CASE AUTH/3295/1/20 and AUTH/3296/1/20

ONCOLOGIST V ASTRAZENECA AND MERCK SHARP & DOHME

Advisory Board meeting

An anonymous complainant who described him/herself as a practising oncologist complained about the arrangements for an advisory board meeting organised jointly by AstraZeneca and Merck Sharp & Dohme. The meeting was held in London on 8 November 2019 to seek advice on new clinically significant data in the treatment of ovarian cancer. The advisory board was part of a strategic collaboration between AstraZeneca and Merck Sharp & Dohme with regard to Lynparza (olaparib). AstraZeneca was the marketing authorisation holder for Lynparza which was indicated in the treatment of ovarian cancer.

The complainant stated that he/she was often approached and had attended several advisory boards but the AstraZeneca and Merck Sharp & Dohme alliance advisory board left him/her speechless; in summary it was an interrogation of the worst sort by all.

Firstly, the complainant noted that there was a large number of company staff, with most attendees coming from AstraZeneca. In particular, the complainant noted that there were 6 different AstraZeneca people from different parts of the company, ie sales and marketing, global, medical, market access and there was even an agency representative with a laptop throughout. In short, the advisory board was more of a 'show and tell' with a comprehensive presentation on the clinical data from PAOLA-1 and then an interrogation by pretty much several different departments from AstraZeneca and Merck Sharp & Dohme.

It was not made clear in the meeting invitation that delegates would face interrogation by different people, including a chairperson from AstraZeneca. Normally at advisory boards the chair was a fellow peer, ie a reputable health professional.

The complainant stated that he/she was concerned about the way in which some of the sessions were run. In one session, delegates were split into groups and, using flip charts, were subjected to a humiliation by brain storming. The complainant stated that he/she had never seen this happen at any other advisory board. Normally he/she would expect pharmaceutical companies to understand the advice they were looking for. Usually the chair (a reputable doctor) would have a clear steer and know how to facilitate the discussion. At the meeting in question the delegates were made to work in groups, and then surrounded by staff (a few too many) from both companies and were interrogated. Having people from sales and marketing and market/pricing for an indication that did not even have a licence granted by the European Medicines Agency (EMA) seemed rather unnecessary.

The complainant stated that his/her greatest concern was that AstraZeneca and Merck Sharp & Dohme made the attending doctors sign a confidentiality contract.

The complainant stated that he/she had not remembered signing a contract for people to take his/her picture during an advisory board. He/she did not consent to that and it was reasonable for advisors to expect privacy. The complainant stated that he/she had never been to any other advisory board where industry personnel took pictures without prior written consent. This was very poor and possibly illegal.

The detailed responses from Astra Zeneca and Merck Sharp & Dohme is given below.

The Panel noted from the companies' submissions that the advisory board, entitled 'AstraZeneca and MSD UK: New Treatments in First Line Ovarian Cancer', was planned and led by Merck Sharp and Dohme whilst AstraZeneca played a supporting role in the arrangements and co-chaired the meeting. Both companies collaborated and agreed on the business need, objectives, content and attendees. Merck Sharp & Dohme was solely responsible for inviting attendees and liaising with them regarding the logistics, eg contracts, honoraria, expenses; briefing the external chair and speakers; and contracting a professional medical writer to minute the discussions. According to both companies, the advisory board focused on gaining advice on the strengths, limitations and clinical implications of new clinical data from the Phase III PAOLA-1 study and the Phase III PRIMA study which were presented at the European Society for Medical Oncology (ESMO) meeting in Barcelona on in September 2019. The Panel noted Merck Sharp & Dohme's submission that the advice obtained was to be used for medical and commercial planning purposes of Lynparza in the ovarian cancer setting.

The Panel considered that the invitation sent to possible attendees in June did not include much detail about the agenda and what would be expected from attendees. The Merck Sharp & Dohme sample advisor contract, which appeared to be dated October 2019, included more information about expectations and the objectives for the advisory board. These included reviewing the data and outlining and obtaining feedback on the UK commercial and HTA strategy following marketing authorization. The Panel had no information from the complainant as to whether he/she signed a contract.

