was off-label and that the study must not be proactively discussed under any circumstances. Interviews with the representative concerned and relevant head office staff, and scrutiny of the call records for the relevant territory, had failed to produce any evidence to support the allegations by the anonymous complainant that Bayer employees failed to follow the approved procedures. In addition, the call records did not support that any meeting occurred in the relevant territory which might correspond to the meeting alleged by the complainant. In line with Bayer policy, representatives were never present at customer visits when medical department personnel responded to any off-label enquiry.

PANEL RULING

The Panel noted that the complainant was anonymous. As stated in the introduction to the Constitution and Procedure, such complaints were accepted and like all complaints, judged on the evidence provided by both parties. Complainants had the burden of proving their complaint on the balance of probabilities. The complainant had neither referred to any specific material or claim nor provided any material to substantiate his/her allegations. As the complainant was non-contactable it was not possible to ask him/her for further information.

The Panel noted the complainant's allegation that he/she had had several discussions over the past 18 months [ie since February 2014] with a representative and another Bayer employee about the treatment of patients with diabetic macular oedema (DMO), vein occlusion and (wet) age-related macular degeneration (wAMD). The complainant submitted that the discussions had largely centred around new trial data from the diabetic retinopathy clinical research network group and included ProtocolT, VIVID, VISTA, RISE and RIDE. The complainant found the discussions very informative but was concerned that the data he/she had discussed with the Bayer representative was off-licence and off-label in the UK. The complainant appeared to be particularly concerned about the discussion of the ProtocolT study as it involved an unlicensed dose of Lucentis. The Panel noted that all of the studies cited by the complainant were DMO studies.

The Panel noted Bayer's submission that none of its representatives or other relevant personnel had discussed any aspect of Eylea use in visual impairment due to DMO in field-based customer visits before January 2015 when sales materials for promotion in visual impairment due to DMO were first made available; no promotion of Eylea in DMO by any means occurred in the UK before September 2014; the marketing authorization for Eylea in visual impairment secondary to DMO was not granted until August 2014. Although Bayer had submitted that its sales team was trained and validated in this new indication by September 2014, in order to permit their presence on promotional stands carrying details of the new indication, the DMO sales e-detailer was not released until January 2015.

The Panel was concerned that the complainant had very clearly referred to an 18 month period (ie from February 2014) in which he/she had discussed Eylea/Lucentis data and the treatment of patients with, *inter alia*, DMO with the Bayer representative and/or another employee. The complainant had not stated the context in which those discussions took place and did not refer to any promotional material which might have been used or any claims in particular to which he/she objected. In the Panel's view, given Bayer's submission it was most unlikely that discussions about DMO had taken place over such an extended period of time. Eylea was not licensed for use in DMO until August 2014 and the sales force was not issued with material (an e-detailer) to use in the field until January 2015.

Given the 18 month time period referred to by the complainant and Bayer's submissions regarding the dates when material was released to the representatives, the Panel had some concerns about the robustness of the complaint. Nonetheless, the Panel noted that the complainant referred to discussions over the last 18 months not only about DMO but also about vein occlusion and wMAD. The complainant however bore the burden of proof and bearing in mind all the evidence, the Panel considered that the complainant had not established that any meetings or discussions had taken place between February 2014 and January 2015. No breach of Clauses 3.2, 7.2 and 7.3 were ruled.

The Panel noted that the e-detailer provider provided by Bayer (available for use from January 2015) discussed the use of Eylea in visual impairment due to DMO and presented, in tabular form, a comparison of data from the RESTORE (Lucentis, 0.5mg/month for 3 months and then as required), VIVID/VISTA (Eylea) and RISE/RIDE (Lucentis, 0.3mg or 0.5mg monthly) studies. Below the tables of data, in small print, was the statement 'The dosing regimen for [Lucentis] used in the RESTORE, RISE and RIDE studies does not represent its current UK posology. For the current UK [Lucentis] posology, please refer to the [Lucentis] Summary of Product Characteristics'. The Panel noted that the supplementary information to Clause 7.2 stated that in general, claims should not be qualified by the use of footnotes and the like. The Panel did not consider that the page detailing the limitations of cross-over comparisons negated the misleading nature of the page in relation to the licensed dose of Lucentis as implied by Bayer. The Panel also noted that a subsequent slide described the design of the RESTORE and RISE/RIDE studies and referred to the unlicensed Lucentis dosing. The Panel noted Bayer's submission that although the 0.3mg dose of Lucentis was referred to on the slide about the study design of RISE/RIDE, the outcome data for this dose was not included. The Panel noted that the fact the results shown only related to the 0.5mg dose of Lucentis only became apparent if the representative 'tapped' on the study to reveal an additional dialogue box ie that information was not otherwise apparent to the reader and it appeared to be optional whether the representative revealed it or not. In addition the Panel noted that those pages of the representatives' briefing material provided by Bayer expressed caution about the cross-study nature of the comparisons but were silent on the caution required in relation to the reference to the unlicensed dose of Lucentis and the results. The Panel considered that given the content of the e-detailer and briefing material, the balance of probabilities was that since January 2015 the representative would have referred to the use of unlicensed doses of Lucentis with customers. The implied comparison of Eylea with an unlicensed dose of Lucentis was misleading as alleged. A breach of Clause 7.2 and 7.3 was ruled. The Panel noted that Clause 3.2 required the promotion of a medicine to be in accordance with the particulars listed in its SPC. The definition of promotion given in Clause 1.2 related, *inter alia*, to an activity undertaken by a pharmaceutical company, which promoted the administration, consumption, prescription, purchase, recommendation, sale or supply of *its* medicines (emphasis added). The Lucentis studies cited in the e-detailer did not use the medicine as per the UK marketing authorization, but as Lucentis was marketed by Novartis then Bayer could not promote that product. No breach of Clause 3.2 was ruled.

