CASE AUTH/3809/8/23 ***NO BREACH OF THE CODE***

COMPLAINANT v BAYER

Allegations regarding a Bayer advisory board

CASE SUMMARY

This case was in relation to a Bayer advisory board . The complainant alleged that it was not a legitimate advisory board and was instead pre-license promotion of its new Eylea indication. The complainant provided a number of reasons including a lack of pre-work, presentation and discussion time did not meet requirements and that there was no legitimate unanswered question given a previous advisory board had been conducted some 3 months prior.

There was an appeal by Bayer of six of the Panel's rulings.

The outcome under the 2021 Code was:

No Breach of Clause 2 [Panel's breach ruling overturned at appeal]	**Requirement that activities or materials must not bring discredit upon, or reduce confidence in, the pharmaceutical industry**
No Breach of Clause 3.1 [Panel's breach ruling overturned at appeal]	**Requirement that a medicine must not be promoted prior to the grant of its marketing authorisation**
No Breach of Clause 3.6 [Panel's breach ruling overturned at appeal]	**Requirement that materials and activities must not be disguised promotion**
No Breach of Clause 5.1 [Panel's breach ruling overturned at appeal]	**Requirement to maintain high standards at all times**
No Breach of Clause 10.1	**Requirement that companies must not provide inappropriate hospitality**
No Breach of Clause 19.1 [Panel's breach ruling overturned at appeal]	**Requirement that no gift, pecuniary advantage or benefit may be supplied, offered or promised to health professionals or other relevant decision makers in connection with the promotion of medicines, or as an inducement to prescribe, supply, administer, recommend, buy or sell any medicine**
No Breach of Clause 24.2 ×2 [Panel's breach ruling overturned at appeal]	**Requirement that arrangements for contracted services fulfil specific criteria, including agreeing a written contract or agreement in advance of the commencement of services, and clearly identifying and documenting a legitimate need for the services in advance of requesting the services and entering into arrangements**

This summary is not intended to be read in isolation.
For full details, please see the full case report below.

FULL CASE REPORT

A complaint was received from an anonymous, contactable complainant about Bayer.

COMPLAINT

The complaint wording is reproduced below:

> "I am writing to complain about a recent Bayer advisory board conducted on 31st July 2023, in the USA. The slides presented were pre-license promotion. The advisory board was not a genuine advisory board. It was warming the market for the new Eylea indication. There was no pre-work sent, you were invited to attend two optional lectures if you had time. The presentation and discussion time during the meeting did not meet the requirements of an advisory board. The participants of the advisory board were also sponsored by Bayer to attend the ASRS conference, and this contradicts the PMCPA guidance on advisory boards. The integrity of the advisory board was compromised. The company did not have a legitimate unanswered business question. The advisory board was not the most appropriate way of obtaining the information. Experts in the field were promoted to and prepared for the upcoming Eylea indication. Bayer had members of the commercial team present. The number of participants was not limited to allow active participation by all. The agenda did not allow adequate time for discussion. A significant majority of the time spent was not spent on feedback from the participants. The attendees were already in talks with Bayer and were also attending ASRS sponsored by Bayer. This was the second advisory board conducted, the previous only being conducted a few months prior on the 27th April 2023 in New Orleans. The invitation to participates did not clearly state the purpose of the meeting, the expected advisory role and the amount of work to be undertaken. Some participants were paid more than fair market value. The presentations to participants were very extensive and not all information was relevant to answering the business question. Expected preparatory work was optional. UK healthcare professionals were promoted to prior to grant of license of the 8mg indication for Eylea. The integrity of the advisory board was compromised due to also sponsoring attendees at congress, who would then propagate the information. The information could have been obtained via consultancy or other means. Two advisory boards were conducted within 3 months of each other, both in parallel with congresses."

When writing to Bayer, the PMCPA asked it to consider the requirements of Clauses 2, 3.1, 3.6, 5.1, 10.1, 19.1 and 24.2 of the 2021 Code.

BAYER'S RESPONSE

The response from Bayer is reproduced below:

> "The Complaint is in relation to an advisory board meeting organised by Bayer and held on 31 July 2023 in Seattle, US. Bayer has been asked to consider the following clauses of the 2021 UK APBI Code of Practice in relation to its response: 2, 3.1, 3.6, 5.1, 10.1, 19.1, and 24.2 respectively.

Bayer takes its responsibility to comply with the ABPI Code of Practice and to maintain high standards extremely seriously. We welcome the opportunity to respond to this complaint and provide a full rebuttal to the satisfaction of the Panel. Bayer does not accept that the arrangements for this meeting breached the requirements of the Code.

Background

Bayer's product aflibercept (Eylea) is a biological medicine in the anti-vascular endothelial growth factor (anti-VEGF) class. It has been available in the UK since 2012 in a 2mg dose formulation where it is approved in vial and pre-filled syringe formulations for a number of indications in the medical retina area in adults (neovascular (wet) age-related macular degeneration (nAMD), visual impairment secondary to diabetic macular oedema (DMO), visual impairment secondary to retinal vein occlusion (RVO, visual impairment due to myopic choriodal neovascularisation (mCNV)), and (in pre-filled syringe formulation only) for the treatment of retinopathy of prematurity (ROP) in preterm infants [1] (Eylea SPCs). Aflibercept, like other medicines in its class, is administered by intravitreal injection i.e., by injection directly into the eyeball of the patient.

The market landscape for anti-VEGF medicines in medical retina is currently undergoing a period of unprecedented rapid change following a period of several years when there were only two licensed products in this class. Multiple new products in this class have been licensed and launched for nAMD and DMO in the UK (the two largest indications in this area) over the past 1-2 years, including several biosimilar ranibizumab products and [named competitor andpharmaceutical company]. In parallel, the NHS is facing significant challenges with funding and capacity in the recovery from the Covid pandemic, with evolving and uncertain implications for medical retina services. New commissioning guidelines for anti-VEGFs in medical retina were issued in August 2022 by NHS England and have already required revision, with the updated version being released only on 26 July 2023 five days before the 31 July advisory board was held. The priorities of health professionals, NHS commissioners and patients in this therapeutic area are thus changing rapidly and in ways that can be difficult to predict without consulting those involved.

[Bayer provided details about the approval for a higher dose formulation of aflibercept (Eylea 8mg) and clinical features of the 8mg dose and health environment on which it sought advice.]

[General details about the differences between the 2mg and 8mg afibercept formulation on which advice was sought]

This uncertain and rapidly changing landscape has created a need for Bayer to be particularly agile and responsive in our business strategy in medical retina, particularly in relation to developing and refining plans for the launch of aflibercept 8mg, and this requires us to seek regular feedback from health care professionals to guide our plans for external communication, research and other activities. This is particularly so as we shape our plans in response to release of new data and NHS changes relevant to [named competitor], ranibizumab biosimilars and aflibercept 2mg/8mg in order to ensure our planned activities across our ophthalmology portfolio meet the anticipated needs of patients and the NHS in 2024 and beyond.

Details of the Bayer Advisory Board
Bayer conducted an advisory board titled 'Congress advisory board: Considering forthcoming developments in the UK anti-VEGF treatment landscape' on 31st July 2023 14:30–18:00 (GMT -7) in Seattle USA.

Clause 10.1 of the Code and guidance from the PMCPA on the conduct of advisory boards both mandate that the meeting is held in an appropriate venue conducive to the business purpose of the meeting and that hospitality is secondary to that purpose and of an appropriate standard.

The venue of the meeting was a boardroom style meeting room booked at the [named hotel], Seattle, USA. Attendees were staying at this hotel to attend the American Society of Retina Specialists (ASRS) annual Meeting.

The Complainant challenges multiple aspects of the advisory board as listed below. We will take each one in turn.

1. Rationale for conducting advisory board in conjunction with an external congress
2. Advisory board objectives
3. Scheduling of the advisory boards
4. Selection of advisors
5. Invitation to advisors
6. Composition of advisory board; Bayer and other attendees
7. Remuneration of advisors
8. Travel arrangements
9. Pre-work
10. Balance and suitability of agenda
11. Side deck

1. Rationale for conducting advisory board in conjunction with an external congress

The Complainant stated that '*The participants of the advisory board were also sponsored by Bayer to attend the ASRS conference, and this contradicts the PMCPA guidance on advisory boards. The integrity of the advisory board was compromised'.* Bayer refutes the suggestion that the arrangements for this meeting compromised its integrity and did not comply with the Code.

The advisory board was conducted in conjunction with the annual meeting of American Society of Retina Specialists (ASRS), an international learned society congress which took place from 28th July to 1st August 2023 in Seattle USA. Providing other requirements of the Code are met, conducting UK advisory boards at international scientific symposia is not specifically restricted by the Code nor PMCPA Guidance, is common industry practice and has significant advantages in term of the quality of discussion and outputs that can be achieved, as well as time efficiency for advisors and minimisation of absence from clinical work. The PMCPA Guidance on advisory boa[r]d conduct does, however, require careful consideration when holding an advisory board in association with an external scientific congress. Matters considered by Bayer when deciding to hold this advisory board at ASRS included the following:

- Advantages of conducting an advisory board in association with a congress:
    - Ability to discuss new data in a face-to-face setting very soon after new data have been presented, when advisor recollections of the data and associated formal and informal discussion at the conference amongst their peers are still clear. This leads to increased quality and relevance of advice obtained compared to advisory boards held later in the UK after data presentation, most of which now have to be virtual because of advisor time restrictions.
    - Efficient use of advisor time, minimising impact on clinical services i.e., avoiding the need to take days of leave and reschedule clinics, which would be necessary for an advisor to attend a face-to-face half-day advisory board in the UK.
- Timing of the advisory board:
    - The advisory board meeting was arranged on the afternoon of Monday 31 July 2023 from 14:30 – 18:00 after careful consideration to avoid any clash with scientific sessions on adult medical retinal conditions which might be of educational interest to the participating advisors. This date/time also fell after the scientific sessions of greatest relevance to the advisory board discussions.
- Selection of advisors
    - Advisors attending the advisory board were selected and invited from those already attending ASRS who also possessed the necessary qualifications and experience to contribute usefully to the advisory board discussions. Not all advisors attending the congress were on the short list for invitation, and within suitable candidates for invitation on the short list there was a primary and secondary list for invitation. No advisors were supported to travel to the US by Bayer solely for the purposes of attending the advisory board. Further detail of the rationale for advisor selection is given in section 4 below.

2. Advisory board objectives:

The complainant states that '*The company did not have a legitimate unanswered business question. The advisory board was not the most appropriate way of obtaining the information'* and '*The information could have been obtained via consultancy or other means'.* Bayer refutes this, as explained below.

Bayer's objectives for the advisory board were recorded and certified prior to the meeting in the Concept document and are as follows:

a) To seek expert feedback and advice on the latest Phase IIb/III clinical data with aflibercept 8 mg for nAMD and DMO, and practical implications for its UK launch

Major congresses in ophthalmology over the course of 2023 have seen and will continue to see the release of further data and post-hoc analyses of the Phase IIb/III PULSAR and PHOTON trials with aflibercept 8 mg. We have explained in the 'Background' above why new data releases from ongoing studies are of critical importance in this therapy area. These later data (year 2 and beyond) give access to new information about the longest

treatment intervals which can be achieved in the later stages of 'treat and extend' regimens with a new anti-VEGF drug formulation in clinical practice. In addition to treatment intervals and impact on service delivery, the longer-term efficacy and safety of extended treatment intervals, [general information relating to aflibercept 8mg and the anticipated impact of the later data on NHS practice]

Bayer therefore sought timely, comprehensive feedback on these data, and the evolving attitudes of ophthalmologists towards aflibercept 8 mg in the light of these data, to ensure reactive communications pre-launch and planned communications and activities post-launch were tailored to the needs of retinal physicians and NHS commissioners. This particular advisory board allowed Bayer to seek up-to-date advice on new aflibercept 8 mg data presented at the ASRS Annual Meeting and data reported at ARVO 2023 that were not available to the UK Bayer team for presentation at earlier advisory board meetings. It also provided an opportunity to gain insights on how aflibercept 8 mg can be best supported as it enters the UK medical retina market and how the latest data on treatment intervals achievable with 8mg aflibercept may impact UK clinical practice, including on how Bayer can most effectively communicate key messages and data, what additional data ophthalmologists would require before they could consider using aflibercept 8 mg, what data NHS commissioners might request from Bayer and from clinicians, and practical considerations for the implementation and use of aflibercept in clinical practice.

It can be seen in the minutes of the meeting that the discussions and insights gained around aflibercept 8mg were wide-ranging and included [slide numbers for each of the bulleted discussions below were provided]:

- Need for more communication from Bayer around the pharmacological rationale for the 8mg dose
- Critique of retreatment criteria for aflibercept 8 mg in PULSAR and PHOTON , useful for assisting Bayer in developing appropriate messaging to explain these criteria vs current practice post-launch
- Insights on posology, presentation and implications for upcoming regulatory discussions and further formulation development
- Impact of likely posology and longer extensions on clinical services
- Proposals for further data collection and/or analyses to meet clinical needs for efficacy and safety data e.g. real-world evidence, post-hoc analyses, comparative studies
- Practical implications of introducing the 8mg dose (higher volume etc)
- Factors influencing choice of drug, including decision to switch patients from 2mg to 8mg aflibercept
- Advice around appropriate messaging for Bayer to consider in relation to launch of aflibercept 8mg

b) To seek perspectives on new Phase III data with [named competitor] (competitor) in RVO

[nature of advice sought about new competitor data]

c) To share and discuss real-world outcomes and experiences with [named competitor] and ranibizumab (competitor) biosimilars in UK clinical practice.

[general information on changes in the medical retina treatment landscape including use of a named competitor of which a previous advisory board had reported clinical experience remained limited]

In addition, Bayer also had the opportunity to understand perspectives on the latest real-world data with a named competitor reported at ASRS, including [named studies] and any real-world evidence from [named competitor] use in UK centres.

Furthermore, Bayer needed to gain insights on how the entry of ranibizumab biosimilars into the UK market, including the recently released drug Ximluci, is affecting the current medical retina treatment landscape and how this may affect use of aflibercept 2mg and the forthcoming launch of aflibercept 8 mg. This offers opportunity for lower-priced competition and so insights are important. An updated version of NHS England commissioning guidelines for anti-VEGFs in medical retina had been released on 26 July 2023 [link, slide number and full title provided]. These new guidelines were discussed verbally as release was too late to be captured in the slide deck. Outputs were captured in the minutes].

The advisory board objectives were thus designed to meet valid business needs in the context of the current market for aflibercept 2mg and the planned launch of aflibercept 8mg. The questions asked at this advisory board could not have been asked at previous advisory boards as the data forming the basis for discussion were not yet available. Informal conversations around Bayer strategy with advisors attending ASRS, outside the context of a formal advisory board, would not have been appropriate or sufficient for the following reasons:

- Lack of confidentiality agreement: such discussions are highly commercially sensitive and so need to take place only under contract where all parties understand their obligations to confidentiality.
- Difficulty of conducting informal discussions in private at a busy congress: private space is in high demand and often needs to be booked and pre-planned; attendees reasonably want to spend their time during the congress day attending educational sessions and meeting with their peers, they would prefer business discussions with Bayer personnel to be held at a separate, dedicated time and place.

Individual consultancy agreements may have enabled Bayer to meet some of the objectives above whilst ensuring confidentiality but would not have permitted any group discussion between advisors, something that is both valuable and necessary to ensure such things as data interpretation, trial design, opinions, strategies, and concepts are challenged and debated robustly in an open manner.

With insights gained from this advisory board meeting, Bayer gained deeper understanding of how the latest clinical data, emerging real-world outcomes and experiences, and current healthcare system challenges are affecting the approach and treatment choices of Ophthalmologists in clinical practice. Bayer also received insights into the economic imperatives and regulatory considerations that are reshaping the anti VEGF treatment landscape in the UK. Insights from this meeting will inform the business-critical decisions in shaping communication strategy as well as future data generation

strategies for aflibercept 8mg. These insights have been captured in the minutes of the meeting.

3. Scheduling of advisory boards

The Complainant stated that '*This was the second advisory board conducted, the previous only being conducted a few months prior on the 27th April 2023 in New Orleans'* and also '*Two advisory boards were conducted within 3 months of each other, both in parallel with congresses'.* Both statements are correct, however Bayer believes that there was a strong business justification for the ASRS advisory board on 31 July 2023, driven (i) by unanswered questions from the previous advisory board and also (ii) the release of new data at the ASRS meeting and (iii) new NHS England commissioning guidelines on 26 July 2023. The advisory board was therefore compliant with the Code, relevant PMCPA Guidance and Bayer SOPs. **It is also important to note that, as stated in the concept document, the advisory board at ASRS held on 31 July was only the second advisory board to be held by Bayer in this therapy area since the start of 2023.**

At the only other advisory board meeting in 2023, held alongside the Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting on 27 April, Bayer was advised that, while the latest Phase IIb/III data with aflibercept 8 mg were promising, further clarification of, and additional data on, durability and safety outcomes were required, [information gathered on named competitor]. This point was captured in the certified concept document for the ASRS advisory board. [general expectations of the advisory board in relation to a named competitor and NHS experience and real world data data]

Bayer does not believe that holding UK advisory boards in association with international congresses is in breach of the Code, providing careful consideration is given to the arrangements and all other requirements of the Code are met. Indeed, this is common industry practice and brings several advantages. Section 1 (above) discusses these advantages at length and sets out the steps taken by Bayer to consider the appropriateness of the advisory board held at ASRS, as recommended by PMCPA guidance. Section 4 (below) explains the rationale for selection of advisors from those clinicians attending the congress. In addition, we have already provided a strong rationale why an advisory board, and not informal discussions during the congress or individual consultancy agreements, were the only means of acquiring the insights which we sought to meet the stated objectives of the activity.

4. Selection of advisors

The Complainant stated that '*The number of participants was not limited to allow active participation by all'.* This is incorrect.

Robust selection criteria were applied to identify advisors for the advisory board. Expertise and experience in the subject matter of interest drove the identification process.

Bayer selects congress delegates with sufficient experience to appreciate the value of the data presented at congresses and sufficient seniority to share their insights and learning from the congress sessions with colleagues on their return, in order to advance local and national clinical practice and pursue new research avenues where appropriate. In some

cases, these clinicians will be presenting their own new data at the congress. These clinicians would fall under the definition of Exceptional, Tier 1 or Tier 2 thought leaders within the third-party Fair Market Value (FMV) tool used by Bayer Pharmaceuticals in the UK (more details of this tool are provided in section 7 below).

Exceptional thought leaders are defined in the tool as being amongst the most experienced clinicians in their field with '*international influence and a unique perspective'* but by definition there are few of them in the UK. Tier 1 thought leaders are defined as experts in their field with national or in some cases, international influence. Tier 2 thought leaders are experienced consultants who have wide clinical experience and important regional influence, although this is not yet national in reach. Any thought leaders from Tier 2 up to Exceptional would be considered suitable for consideration for advisory board participation because of their extensive clinical experience and knowledge of regional (all), national (Tier 1 and Exceptional) and international (Exceptional, more experienced Tier 1) clinical practice and likely future directions of travel.

The advisory board at ASRS was considered a national advisory board as it was convened to give insights into overall UK strategy. Typically, a national advisory board would have a majority of advisors at Tier 1, a smaller number at Tier 2 and perhaps one Exceptional thought leader.

The concept document shows that 8 advisors were selected as primary attendees for the advisory board meeting from a group of 15 consultant ophthalmologists who were all Tier 1 or 2 (or unassigned in the external FMV tool but considered Tier 1 or 2 by Bayer based on the criteria above) and already attending ASRS congress as Bayer-sponsored delegates. All the 8 primary advisors accepted the invitation. Of these, 5 were rated as Tier 1 by the FMV tool, 2 were rated Tier 2 by the FMV tool and one was unrated in the tool but worked at a major teaching and research centre and was considered by Bayer to be Tier 2.

- A total of 8 advisors is within accepted norms for advisory board numbers as it allows sufficient advisors to generate challenge and discussion, and contribute a range of viewpoints, whilst still allowing active participation by all present.
- Consideration was given to including a balanced geographic sp[r]ead of advisors from across the UK, important for a national advisory board as regional NHS practice varies: 2 advisors were from the north-west of England, 2 from the north-east, 2 from the south-east, one from the south-west and one from Scotland.
- Of the 15 total congress attendees, a further 4 (3 rated Tier 2; one unrated but judged to be Tier 2) were considered to be valuable alternative advisory board participants but (marginally) less appropriate for invitation based on their experience; these were therefore selected as secondary invitees in the event the primary advisors were unable or unwilling to accept the invitation.
- Location of the advisor would have been the major driver of which of these 4 secondary advisors were selected first in the event one or more of the primary advisors declined the invitation, to ensure a good overall geographic spread across the UK was maintained.
- A further 3 congress attendees (all Tier 2) were considered slightly less appropriate for invitation than the 4 secondary invitees, based on their experience. It was felt unlikely that we would be unable to find a suitable

minimum number of attendees to ensure a productive discussion with wide geographic coverage from a choice of 12 primary and secondary invitees, so these 3 individuals were not included on the concept document as alternatives.

- No advisors were taken by Bayer to the US only for the purpose of participating in the advisory board. None of the advisors invited to join the ASRS advisory board had been present at the previous advisory board held in April.

[Further confidential information about two advisors was given]

Attached is the full list of advisors who attended the advisory board meeting with the relevant reason for their selection, details of the work undertaken and the corresponding honoraria. [It] also sets out the second line invitees. In order to comply with data protection laws, we have redacted their names and places of work from both documents. If you feel that is not possible to verify Bayer's rationale for choosing the attendees without this information, please revert to us.