The Panel noted its comments above about the representatives' briefing material for the e-detailer. The Panel considered that to cite an unlicensed dose in the e-detailer and then not to make the status of that dose clear in the briefing material and further fail to make it clear that the data discussed from RISE/RIDE related solely to the licensed dose was a significant omission which was likely to lead to representatives having discussions which were contrary to the Code. A breach of Clause 15.9 was ruled in relation to the briefing material for the e-detailer.

The Panel noted its ruling of breaches of the Code above with regard to the e-detailer and the representatives' briefing material. In so much as a representative had used the material provided, the Panel ruled a breach of Clause 15.2.

With regard to possible discussions of Protocol T (which did not feature in the e-detailer), the Panel noted Bayer's submission that since the publication of the first interim results from Protocol T in February 2015 (Wells *et al*) there had been no sales calls recorded in the region in question where the representative and a head office employee had met with customers, nor any calls by the head office employee alone. The company thus could not identify the meetings in question. In any event, representatives had been briefed immediately after publication of Wells *et al* not to discuss the study proactively and to refer any unsolicited queries to medical information; the representative in question had confirmed that this indeed was what he/she had always done. The Panel did not consider that the complainant had shown that from February 2015, on the balance of probabilities and bearing in mind all of the evidence, Bayer personnel had discussed and compared Lucentis and Eylea in the context of the Protocol T study as alleged. No breach of Clauses 3.2, 7.2 and 7.3 were ruled. There was no evidence that the representative had failed to maintain a high standard of ethical conduct. No breach of

Clause 15.2 was ruled. Whilst in the Panel's view it would have been preferable if the warning not to discuss the results proactively had appeared at the beginning of the briefing material, it did not consider that the Protocol T briefing material had advocated, either directly or indirectly, any course of action that would be likely to lead to a breach of the Code. On balance the Panel ruled no breach of Clause 15.9.

The Panel noted that the complainant was further concerned that there was a meeting planned that would promote the unlicensed 0.3mg dose of Lucentis. The Panel presumed this was because the meeting would include discussion of the Protocol T study although the complainant had not been clear in this regard; it was not possible to contact him/her for further details. Bayer had submitted that, on the information provided, the meeting appeared to be one of four which Bayer described as non-promotional about the work of the diabetic retinopathy clinical research network group. The Panel noted Bayer's submission that these meetings would discuss several studies including Protocol T. No speakers' slides had yet been submitted for its approval. The Panel noted that the invitation to one of the meetings described it as 'a scientific meet-the-expert session, exploring the latest updates from the [diabetic retinopathy clinical research network group]'. The Panel noted Bayer's general submission about the likely considerable interest from UK ophthalmologists in the Protocol T data. In these circumstances and given Bayer's role and commercial interest, the Panel queried whether such meetings would be considered promotional. However, the complainant had made a very broad allegation about 'a forthcoming meeting' and no further details had been provided. In any event and as noted above, Lucentis was marketed by Novartis and in that regard a pharmaceutical company could not promote another company's medicine. No breach of Clause 3.2 was ruled.

The Panel noted its ruling of a breach of Clauses 7.2, 7.3 and 15.9 above with regard to the e-detailer and considered that Bayer had not maintained high standards. A breach of Clause 9.1 was ruled. However the Panel did not consider that the rulings were such as to merit particular censure and in that regard no breach of Clause 2 was ruled.

Complaint received **3 August 2015**

Case completed **20 October 2015**