5. Invitation to advisors

The Complainant states that '*The invitation to participates [sic] did not clearly state the purpose of the meeting, the expected advisory role and the amount of work to be undertaken'.*

A certified invitation was issued to advisors in advance of the advisory board. The invitation states clearly that this meeting was an advisory board, the duration of the meeting from 14:30 – 18:00 and its location. The title of the meeting ('Considering forthcoming developments in the UK anti-VEGF treatment landscape') is provided along with more detail of meeting content, specifically that Bayer would be seeking feedback and advice on the latest phase III clinical trial data with aflibercept 8mg in nAMD and DMO and the implications for the launch of this product in the UK, and also that there would be discussion of real-world outcomes and experiences with [named competitor] and ranibizumab biosimilars in UK clinical practice. Bayer believes this is sufficient information for experienced clinicians to understand the workload required from them and the content of the meeting, and fully meets the recommendations of PMCPA guidance in this regard. It is not usual to share full agendas for advisory boards in advance of the meeting with invitees, as the contents are highly commercially sensitive and at the point of invitation a contract and confidentiality agreement with the advisor has not been signed.

6. Composition of advisory board; Bayer and other attendees:

The Complainant states that '*Bayer had members of the commercial team present'.* In fact, only one Bayer colleague with a reporting line into the commercial department attended the meeting. It is our belief that the Bayer attendees selected/attending were fully justified by the meeting content.

The details of the Bayer attendees at the advisory board are as follows:

Initials	Job title	Reason for attendance
	[Senior member of staff] Ophthalmology, Bayer	• Meeting chair • To deliver presentations to inform discussion • To contribute to discussion to gain advice on brand strategy for Eylea
	[Senior member of staff], Bayer	• To open and close the meeting • Contribution to discussions, ensure all questions answered in line with objectives
	[Member of Franchise Team] Ophthalmology, Bayer	• *Listed and approved in concept document but did not attend the meeting owing to personal reasons*.
	[Senior member of staff] Cell & Gene Therapy & Ophthalmology, Bayer	• Replaced [initials] in the meeting at short notice therefore not mentioned in concept document but minutes capture presence of [initials] • To contribute to discussion and to gain advice on medical strategy for Eylea relevant to Bayer global
Representative from medical communications agency partner	Medical Writer	• To facilitate the presentation of slide content (technical support only) and the writing of the post-meeting report

- The meeting was led and chaired by [initials], an experienced medical advisor, [qualifications and expertise] with expertise in presentation and discussion of scientific data in this therapy area. Bayer SOPs state that advisory boards including discussion of unlicensed products must be organised and led by medical personnel.
- [initials] is a [Senior member of staff] who is responsible for liaison with the medical communications agency partner and general organisation of congress attendance and speaker selection within Bayer UK. [initials] has a background as a health professional, [experience] and in their current role attends all ophthalmology advisory boards and all national and international scientific meetings and congresses, so is able both to contribute usefully to scientific discussions and to ensure the discussion is always exploring new ground rather than revisiting questions which have already been asked and answered in previous meetings. [initials] reports into the commercial function but works closely and cross-functionally with medical and is not in a sales or marketing role.
- [initials] is in a senior management role within ophthalmology marketing and was intending to be present to ensure the discussions answered key questions about future commercial strategy relevant to the launch of aflibercept 8mg and current marketing of aflibercept 2mg. Unexpectedly [initials] was unable to attend for personal reasons and their place was taken by [initials] at short notice. Questions relating insights relevant to commercial aspects of launch strategy were therefore picked up by [initials] on behal[f] of [initials]. Although it would never be appropriate for sales personnel to take part in an advisory board, participation by appropriately senior head office personnel in the

commercial department is not necessarily in breach of the Code, providing their presence can be justified by the objectives of the meeting.

- [initials] is a [health professional qualification] in a senior position within the medical division of Bayer Global; although not anticipated in the concept document, their presence at the advisory board was very useful to gather input relevant to global medical strategy and to answer clarifying questions from advisors on data and potential further analyses from global studies which were being presented.
- There were no Bayer participants at the advisory board with a role in sales.
- A medical writer from a third-party agency under contract to Bayer also attended the advisory board for the sole purpose of providing minutes of the meeting and attending to any audio-visual technical issues. They did not contribute to discussions. The third-party agency was the same agency which had organised the advisory board on behalf of Bayer.
- The ratio of company staff to advisors did not exceed 1:2 at any point. All company representatives had a substantive and identifiable role in the advisory board.

7. Remuneration of advisors

The Complainant states that '*Some participants were paid more than fair market value'.* This is incorrect.

The honoraria were calculated based on the hours of engagement and a validated third-party Fair Market Value (FMV) rate calculation tool [website link provided] which is used across all Bayer Pharmaceutical functions in the UK. See also Section 4 above for Tier definitions.

All advisors received the same honorarium payments, which were calculated at a rate of £[amount] per hour. This figure is well within the limits of what would be considered fair market value for their seniority and experience. The FMV rate calculation tool used by Bayer recommends a rate of no more than £[amount] per hour for advisory board consultancy for health professionals classified as Ophthalmology (retina) Tier 1, and no more than £[amount] for Tier 2. £[amount] per hour would be considered modest by these criteria.

These arrangements therefore did not amount to a pecuniary advantage or inducement to prescribe as defined by Clause 19.1 of the Code. Contracts for services were signed by advisors and Bayer before the advisory board, in line with the requirements of Clause 24.2 of the Code. The contracts clearly specified the services to be provided by the advisors and the basis of payment for those services. The expected hours of engagement were clearly documented. High standards were maintained.

8. Travel arrangements

The complainant did not raise any concerns related to the travel arrangements for clinicians attending the advisory board meeting, but in the interests of transparency and demonstrating Bayer's intent to comply with the requirements of clauses 10.1 and 5.1 of the Code, we would like to provide the following information concerning these arrangements.

The concept document for this meeting states that '*Travel to Seattle for HCP consultants participating in the advisory board under contract will be premium economy (refer to concept for delegate attendance) but in exceptional circumstances HCP contractors may be offered business class flights. Acceptable reasons for business class travel might be, e.g., medical issues requiring additional leg room to ensure safety and equality of participation opportunities. Any decision to offer a business class fare to an HCP contractor will require approval from a senior medical signatory within ophthalmology'.*

It is not usual practice for Bayer to offer business class travel to health professionals participating in advisory boards whilst attending an international congress with Bayer. Very exceptionally (there has been only one instance of this ever occurring in ophthalmology at the time of writing) an upgrade to a business class flight was organised for a US congress where there was a significant medical issue requiring this reasonable accommodation in order to allow safe long-haul travel and congress/advisory board participation by an advisor without detriment to their health. Such a decision would be taken at a senior level in the Bayer medical department with regard to the relevant personal circumstances. The concept document has been designed to allow for this exceptional circumstance should it arise again in future.

For this event, 6 of the 8 advisors travelled to and from the congress either with premium economy tickets purchased by Bayer or self-purchased tickets which were reimbursed by Bayer to the value of a premium economy return; 2 advisors travelled in business class with tickets purchased by Bayer because they were conducting other Bayer consultancy duties at the congress not linked in any way to the advisory board and covered in each case by a separate consultancy contract.

9. Pre-work:

The Complainant stated that '*There was no pre-work sent, you were invited to attend two optional lectures if you had time'* and also '*Expected preparatory work was optional'.* These statements are incorrect.

Attendees of the advisory board meeting were required to complete 1 hour of pre-work which comprised:

a) Attendance at a selection of presentations given at ASRS, chosen by the advisor at their professional discretion from a list of 10 presentations provided by Bayer. Not all presentations were on aflibercept, some were on [named competitor]. It was appreciated that for various reasons it would be unlikely for the advisors to be able to attend all presentations, but Bayer had full confidence that the advisors would discharge their professional duty in this regard and they were briefed accordingly. Data were selected for presentation for novelty and relevance to the topics under discussion at the advisory board.

b) To read a press release by Regeneron, to inform discussions during the advisory board, relating to two-year results for aflibercept 8 mg from the pivotal PHOTON trial; the press release was the only written source of these data available to Bayer UK at the time the advisory board was planned [3] [Two-year results for aflibercept 8mg from Pivotal

Photon Trial demonstrate durable vision gains at extended dosing intervals in diabetic macular edema. Link: website link provided: June 2023]

The concept document had originally proposed provision of a selection of advisory board slides as pre- work, but it was felt that attendance at presentations and exposure to critique of new data during the conference sessions, together with reading through new data from the PHOTON trial, would be more valuable in terms of informing advisory board discussions. A new pre-work schedule was therefore drawn up and certified before circulation to attendees. Further verbal briefings regarding pre-work requirements, based on the certified document, were conducted in person by Bayer medical staff with the advisors after arrival in the US to ensure the advisors understood what was expected. The medical advisor chairing the advisory board has confirmed that it was evident from the discussions during the meeting that all advisors had completed the prework as per the verbal and written briefings and had clearly attended the majority of presentations suggested.

10. Balance and suitability of agenda:

The Complainant stated that '*The presentation and discussion time during the meeting did not meet the requirements of an advisory board'* and that '*the agenda did not allow adequate time for discussion'.* This is incorrect.

The agenda consisted of three main components, all specifically designed to address the objectives set out for the advisory board. Due diligence was applied to minimise any presentation time on the agenda and maximise the time available for discussion. The agenda order had changed between the concept and the certified slide deck as the importance of discussion of new data on [named competitor] in RVO resulted in this topic being placed first on the agenda.

The total duration of the meeting was 3 hours and 30 minutes (210 minutes). Guidance from the PMCPA recommends that '*a significant majority of the time'* at advisory boards is spent on discussion/feedback rather than presentation. Bayer SOPs on advisory board conduct specify that 65-80% of the meeting should be spent obtaining advice.

i) Excluding the opening introduction (5 minutes) and the summary and close (5 minutes) there were three clinical presentations totalling 40 minutes. **Of the 40 minutes of presentations, only half (i.e., 20 minutes) related to aflibercept 8mg;** the other half was devoted to presentations on competitor products ([named competitor] and ranibizumab biosimilars).
ii) There was discussion time of 145 minutes excluding the coffee break (15 minutes) including one uninterrupted period of 75 minutes for discussion of adlibercept 8mg.
iii) Total presentation and discussion time was 185 minutes, exclusive of introduction, conclusion and coffee break ('active meeting time').
iv) Overall, 22% of the active meeting time was allocated to presentations and 78% to discussion.
v) Specifically, of the total active meeting time, only 11% was allocated to presentation of aflibercept 8mg data and 40.5% to discussion of aflibercept 8mg.

The above demonstrates that the agenda was designed to deliver adequate time for all advisors to share their insights and to allow detailed discussion and feedback. Presentation time devoted to aflibercept 8mg data occupied a minority (11%) of active meeting time and was thus proportional to the meeting objectives and not excessive. The requirements of the Code, the PMCPA Guidance on Advisory Boards and Bayer SOPs were all met.

11. Slide deck:

The Claimant asserts that '*the slides presented were pre-license [sic] promotion'* and that '*UK healthcare professionals were promoted to prior to grant of licence of the 8mg indication of Eylea.'* They also assert that '*The advisory board was not a genuine advisory board'* but an attempt to '*[warm] the market for the new Eylea indication'.* Bayer denies such claims.

A slide deck reel for the advisory board meeting was reviewed and certified before the advisory board meeting. The scientific contents of the slides were relevant and aligned to the objectives stated in the agenda. The number of slides were optimal to provide an overview and inform the subsequent discussion that followed these presentations.

The slides covered data available in advance only for background and context, but the discussion was devoted mainly to new data presented at the congress at sessions attended by the advisors as part of pre-work. These superseded the relevance of the data presented on the slides. For example, the [named competitor studies] data included in the slide deck reflected data presented at ARVO in April 2023, however the advisors attended sessions at ASRS as part of their pre-work, which provided further updates to these data. This pre-work therefore played a significant role in the discussion to inform how [named competitor] was performing in real world practice over a longer period of time, with an increased number of patients and centres recruited since the last data presentation at ARVO, thus providing further and more valuable context to the discussion – something that had been flagged as a need at the previous advisory board held in April 2023. Similarly, the slides included in the deck for the aflibercept 8mg PHOTON year 2 data covered the contents of the press release provided as pre-work, whereas the actual data presentation of PHOTON, recommended for attendance in pre-work, was a late breaking 96-week data presentation with much more detail which formed the basis for most of the discussion.

In total, 13 slides were presented on clin[i]cal data on [named competitor] in RVO in the first session and 10 slides were presented in second session on [named competitor] and (ranibizumab) biosimilars in clinical practice, including the licensed posology but excluding introductory, title and question slides. Finally, 55 slides were included for the third session on aflibercept 8mg clinical data (including posology) although not all were presented. The meeting chair [initials], who also presented the slide deck, confirms that 37 slides of these 55 were presented (including posology slides) with the remainder being hidden or skipped. In some places the slides were skipped because the pre-work made reference to them unnecessary; in other cases, the topic was dropped from the agenda in order to allow more discussion of other topics such as [named competitor] in RVO (data for aflibercept 8mg in PCV, a subtype of nAMD, were not discussed at all, as recorded in the minutes. 70 slides (excluding title slides) were included in the slide deck clearly marked as backup. These backup slides were certified as part of the reel and available at the discretion of the

presenter/Chair, [initials], in the event that an advisor raised a scientific query during the discussion requiring a response. The backup slides were not presented to the advisors or provided to advisors proactively.

ABPI's advisory board guidance states that '*Discussion of clinical data about a particular medicine should only take place at an advisory board if such discussion is essential to meet the stated objective.'* New clinical data often relates to pre-licence products and (as demonstrated by the ABPI guidance) discussion of it does not automatically make an activity promotional. Clinical data on an unlicensed product were discussed at this advisory board, but such discussion was essential in order to achieve the objectives set out at points 2(a) and 2(b) above.

Discussion about clinical data was not limited to aflibercept but also included [named competitor] and biosimilars of ranibizumab, including the potential impact of the newest biosimilar entrants to the UK market. This further reinforces that the aim of the meeting was to understand this complex and evolving market as a whole and how the approach and treatment choices of ophthalmologists in clinical practice may change. In order to garner the opinion of experts in relation to the likely response of users to new products and indications, it is necessary to discuss clinical data. Insights from this meeting will inform the business-critical decisions in shaping communication strategy as well as future real-world data generation strategies and post-hoc analyses of phase III data for aflibercept 8mg. These insights have been captured in the minutes of the meeting.

Conclusions

The Complainant made several allegations that this advisory board was promotional. Bayer strongly denies that this advisory board constituted promotion, whether off-label, on-label or disguised.

- The field of medical retina is undergoing significant change both in terms of the introduction of new products and changes in commissioning practices. Within this context, it is essential that Bayer obtains effective and timely advice, especially in regard to the future authorisation of aflibercept 8mg which differs markedly from the 2mg formulation in terms of both clinical and practical considerations. The rationale for the advisory board was therefore legitimate and addressed questions that could not be answered at previous meetings because new data had since become available (in some cases presented for the first time at the congress where the advisory board was held). No other route of gaining insights would have satisfactorily met the stated objectives of the meeting.
- Updated NHS commissioning guidance on biosimilars had very recently been published and clinical practice and experience in this therapy area is evolving unusually rapidly owing to an unprecedented number of new market entrants over a short period of time.
- The advisory board held at ASRS was only the second advisory board in this therapy area held in 2023, which in the view of Bayer is not excessive frequency in a rapidly evolving therapy area.
- The presentation of data was balanced, non-promotional in nature and limited to those data relevant to meet the objectives of the meeting. Presentation of data on aflibercept 8mg formed a minority of the active meeting time (11%). Several competitor products were also discussed, including new data/guidelines relating

to these products. The agenda devoted a significant majority of the time available to discussion. Suitable pre-work was provided.
- All participants (internal and external) that attended the advisory board had clearly defined roles and the ratio of Bayer to health professional attendees was not excessive. No sales personnel were in attendance.
- The minutes available following the meeting confirm that the discussions met the stated objectives.

There was thus no breach of Clauses 3.1 or 3.6 of the Code.

Further, Bayer submits that the venue and other arrangements were appropriate and conducive to the main purpose of the meeting.
- Providing other requirements of the Code are met, conducting UK advisory boards at international scientific symposia is not specifically restricted by the Code nor PMCPA Guidance. Indeed, this is common industry practice, having significant advantages in term of the quality of discussion and outputs that can be achieved, as well as time efficiency for advisors and minimisation of absence from clinical work. Companies are required to carefully consider the suitability of the arrangements where an advisory board is held in conjunction with a congress, and we have shown that this was done.
- No advisors were supported to travel to the US by Bayer solely for the purposes of attending the advisory board and the travel arrangements were appropriate to congress attendance and would not encourage participation in the advisory board. Bayer therefore denies that the meeting arrangements were in breach of Clause 10.1.

Advisors were selected according to their relevant expertise and experience, and to give appropriate geographic balance to the discussions. Advisors were remunerated under contract and in line with fair market value for their professional time. Appropriate invitations were issued in advance of the meeting. No other form of interaction with the advisors would have delivered the required output to fulfil the objectives of the advisory board. Bayer therefore denies that the arrangements for this meeting breached Clauses 19.1 or 24.2 of the Code.

Bayer maintains that the intent, planning and conduct of the advisory board was to the highest standard possible. Bayer considers that the way in which the advisory board was developed and held was in accordance with the letter and spirit of the Code, internal SOPs and PMCPA guidance on advisory boards. Clause 5.1 was not breached.

Summary

The Bayer meeting held on 31 July was a *bona fide* advisory board with clear objectives held for legitimate reasons in accordance with the Code, additional PMCPA guidance and relevant Bayer SOPs. All arrangements and materials for the meeting were reviewed and certified in advance to be in accordance with the requirements of Code and specifically the requirements of Clauses 3.1, 3.6, 10.1, 19.1 and 24.2.

High standards were maintained by Bayer at all times. There was nothing in the arrangements to bring discredit upon or reduce confidence in the pharmaceutical industry.

Bayer therefore considers that the arrangements for this meeting do not breach Clauses 2 or 5.1 of the Code."

FURTHER RESPONSE FROM BAYER

The PMCPA wrote to Bayer for further information. The response from Bayer is reproduced below:

"Thank you for your email of 28 October 2024 requesting further information from Bayer in relation to the complaint in Case AUTH/3809/8/23. We are pleased to provide the information you requested.

1. *Copies of the written, signed contracts with each of the advisors* - all 8 contracts from the ASRS 2023 advisory board are appended, redacted only to remove names, emails, addresses and bank details where appropriate for confidentiality.

2. *A copy of the 'press release by Regeneron' submitted to have formed part of the preparatory work* – this was previously included in Bayer's original letter of response to this complaint (01 September 2023) via hyperlink.

3. *A copy of the updated NHS commissioning guidelines of 26 July 2023 referred to in Bayer's letter of response* - this was previously included in Bayer's original letter of response to this complaint (01 September 2023) via hyperlink.

    a) Please confirm whether Bayer had sight of the guidelines, e.g. a draft version, prior to the date of publication

    To the best of Bayer's knowledge, Bayer did not have sight of the updated NHS England commissioning recommendations in draft form prior to their publication in July 2023. In our experience, it would be unusual for NHS England to seek input from pharmaceutical companies on commissioning guidance at the pre-publication stage. For further context and clarity regarding the inclusion of this document in the July 2023 advisory board, Bayer would like to make the following points:

    - At the time of the July 2023 advisory board, Bayer expected the growing number of ranibizumab biosimilars to increase the impact of biosimilars on NHS commissioning practice in retina. Biosimilar use in medical retina was still continuing to evolve significantly in 2023, and ranibizumab biosimilars had not been addressed in Bayer's previous 2023 advisory board (April 2023), as can be seen in the outputs of that meeting.

    - The publication of updated NHS England commissioning recommendations in July 2023, less than a year after the original version was issued in August 2022, is a clear example of the rapid changes occurring in this area within the NHS in 2022 – 2023..

    - Biosimilars to ranibizumab were therefore still of high relevance to Bayer in 2023, and advice from experienced UK clinicians was required to shape Bayer's strategy in a rapidly changing commissioning landscape. As a result,

this topic was included in the July 2023 advisory board meeting, even before the updated NHS England commissioning recommendations were published.

b) Please also confirm that the only change related to the introduction of Ximluci as indicated in Bayer's response

The original NHS England commissioning recommendations for medical retinal vascular medicines, issued in August 2022, have now been superseded by the updated recommendations from July 2023. Only the most recent recommendations are currently available on the NHS England website. However, we are pleased to attach a PDF copy of the original August 2022 version, which was downloaded at the time. There are some formatting changes between the August 2022 and July 2023 versions, including a more prominent positioning of biosimilars to ranibizumab among the main list of approved medicines for these indications. However, the main difference in content between the two versions is the inclusion of Ximluci in the July 2023 update.

4. Copies of the concept form, slides and output from the April 2023 advisory board referred to in Bayer's letter of response - concept form, slides and output (minutes) from the April 2023 advisory board are attached as requested. These have been redacted only to remove names and locations of attendees, as appropriate for confidentiality.

For further context and clarity, Bayer would like to make some additional points in relation to the April 2023 advisory board meeting materials:

- [Information about named competitor]
- The advisers in April 2023 highlighted the importance to Bayer's strategy of longer-term (2 year) phase III data on aflibercept 8mg, beyond the 48-week data available at the time, in order to characterise the product's durability (ability to extend intervals between treatments) and to deternine whether vision outcomes can be maintained with less frequent injections long term, even in the presence of some fluid. By the July 2023 advisory board, 96-week data for aflibercept 8mg had recently become available, including interval extensions to 20 weeks. These new data were included in the July agenda so that Bayer could obtain insights from the advisers to assess the data's strengths, weaknesses and significance to future strategy and communications.
- Meeting slides: Please note that slides 95 to 174 are backup slides only. These slides were certified as part of the reel and were available at the discretion of the presenter/Chair in the event that an adviser raised a scientific query during the discussion that required a response supported by data. The backup slides were not proactively presented to the advisers nor proactively provided to them.

I trust that this additional information assists the Panel in its deliberations regarding this case. Please contact us again if you require anything else from Bayer."

PANEL RULING

This case was in relation to a Bayer advisory board that was held in the USA on 31 July 2023 during an American Society of Retina Specialists (ASRS) conference which the health professionals were already attending as Bayer sponsored attendees. Bayer submitted that its medicine, Eylea (aflibercept) had been available in the UK since 2012 in a 2mg dose formulation in vial and pre-filled syringe formulations for a number of indications. At the time of the conference a new marketing authorisation for an 8mg dose of Eylea was being considered for the treatment of neovascular (wet) age-related macular degeneration (nAMD) and diabetic macular oedema (DMO) and Bayer submitted that it wanted to seek insights from the clinical community on a number of questions it needed answering before its launch. Bayer submitted that the marketing authorisation for the 8mg dose was expected in quarter 1 of 2024. The complainant's allegations related to multiple aspects of the meeting, including the rationale for it and whether the arrangements were such that it was a legitimate advisory board.

The Panel noted that it was acceptable for companies to pay health professionals and others for relevant advice so long as the arrangements complied with the Code including the consultancy arrangements set out in Clause 24 of the 2021 Code. It was important that when a company interacted with health professionals as consultants rather than prescribers that the arrangements withstood independent scrutiny given that such arrangements invariably involved payment. To be considered a legitimate advisory board the company must have a legitimate unanswered business question which the company could not itself answer. The selection and number of participants should stand up to independent scrutiny; each should be chosen according to their expertise such that they would be able to contribute meaningfully to the purpose and expected outcomes of the advisory board. The number of participants should be limited so as to allow active participation by all. The agenda should allow adequate time for discussion. The number of meetings and the number of participants should be limited and driven by need and not the invitees' willingness to attend. The nature of the meeting should be made clear to invitees and participants: invitations to participate should clearly state the purpose of the advisory board meeting, the expected advisory role and the amount of work to be undertaken. If an honorarium was offered, it should be made clear that it was a payment for such work and advice. Honoraria must be reasonable and reflect the fair market value of the time and effort involved.

The Panel noted the complainant's concern that the participants of the advisory board were also sponsored by Bayer to attend the ASRS conference and in the complainant's view this contradicted PMCPA guidance on advisory boards and they alleged that the integrity of the advisory board was thereby compromised. The Panel noted that whilst there was no prohibition on holding an advisory board during a conference or similar event, it was particularly important to ensure that the arrangements complied with the Code, that the non-promotional nature of the event was clear and to be mindful of the impression created by the arrangements given that invariably advisors were paid for attendance. Whether such arrangements were acceptable would be decided on a case-by-case basis.

<u>General comments about the advisory board arrangements</u>

In the Panel's view, certain aspects of the advisory board did not appear to be unreasonable. In this regard, the Panel noted that the complainant had raised concerns that the number of participants did not allow for active participation by all. The Panel noted that the concept

approval form dated 28 June 2023 showed that 8 advisors were confirmed attendees from a group of 15 ophthalmologists who were all Tier 1 or 2 experts and already attending the ASRS conference as Bayer-sponsored delegates. Bearing in mind the agenda and the time allocated for discussion, the Panel did not consider that 8 advisors was unacceptable.

The Panel noted the complainant's concern that some participants were paid more than fair market value and noted that Clause 24.2 required remuneration to be reasonable and reflect fair market value. The Panel noted that the advisors were renumerated equally for their time at the meeting at a rate of £[amount] per hour which included 1 hour dedicated to the pre-work; this totalled £[amount]. The Panel noted Bayer's detailed submission about selection of advisors, their levels of expertise and payment, it selected and invited advisors already attending ASRS who also possessed the necessary qualifications and experience to contribute usefully to the advisory board discussions. Whilst the Panel had concerns about aspects of the overall arrangements and particular concerns about whether any payment at all was acceptable as outlined below, the Panel considered that it had no evidence before it to establish whether the level of payment offered was unacceptable when considered in isolation given the expertise required to participate in the advisory board.

The Panel firstly considered whether overall the arrangements constituted a valid advisory board noting the complainant's allegation that Bayer did not have a legitimate unanswered business question and was warming the market for the new Eylea indication. In this regard the Panel noted that the response provided more detailed information than outlined in the invitation and the advisory board concept form. The Panel also bore in mind that Bayer already had certain internal expertise in this therapeutic area given Eylea was licensed for the 2mg dose.

The Panel noted that the approval concept form for the advisory board in question described 3 objectives: to seek expert feedback and advice on the latest Phase IIb/III clinical data with aflibercept 8 mg for nAMD and DMO, and practical implications for its UK launch; to seek perspectives on new Phase III competitor data in RVO; and to share and discuss real-world outcomes and experiences with a competitor and ranibizumab biosimilars in UK practice. The Panel noted that Bayer's response in addition referred to differences between the 2mg and 8mg Eylea doses, updated NHS commissioning guidance and that clinical experience in this therapy area was evolving unusually rapidly owing to an unprecedented number of new market entrants over a short period of time.

When deciding whether the standalone objectives for the advisory board in question were legitimate the Panel considered that it was particularly relevant that according to the advisory board concept forms for the meeting at issue and one held in April 2023, a number of advisory boards had already taken place in this therapeutic area in 2022 in quick succession; one in Quarter 2, two in Quarter 3 and one in Quarter 3/Quarter 4 and a further four had been planned for 2023. The July 2023 advisory board at issue was the second of these in 2023. All of these meetings were timed to coincide with a conference or event and all related to Bayer's medicine aflibercept (2mg and 8mg). The meetings which took place in 2022 were, Bayer submitted, to gain timely feedback on new Phase III data. The Panel noted that this was also an objective for the April 2023 and July 2023 meetings and the Panel was generally concerned about significant similarities in the meetings' objectives in relation to ranibizumab biosimilars, a named competitor and Eylea 8mg clinical data. The Panel noted that the number of advisory board meetings should be limited and companies should have robust reasons for holding more than one meeting on a similar subject matter. The Panel noted that the concept form for the meeting in question stated that it was 'crucial that Bayer gains regular up to date feedback on real world

outcomes and experiences' with a competitor. The Panel queried whether a series of advisory board meetings was the appropriate mechanism to receive such regular updates unless it could be demonstrated that each meeting, as a standalone event, complied with the Code.

The Panel noted that new data releases and post hoc analyses from ongoing trials were presented for the Eylea 8mg dose at the July conference and noted Bayer's submission about the relevance of this data to an advisory board objective. Data presented at the April 2023 conference was also discussed at the advisory board in question. The Panel noted Bayer's assertion that a reason for the July 2023 advisory board was that since the April 2023 advisory board clinicians, in the intervening period, would have greater NHS experience of a competitor. The Panel queried whether meaningful NHS experience would have been obtained in the intervening 2 months that elapsed since the April 2023 advisory board such as to justify an advisory board objective. The Panel also noted the submission that new data on the competitor from ongoing real world evidence studies was presented at the July 2023 advisory board.

The Panel noted Bayer's submission about the advisory board objectives and the need to discuss the 'updated NHS commissioning recommendations for medical retina vascular medicines following the national procurement for ranibizumab biosimilars'. The Panel noted that the main update appeared to relate to the addition of a fourth ranibizumab biosimilar, Ximluci, and queried whether there was a genuine need for advice on this.

The Panel noted that one of the criteria set out in Clause 24.2 in relation to consultancies is the legitimate need for services to be clearly identified and documented in advance of requesting the services and entering into arrangements. The Panel was concerned that Bayer had planned to hold an advisory board meeting before understanding what the legitimate unanswered business question was that could not be addressed either within the company or by a preceding or subsequent advisory board. It appeared from the documentation provided by Bayer that plans had been made to hold and approve these meetings throughout the year to coincide with other events before it properly understood whether there were sufficiently robust reasons to support each individual meeting within the series.

The Panel therefore queried whether, within the context of a series of meetings in 2022 and 2023, there were robust legitimate standalone objectives to support the advisory board at issue in 2023.

Invitation and preparatory work

The Panel noted the complainant's concern that the invitation did not clearly state the expected purpose of the meeting and the expected advisory role. The invitation dated Friday 30 June 2023 was headed "Considering forthcoming developments in the UK anti-VEGF treatment landscape". The purpose of the meeting was subsequently described as "to gain feedback and advice on the latest Phase III clinical data with aflibercept 8mg for nAMD and DMO, and practical implications for its UK launch. In addition, Bayer aims to share and discuss real-world outcomes and experiences with [a competitor] and ranibizumab biosimilars in UK clinical practice." The Panel considered that the heading to the invitation set the tone for the invitation and implied that the recipients were invited to a standard company meeting as delegates rather than participants. The Panel accepted that this was qualified by the subsequent reference within the body of the invitation which referred to gaining feedback and advice, but noted this was limited to Eylea data. The Panel considered that it was not clear that the reference to Bayer aiming to "share and discuss real-world outcomes and experiences with…biosimilars in UK

clinical practice" was a subject on which the company sought advice from participants. This lack of clarity was compounded by the heading. The reference to an honorarium for participation might be considered by some to relate solely to their feedback and advice on Eylea. Overall, the Panel considered on balance that the invitation was not sufficiently clear.

The Panel considered that the invitation should be capable of standing alone in relation to the requirements of the Code but further noted that the contracts signed by the advisors made the consultancy arrangements clear.

The Panel noted the complainant's concern that the expected preparatory work was optional. The Panel considered that whilst preparatory work was not mandatory its omission or requirements might on occasion be relevant when considering the overall legitimacy of an advisory board. The Panel noted that the documents before the Panel gave differing accounts of what the preparatory work included.

The email template dated 13 July 2023 sent to advisors who had contractually agreed to participate included a document attachment listing the relevant presentations taking place at ASRS which were expected to inform the discussions that would take place at the advisory board meeting. The email also went on to state: "we completely understand that it may not be feasible for you to attend all presentations; however, we do kindly request that you try to attempt a selection of presentations from the attached list and provide your insights at the meeting". A list of ten presentations concerning Eylea and a competitor were provided however attendance was encouraged rather than mandatory. Bayer submitted that it had full confidence that the advisors would discharge their professional duty in attending the presentations as outlined and that the medical advisor chairing the advisory board confirmed that it was evident from the advisory board discussions that advisors had completed the prework. The Panel accepted that the minute of the meeting demonstrated that a clinical discussion had taken place but did not consider that it was clear whether every advisor had attended the requisite presentations. Within the list of presentations was a pre-reading link to a five-page press release, the reading of which was similarly not mandatory. The Panel noted that the section of the advisory board concept form which covered pre work to be completed by the advisors stated that a version of the slide deck would be provided to attendees as a pre-read to minimise presentation time and inform discussion. It was, however, wholly unclear from the evidence provided whether this was done as it was not referred to in either Bayer's response nor other documentation. The concept form indicated that the pre read of the slides should take one hour and it appeared that such pre reading was mandatory. In addition, the Panel noted that the Annex Scope of Services to the consultancy contracts described the pre-work as 'attending specific sessions at the congress' for which the estimated preparation time was one hour.

The Panel considered that, overall, both the content and optional or mandatory nature of the pre-reading was unclear. This was of particular concern given that the participants were paid for one hour's preparatory work, and the meeting was approved on the basis that the preparatory work comprised a version of the presentation. The basis of any payment to health professionals should always be abundantly clear.

Further considerations

The Panel noted the complainant's concern that the presentation and discussion time did not meet the requirements of an advisory board. The Panel noted Bayer's submission that the agenda was split into 3 components, all designed to address the advisory board objectives. The

Panel noted that the presentation time (excluding the opening and closing times) totalled 40 minutes and discussion time (excluding the coffee break) totalled 145 minutes – overall, the advisory board was made up of 22% presentation time and 78% discussion time which the Panel considered was on the outer limits of acceptability. Bayer submitted that the agenda was designed to deliver adequate time for all advisors to share their insights and to allow detailed discussion and feedback. The Panel noted that the slide deck for the advisory board consisted of 188 slides – 78 slides were "backup" slides, 109 slides contained content for the advisory board and 16 of these slides were title pages. Whilst the Panel was concerned about the overall number of slides from Bayer's submission it appeared that 60 slides were presented on the day and given the presentation time and the number of slides actually presented, did not appear to be unreasonable.

In relation to the number of Bayer attendees, the Panel noted Bayer's submission that the attendees selected, and attending were fully justified by the meeting content and the ratio of Bayer staff to advisors did not exceed 1:2 at any point. The Panel, whilst accepting that a certain level of staff attendance was required, queried whether a ratio of 1:2 was acceptable.

Clause 24.2

Whilst noting that certain elements of the advisory board did not appear to be unacceptable as referred to above, the Panel, bearing in mind the cumulative effect of its various concerns outlined above, did not consider within the context of a series of similar advisory board meetings that the July advisory board was a genuine advisory board. The Panel noted its concerns about objectives and payment of health professionals in this context including payment of preparatory work. The Panel noted the requirements of Clause 24.1 and the concerns raised by the complainant: that a legitimate need for the services must be clearly identified (and documented in advance of requesting the services); the hiring of the contracted party must not be an inducement to prescribe, supply, administer, recommend, buy or sell a medicine. The Panel **ruled breaches of Clause 24.2 in relation to each matter**.

Clause 19.1

The Panel noted the supplementary information to Clause 19.1 which stated "Any payment to an individual for an activity that is ruled in breach of Clause 24 and/or Clause 25.4 is likely to be viewed as an unacceptable payment and thus in breach of Clause 19.1". The Panel also noted its view above that the arrangements were not a genuine advisory board. The Panel considered that where health professionals had been paid to attend a meeting about medicines (including payment for preparatory work) which was not a genuine advisory board and which had also been ruled in breach of Clause 24.2, that payment was contrary to the requirements of Clause 19.1 as an inducement to prescribe, supply, administer, recommend, buy or sell a medicine. The Panel therefore ruled **a breach of Clause 19.1**.

Clause 3.6

Clause 3.6 states materials and activities must not be disguised promotion. In this regard, given the Panel's decision that the arrangements were not a genuine advisory board, that the payment amounted to an inducement to prescribe, supply, administer, recommend, buy or sell the medicine, noting these rulings and bearing in mind the definition of promotion at Clause 1.17 of the Code, the Panel considered on balance that the promotional nature of the advisory board had been disguised. The Panel ruled a **breach of Clause 3.6**.

Clause 3.1

The Panel noted that Eylea 8mg was granted marketing authorisation in the UK on 19 January 2024, which was after the July 2023 advisory board. On this basis, and noting its rulings above, the Panel considered that Eylea 8mg was promoted prior to the grant of marketing authorisation and ruled a **breach of Clause 3.1**.

Clause 10.1

The Panel noted the supplementary information to Clause 10.1, "Events/Meetings held Outside the UK", stated that meetings organised by pharmaceutical companies which involved UK health professionals at venues outside the UK were not necessarily unacceptable. There had, however, to be valid and cogent reasons for holding meetings at such venues. These were that most of the invitees were from outside the UK and, given their countries of origin, it made greater logistical sense to hold the meeting outside the UK or, given the location of the relevant resource or expertise that was the object or subject matter of the meeting, it made greater logistical sense to hold the meeting outside the UK. Consideration should be given to the use of technology to avoid travel outside the UK, e.g. webinars, virtual meetings.

The Panel considered the contracts and observed that the advisors were not renumerated under the consultancy for their hotel stays nor was there any suggestion of the venue being lavish or extravagant. The Panel considered that the meeting of UK health professionals could have been held in the UK and the importance of using technology in this regard. Noting Bayer's detailed response on this point, whilst the Panel had some concerns about the arrangements as outlined above, on balance, the Panel did not consider that the complainant had established that the arrangements were contrary to the supplementary information to Clause 10.1 and on this point ruled **no breach of Clause 10.1.**

Clauses 5.1 and 2

The Panel considered that the cumulative effect of Bayer's actions meant that it had made payments to eight health professionals to attend a promotional meeting. The content of which related to a product which at the time did not have marketing authorisation. Bayer had therefore failed to maintain high standards and a **breach of Clause 5.1** was ruled.

The Panel noted that Clause 2 was reserved for use as a sign of particular censure which, according to its supplementary information, included matters of inducement to prescribe and promotion prior to the grant of a marketing authorisation. The Panel noted that the minutes of the advisory board indicated that a discussion about certain scientific matters had taken place. The Panel noted that not all aspects of the advisory board were unacceptable in relation to the requirements of the Code. However, bearing in mind its comments and rulings above the Panel, noting that the supplementary information to Clause 2 referred to unacceptable payments, inducements to prescribe, and promotion prior to the grant of a marketing authorisation as examples of activities that were likely to be in breach of Clause 2, decided that the arrangements had brought discredit to and reduced confidence in, the pharmaceutical industry. A **breach of Clause 2** was ruled.

BAYER'S APPEAL

"Thank you for the PMCPA's letter of 31 January 2025, notifying Bayer plc ("Bayer") of the initial outcome of the above case relating to an ophthalmology advisory board held on 31 July 2023. Further to our previous letter of 10 February 2025, Bayer would like to appeal all breaches ruled in this case (clauses 24.2 (x2) 19.1, 3.1, 3.6, 5.1 and 2) and to attend the hearing of the Appeal Board in due course.

Bayer takes its responsibilities to abide by the ABPI Code of Practice ("the Code") and to maintain high standards within our industry very seriously.

The Panel's ruling of multiple breaches of the Code appears to rest chiefly on its view that the 31 July 2023 advisory board subject to complaint was not legitimate and was, in fact, a promotional meeting. Bayer wishes to challenge this opinion at appeal and demonstrate that this advisory board was, in fact, legitimate and not a promotional meeting either in intent or execution.

In our response, Bayer will address other concerns raised by the Panel which contributed to their view of the advisory board meeting as promotional. Bayer will also highlight areas where the ruling in Case AUTH/3809/8/23 appears inconsistent with previous Code case precedent that has shaped Bayer's interpretation of the Code and PMCPA guidance in terms of what constitutes high standards for advisory board conduct.

Accordingly, Bayer would be grateful for the Appeal Board's fresh scrutiny of evidence supporting the legitimacy of the 31 July 2023 advisory board.

[Bayer raised confidentiality matters]

Summary of grounds for appeal

The meeting held on 31 July 2023 was a legitimate advisory board. Expert advice was required, obtained and documented in the minutes on a number of anti-VEGFs - not just aflibercept.

- Inclusion of aflibercept 8mg on the agenda was justified by business need and thus was not pre-licence promotion nor was there disguised promotion.
- Aflibercept 8mg is a very different product to 2mg, in terms of formulation, pharmacokinetics, posology and NICE appraisal status.
    - [information relating to use of 2mg and 8mg]
- In 2022-23, Bayer was preparing to launch 8mg into a very rapidly changing UK medical retina environment with evolving clinical understanding of multiple new competitors:
    - [Bayer provided information on what could impact the launch of 8mg]
- While the Panel referenced previous advisory boards, it is crucial to note that the context and specific questions addressed at each meeting were distinct. The evolving nature of the anti-VEGF treatment landscape meant that even topics appearing similar in outline could yield very different insights over time. Bayer's approach to monitoring these changes through these discussions was both strategic and necessary.

  - The Panel was, respectfully, in error in stating that only 2 months elapsed between meetings in April and July 2023.
  - The timing of the July meeting vs the April meeting was of demonstrable clinical and business relevance
  - Apparent similarity of top-line topics (appearing in concept documents for other meetings) does not equate to similarity of detailed content or outputs - especially not in the context of a dynamic market/data environment.
  - Advisory boards tentatively considered in advance ("TBC") are reviewed nearer the time to confirm legitimate business need; not all will take place.
- The total number, selection and justification of the role of participants was deemed acceptable by the Panel.
- Bayer's rationale for holding advisory boards at international congresses was not disputed by the Panel.
- The ratio of Bayer staff:advisers was 1:2, consistent with ratios previously deemed acceptable in Code case precedent.
- 78% of meeting time was spent in discussion, a "significant majority" of the agenda consistent with PMCPA guidance; the number of slides presented was deemed reasonable by the Panel.
- The invitation was clear that the 31 July 2023 meeting was an advisory board and not any other type of meeting:
  - Prominent identifying wording ("Bayer advisory board") was used in invitation email title, invitation heading and contract heading, but this was not mentioned in the ruling – a misleading omission.
  - There was no possibility advisers could have been left uncertain as to the nature of the meeting nor the services they were being contracted to provide.
- All advisers were contracted in advance and remunerated for their time in line with Bayer fair market value guidance in the UK and Clause 24.2. The Panel accepted the contract was clear. Honoraria offered were very modest in terms of permitted FMV (less than half acceptable maximum) and the total reimbursement justified by the total work required. There was no inducement to prescribe.
  - Pre-work occupied 1 hour. Completion of pre-work was documented in 3 places in the meeting minutes; the complainant's specific assertions that there was *"no"* pre-work and only *"two optional lectures"* set as pre-work are not supported by evidence.

Detailed appeal reasoning

In page 2 of its ruling of 31 January 2025, the Panel has listed nine conditions under which an advisory board can be considered a legitimate, nonpromotional activity. Bayer reproduces these below and would like to take each point in turn as they apply to the advisory board held on 31 July 2023, in order to address the concerns raised by the Panel.

1. **The company must have a legitimate unanswered business question which the company could not itself answer.**

Lack of relevance of aflibercept 2mg experience to aflibercept 8mg strategy

Bayer notes the comment of the Panel that *"Bayer already had certain internal expertise in this therapeutic area given that Eylea was licensed for the 2mg dose".* Bayer would like to

draw the attention of the Appeal Board to the points made on pp2-4 of Bayer's original response to the PMPCA of 1 September 2023 [A] about the features of aflibercept 8mg and its significant differences from aflibercept 2mg, the points on pp 7-8 [A] relating to the relevant outputs from the advisory board [B] and Table 1 summarising the differences between 8mg and 2mg, with relevance to advice needed.

Aflibercept 8mg is a very different formulation to 2mg, not simply a higher dose [Table 1] and these differences have direct clinical implications e.g. formulation, presentation, pharmacokinetics, dosing regimen. These factors necessitated expert input to inform Bayer's launch strategy, as can be seen from the minutes [B], and examples are given below.

At the July 2023 advisory board, advisers recommended that Bayer prepared a simple primer on the pharmacokinetic rationale for 8mg for UK clinicians, as pharmacokinetics as a topic is often not well understood [B, p20 – action now completed by Bayer, publication pending]; advisers also made detailed clinical recommendations [B p28] relating to injector training, drug naming in patient electronic records, practical steps to avoid confusion between 2mg and 8mg in clinic and suggestions for an 8mg pre-filled syringe, all relevant to NHS practice and patient safety.

The 8mg product was also preparing for launch (early 2024) in a rapidly evolving competitive and pricing environment through 2022-2023, vastly different to the landscape in any of the preceding years since the launch of aflibercept 2mg, [general information about a competitor and the market]

Bayer was thus preparing to launch aflibercept 8mg in a rapidly evolving competitive environment marked by the introduction of therapies such as [named competitor] and various ranibizumab biosimilars. Input from advisers was sought and received [B, pp10-18] on factors affecting drug choice, practical implications of switching treatment, patient consent, stock/supply chain issues and impact of longer treatment intervals on clinic capacity.

This context underscores the need for timely expert insights in 2022 – 2023 to navigate the complexities of market entry and positioning, and to ensure patient safety.

<u>Rationale for seeking advice via an advisory board vs other means</u>

Bayer will not restate but would like to draw the attention of the Appeal Board to p9 of its original submission [A], containing a detailed rationale for seeking the required advice in an advisory board, and not by other means.

<u>Apparent repetition of similar topics across different advisory boards</u>

The Panel points out that several advisory boards in 2022 – 2023 appeared to cover similar topics. However, the Panel's view of these other meetings was based solely on topline summaries of previous advisory board content listed in the two concept documents of the April and July advisory boards. With respect, whilst the topics might appear superficially similar in concept documents pertaining to other meetings, similar topics may result in very different outputs over time in a dynamic area, nor is it possible to assess

differences in detailed meeting content from such limited information. Prior Code case precedent shows multiple advisory boards are acceptable, even across short time periods, if justified by business need e.g. Case AUTH/3158/2/19 [1].

For example, the July 2023 advisory board involved significant discussion of new longer-term data and clinical experience with various products, including aflibercept 8mg (e.g. 96-week data in DMO [B]) and [named competitor], as discussed below. A key factor in anti-VEGF injections is the dynamic interval between treatment doses, as the disease fluctuates ("treat and extend", a proactive treatment regime to allow the fewest injections required to control disease activity). Similarly, increasing NHS experience with [named competitor] and biosimilars allowed answers to questions on these topics in July 2023 that had not been possible earlier. Long-term data provide information on maximum treatment intervals reached, whether or not these can be maintained, and also on longer term safety. All these impact choice of treatment and clinic capacity, and would influence Bayer launch strategy for 8mg. The meeting minutes [B] record the outputs of these discussions.

Bayer therefore contends that, given the rapid evolution of the anti-VEGF treatment landscape in this period and the availability of new treatments and new data, **it is entirely possible to ask the same questions at different points in time and receive very different answers**. Indeed, this was the objective of repeating some questions and topics in successive advisory boards, to monitor and respond strategically to this rapidly evolving landscape. The point made directly below, concerning evolving NHS experience with a competitor, is an excellent example of this.

<u>Increased NHS experience of competitor in period 27 April – 31 July 2023</u>

The Panel also *"queried whether meaningful NHS experience would have been obtained [of use of a competitor] in the intervening 2 months that had elapsed since the April 2023 advisory board"*. Bayer would like, respectfully, to point out that the time between the 27 April and 31 July advisory boards was **slightly over 3 months**, not 2 months as stated in the ruling.

This period was significant as [reference to use of a competitor and the posology of anti-VEGF treatments].

<u>Discussion of updated NHS commissioning recommendations/Ximluci</u>

With regard to the Panel's comments on p4 of the ruling on the inclusion of updated NHS commissioning recommendations for medical retinal vascular medicines, Bayer would like to draw the attention to the Appeal Board to page 3 of its letter to the PMCPA of 5 November 2024 [C]. As stated there, Bayer had always intended to discuss biosimilars in the July 2023 advisory board due to their increasing prevalence in the NHS in 2023 compared to 2022. Bayer thus disagrees, respectfully, with the Panel's conclusion on this point [general information on the relevance of the guidance]

It is relevant here that **there had not been a Bayer advisory board discussion on the status of biosimilars in the NHS since 2022.** The first ranibizumab biosimilar (Ongavia) was only launched in the UK in 2022. **By July 2023 the biosimilars were several in number and increasingly well-established in NHS practice, a very different situation**

to 2022. [general information on the relevance of the guidance] Respectfully, the Panel appears inadvertently to have misunderstood the point Bayer had made in [C].

2. The selection and number of participants should stand up to independent scrutiny

The Panel raised no concerns in relation to this point.

3. Each [participant] should be chosen according to their expertise such that they would be able to contribute meaningfully to the purpose and expected outcomes of the advisory board.

The Panel raised no concerns in relation to this point.

4. The number of participants should be limited so as to allow active participation by all.

The Panel accepted that 8 advisers was an appropriate number for this meeting but queried whether a ratio of 1:2 Bayer staff:advisers was acceptable. This opinion is in conflict with a previous ruling of the Panel, in Case AUTH/3295/1/20 - AUTH/3296/1/20 [2], where a ratio of 1:2 staff:advisers was ruled to be acceptable under the Code.

Bayer ensured that the selection of advisory board participants was based on their expertise and relevance to the topics discussed, as the Panel has acknowledged. The ratio of Bayer staff to advisers was 1:2, consistent with acceptable standards in prior rulings. The presence of three Bayer staff members, plus one medical writer who did not participate in discussions, maintained the integrity of the advisory process, ensuring Bayer's questions were answered and outputs recorded.

5. The agenda should allow adequate time for discussion.

The ruling states that the amount of discussion at the 31 July 2023 meeting was *"on the outer limits of acceptability"* but stops short of deeming it unacceptable. Discussion time occupied 78% of the meeting. Presentation time was 22% and the Panel accepted the number of slides presented was reasonable. The structure of the meeting allowed for meaningful engagement and feedback from all participants, as proven in the detailed minutes [B] which demonstrate all objectives of the advisory board were met.

Bayer believes that a discussion:presentation ratio of 78:22 meets the requirements of the Code and also follows PMCPA advisory board guidance i.e. *"a significant majority of the time spent on feedback"* [3]. The PMCPA has never defined "significant majority" but the ruling in Case AUTH/3335/4/20 [4] suggests that a ratio of discussion to presentation of 70:30 might be considered as the point at which discussion becomes insufficient, in that the Panel queried the sufficiency of discussion in that case but did not make a clear statement that it was unacceptable. No breach of Clause 2 was ruled in that case.

6. The number of meetings and the number of participants should be limited and driven by need and not the invitees' willingness to attend.

The Panel states in its ruling that it had considered the legitimacy of the 31 July advisory board *"within the context of a series of meetings in 2022 and 2023"* and it is therefore

clear that these other meetings had formed a key foundation to the ruling of breaches of the Code.

Please note that points already made in section (1) above under *"Apparent repetition of similar topics across different advisory boards"* are also relevant here.

The Panel wrote to Bayer on 28 October 2024 [D] requesting more information specifically on the 27 April 2023 advisory board mentioned by the complainant. Following our response [C], the Panel in its ruling has taken into consideration advisory boards held in 2022 which were mentioned in outline in the concept for the April meeting, provided as an enclosure to [C]. No 2022 advisory boards had been part of the original complaint.

Bayer would like to emphasise that, prior to this appeal, it has not had opportunity to explain the number and timing of any advisory boards outside those in the original complaint, nor to justify the general way in which advisory boards are planned in our organisation. The Panel did not request any further information on these points at the end of last year before making its ruling. **The Panel has ruled based only on top-line information about earlier or later meetings appearing in concept documents not pertaining directly to those meetings**. Bayer believes this has resulted in inadvertent misperception, as this limited information provided insufficient evidence on which to judge the legitimacy of the total number of meetings held, or indeed whether those meetings had been held (one meeting listed tentatively for Q4 2023 in the July 2023 concept [E] was cancelled).

<u>Forward-planning of advisory boards</u>

The Panel expressed concern that Bayer had planned a number of advisory boards in advance, all at international congresses. Bayer's arguments for conducting advisory boards at international congresses have been set out in our response to the Panel of 1 September 2023 [A, pp5-6] and were not disputed in the Panel's ruling. We will therefore not restate them here.

Bayer UK will be informed of which major congresses are targets for Bayer Global to release new clinical trial data, typically year or more in advance. There were a large number of major phase III data releases for aflibercept 8mg and [named competitor] in 2022-23, and real-world evidence for [named competitor] plus data on new [named competitor] indications in 2023. Bayer needed advice on how these new data might affect the views of UK clinicians/NHS practice, and thus how Bayer UK will need to adapt its business strategy in response.

All advisory boards tentatively considered at the start of the year are reviewed much nearer the time to reassess the business need for advice. Only meetings where there is a clearly defined advice requirement will proceed. The concept document for the 31 July advisory board [E] marks the two advisory boards which follow it in Q4 2023 as "TBC", meaning to be confirmed. Following the standard review of business need, one of the pre-planned Q4 2023 advisory boards (Euretina) was cancelled as it was deemed unnecessary.

7. **The nature of the meeting should be made clear to invitees and participants: invitations to participate should clearly state the purpose of**

the advisory board meeting, the expected advisory role and the amount of work to be undertaken.

Bayer disagrees, respectfully, with the Panel's conclusions concerning the clarity of the invitation to the 31 July 2023 advisory board [F].

The Panel ruling states on page 4 of its ruling that the heading of the invitation to the 31 July meeting was *"Considering forthcoming developments in the UK anti-VEGF treatment landscape".* Respectfully, we wish to highlight that **this statement is incorrect, as the heading quoted by the Panel is incomplete**.

The full heading appearing on line 1 of the invitation, in prominent bold typeface, was *"Bayer Advisory Board: Considering forthcoming developments in the UK anti-VEGF treatment landscape".* This is not quoted in full in the ruling and such omission of full detail / context is misleading.

The title of the email containing the invitation was also *"Invitation from Bayer: Advisory Board, 31 July 2023"* [F], not mentioned in the ruling.

It was thus entirely clear from the outset, in both the title and heading on the invitation email that the invitation was specifically for an advisory board and not for a promotional meeting or any other sort of Bayer meeting. Contracts were also titled *"Advisory board agreements".*

Ophthalmology is a relatively small speciality in the UK, and the medical retina subspecialty relatively new, having only evolved since the late 00s when anti-VEGF therapies were first introduced. Medical retina clinicians of sufficient seniority and experience to act as advisers are therefore relatively few in number. All invitees would therefore, by reason of their seniority, likely have attended previous advisory boards with Bayer and/or other companies. They would have understood exactly what was meant by the term "advisory board" and would know that an advisory board only has active participants, contracted to deliver advice, not passive "delegates".

The Panel has accepted that the body of the invitation provided further detail, and the contracting arrangements were clear, but expressed concerns about the distinction between "advice" and "discussion" in the description of the meeting, concluding that "advice" referred only to the aflibercept part of the agenda. Respectfully, Bayer disagrees with the Panel on this point. The terms "advice", "feedback" and "discussion" were used broadly and synonymously in the invitation, in the same way as these terms are used broadly and synonymously in the PMCPA guidance on advisory board conduct [3]. Advice obtained through discussion was required on all topics on the agenda, not just aflibercept, and this was clear from the invitation.

For example, the PMCPA refers to *"adequate time for discussion"* in its guidance, not "adequate time to obtain advice", recognising that it is only through discussion that advice can be obtained. In the context of the prominent statements in the invitation that this was an advisory board and the past experience of the invitees, Bayer does not believe any invitees could have misunderstood the nature of the work they were being invited to do at the meeting i.e to discuss and thus to provide advice to Bayer on anti-VEGF products, including aflibercept, in UK clinical practice.

8. If an honorarium was offered, it should be made clear that it was reimbursement for such work and advice.

Please see comments under point (7) above, in relation to the invitation. Bayer disagrees, respectfully, with the Panel's view that the invitation was insufficiently clear. There was no ambiguity in the wording of the invitation. The contract was likewise very clear that this was an advisory board and that 1 hour of pre-work was also required. These experienced advisers would have understood immediately from the invitation that this was an advisory board, not a promotional meeting, and that the honorarium would be for their professional expertise and advice, not simply for their attendance. The requirements of Clause 24.2 were met.

9. Honoraria must be reasonable and reflect the fair market value of the time and effort involved.

Fair market value

The Panel did not uphold the complainant's concerns about the fair market value (FMV) of the honoraria offered by Bayer to its advisers, considering the amount to be acceptable in relation to the expertise required.

Pre-work to 31 July 2023 advisory board

This comprised a list of 10 congress sessions of relevance to the advisory board agenda plus reading a 5-page press release containing a summary of unpublished data, total work 1 hour. In regard to pre-work, the complainant alleged *"there was no pre work sent"* and *"Expected preparatory work was optional",* describing this as *"two optional lectures"* when in fact there were ten listed. Bayer has always maintained that both complainant statements are false [A].

The Panel stated that pre-work is not mandatory in the Code and did not dispute that pre-work was set, nor that clinical discussions occurred, but nevertheless expressed certain concerns about the pre-work.

- On p5 of the ruling, the Panel states that reading the press release was *"not mandatory".* With respect, the Panel is in error on this point. The pre-reading directions [G] state in regard to the press release *"In addition to attending the above sessions where possible, we kindly request that you read the following press release to inform discussions during the advisory board at ASRS:"* This is a polite but clear direction to read the press release; the activity is mandatory. The instruction in [G] relating to the press release was reinforced in pre-advisory board face-to-face verbal briefings to advisers by Bayer UK medical staff as stated in [A].
- The pre-meeting verbal briefings likewise reinforced the importance of attending as many of the pre-work presentations as possible, but Bayer did not at the time feel it was possible to make attendance at all 10 mandatory within the 1 hour period allocated to pre-work, not least as in total this would total 48 minutes of presentations leaving no time for reflection on the data nor reading the press release in detail and preparing for the advisory board questions. The verbal briefing made clear the expectation to complete one hour of work prior to the

meeting, likewise this was clear in the contracts, and the advisory board chair was confident from the clinical discussions [A,B] that all advisers had come well-prepared having each attended several presentations, read the press release and considered the data i.e. all advisers had done the contracted one hour of pre-work. **There is also explicit reference to pre-work in relation to meeting outputs on pp 12, 22 and 24 of the minutes [B].**

Bayer follows the requirements of Clause 5.3 in recognising the professional standing of its contracted advisers. Doctors are also obliged by the General Medical Council to abide by their professional commitments. One hour of pre-work was in the signed contracts and the nature of the pre-work required had been explained in a certified document and by in-person briefing at the congress. The advisory board organisers were satisfied before the meeting that the advisers understood what was required, and during the meeting that the work had been done (as the minutes confirm). Bayer did not feel it would have been appropriate to demand further proof from the advisers that they had complied with the requirements of the contract.

The Panel commented on some changes in the plan for pre-work, which was originally to send out the advisory board slides. The pre-work plan had changed from the concept, reflecting the dynamic landscape in which Bayer was working in 2023, but the **revised pre-work plan would still have justified one hour's reimbursement and had been appropriately certified as such**.

Overall, the reimbursement to each adviser for total work in relation to the 31 July 2023 advisory board was very modest [reference to amounts paid]

Conclusion

- Bayer contends that the advisory board held in July 2023 was legitimate, was conducted in response to clear business need and constituted neither pre-licence promotion nor an inducement to prescribe.
- The number of advisory boards held in 2022-2023 was legitimate in context of the large number of competitor launches, new data releases and changing NHS landscape in that period.
- The terms under which advisers were invited and contracted by Bayer were abundantly clear as to the nature of the meeting and the reimbursement offered was very modest in terms of fair market value for the work required.
- Pre-work requirements were clear, certified, occupied one hour and completed by advisers, as the minutes reflect.
- Expert advice received and recommendations from the advisory board directly informed our strategy and operational decisions, ensuring alignment with current NHS practices and prioritisation of patient safety.

The Panel acknowledged in its ruling that several aspects of the meeting were acceptable. Bayer believes that its response to the Appeal Board has addressed the concerns raised by the Panel and clarified those areas where there may have been inadvertent misinterpretation or where the ruling appears to conflict with prior Code case precedent.

Bayer therefore respectfully submits that the meeting held on 31 July 2023 was fully adherent to the letter and spirit of the Code. Bayer made every effort to maintain high

standards. The arrangements were accordingly not in breach of clauses 24.2 (x2), 19.1, 3.1, 3.6, nor clause 5.1.

Clause 2 is reserved as a sign of special censure and, respectfully, Bayer does not believe that the facts of this case merit ruling a breach of clause 2.

Bayer would like to thank the Appeal Board in advance for its careful consideration of this matter and looks forward to presenting its case in person in due course."

APPEAL BOARD RULING

The Appeal Board observed that the approval concept form for the advisory board in question described three objectives: to seek expert feedback and advice on the latest Phase IIb/III clinical data with aflibercept 8mg for nAMD and DMO, practical implications for its UK launch; to seek perspectives on new Phase III competitor data in RVO; and to share and discuss real-world outcomes and experiences with a competitor and ranibizumab biosimilars in UK practice. At the July conference, new data releases and post hoc analyses from ongoing trials were presented for the Eylea 8mg dose.

The Appeal Board took account of Bayer's submissions that Aflibercept 8mg was a very different product to 2mg, in terms of formulation, pharmacokinetics, posology and NICE appraisal status. In 2022-23, Bayer was preparing to launch 8mg into a very rapidly changing UK medical retina environment with evolving clinical understanding of multiple new competitors.

The Appeal Board considered the email template dated 13 July 2023 sent to advisors who had contractually agreed to participate including a document attachment listing ten presentations being held at the conference concerning Eylea and a competitor; attendance appeared to be encouraged rather than mandatory. Bayer had submitted that the medical advisor chairing the advisory board confirmed that it was evident from the advisory board discussions that advisors had attended the presentations. Within the list of presentations was a link to a five-page press release as part of the pre reading, which Bayer submitted was mandatory reading. Bayer submitted that the verbal briefing also made it clear that the expectation of attendees to the advisory board was that they completed one hour of work prior to the meeting.

The Appeal Board did not consider that it was unreasonable to stage the advisory board in question at the same time as the conference. This made sense as attendees would already be in the same place and would have been provided with the latest data at the conference.

The Appeal Board acknowledged that there was a rapidly changing market in ophthalmology which helped to explain why there was a short period between the April and July advisory boards. The Appeal Board determined that the questions and responses from the April and July advisory boards were sufficiently different and that the close proximity of the advisory boards was justified in this specific case. The Appeal Board had some concerns about whether the overall number of advisory boards in relation to the product held across 2022 and 2023 in such close succession was necessarily acceptable, but noted that the appeal related to the July advisory board only. The Appeal Board was assured by the representatives from Bayer that the company always planned ahead from a budget perspective to hold a number of advisory boards each year but that advisory boards would be cancelled if there was no legitimate reason to hold them, and had been cancelled previously.

The Appeal Board considered that the concept document was clear and robust, and the minutes were very detailed and highlighted a high level of discussion. The invitation and contract clearly stated the purpose was a Bayer advisory board and the invitation included the objectives. The Appeal Board considered that in the circumstances it was acceptable to discuss the stated objectives to help shape Bayer's commercial, logistical and practical considerations around the launch of the Eylea 8mg dose in such a dynamic market space.

The Appeal Board noted the requirements of Clause 24.2 and it was satisfied that there was a legitimate need for the services and that this was clearly identified (and documented in advance of requesting the services); the hiring of the contracted party was not an inducement to prescribe, supply, administer, recommend, buy or sell a medicine. The Appeal Board **ruled no breaches of Clause 24.2 in relation to each matter and consequently no breach of Clause 19.1**. The appeal on these points was successful.

In the light of its findings that this was a legitimate advisory board the Appeal Board did not consider that Eylea 8mg had been promoted prior to the grant of marketing authorisation and it did not constitute disguised promotion. The Appeal Board **ruled no breach of Clauses 3.1 and 3.6**. The appeal on this point was successful.

Bayer had therefore not failed to maintain high standards nor had it brought discredit to and reduced confidence in, the pharmaceutical industry and no **breach of Clauses 5.1 and 2** were ruled. The appeal on these points was successful.

Complaint received **2 November 2023**

Case completed **13 March 2025**