The Panel noted the complainant's concern that the advisory board was a 'show and tell' with a comprehensive presentation on PAOLA-1. The Panel noted AstraZeneca's submission that, in order to seek advice on the clinical interpretation of olaparib and competitor data in first line advanced ovarian cancer, with a focus on the PAOLA-1 and PRIMA clinical studies, it was necessary to present data on those studies for appropriate context. The Panel noted that, according to both companies and the agenda, a total of 40 minutes was spent on presentations and 295 minutes on obtaining advice (excluding the opening and closing of the meeting). The Panel noted that no pre-reading was sent to attendees. The Panel queried why the data presented was not sent as pre-reading, however, on the information provided, there was no evidence to suggest that there had not been adequate time for discussion at the advisory board meeting. The Panel noted from the minutes of the meeting that the meeting appeared to deliver the stated aims.

The Panel noted the complainant's concern about the number and type of company attendees present at the advisory board including sales, marketing, global, medical and market access. The complainant was particularly concerned with the presence of sales and marketing staff when an unlicensed indication was being discussed. The Panel noted that the attendance of medical and commercial staff at an advisory board was not necessarily unacceptable nor when such an advisory board was about an unlicensed

medicine or indication provided that their presence complied with the requirements of the Code.

The Panel noted AstraZeneca's submission that the medical and commercial expertise from the combined AstraZeneca and Merck Sharp & Dohme team was required to interpret the insights provided by the external attendees.

Although the Panel had some concerns, it did not consider that the complainant had shown, on the balance of probabilities, that the advisory board was disguised promotion or that the presence of commercial staff at the advisory board meant that an unlicensed indication had been promoted. The Panel ruled no breaches of the Code.

The Panel did not consider that the complainant had shown, on the balance of probabilities, that the number or types of company attendees were unacceptable as alleged and no breach of the Code was ruled in this regard.

The Panel noted the complainant's concern that the chairperson was an AstraZeneca employee whereas usually the chair of an advisory board would be a reputable health professional. The Panel noted that it was not necessarily unacceptable for a company employee to act as the chair of an advisory board provided that the way in which it was done complied with the requirements of the Code. The Panel noted that the advisory board at issue had an external and internal chair, both of whom were to participate in the advisory board. According to the companies, the external chair was a highly experienced oncologist with a world-renowned reputation. The internal chair was an AstraZeneca employee who had a background in clinical oncology and was a trained senior pharmacist. The Panel did not consider that the complainant had shown, on the balance of probabilities, that having the meeting co-chaired with an employee of AstraZeneca was unacceptable *per se* or that the meeting was inappropriately facilitated as alleged and no breach of the Code was ruled.

The Panel noted the complainant's concern that the advisory board was an interrogation of the worst sort. He/she also highlighted the way in which the afternoon sessions were run. The purpose of any advisory board would be to obtain advice and feedback. The Panel noted AstraZeneca's submission including that workshops to discuss clinical or commercial scenarios were a common and effective means of gaining insight at advisory boards. The Panel appreciated that attendees might not feel comfortable in that type of setting, however, this did not mean that a workshop type session was, in itself, unacceptable. The Panel was concerned that the complainant felt interrogated as well as humiliated by the workshops but did not consider that the complainant had shown, on the balance of probabilities, that either the way of obtaining feedback or the workshop sessions were inappropriate and no breach of the Code was ruled in this regard.

The Panel considered that it was standard practice for companies to ask health professionals and others to sign confidentiality agreements particularly before sharing data. It was not a breach of the Code for a company to ask an attendee at an advisory board to sign a confidentiality agreement. The Panel did not consider that the complainant had established that asking the attendees to sign confidentiality agreements, meant that the companies had failed to maintain high standards and no breach of the Code was ruled.

The Panel noted Merck Sharp & Dohme's submission that it was not its policy to take photographs during advisory boards and it was not mentioned in the signed contracts of the advisors that photographs would be taken. The Panel noted AstraZeneca's submission regarding the photographs, which included the faces of two health professionals, and that Astra Zeneca submitted that no health professional expressed any reservations about having his/her photograph taken at the time. AstraZeneca submitted that the photographs were deleted when it received notification of the complaint. The Panel considered that by taking photographs which identified individual health professionals and posting them, albeit on AstraZeneca's internal system, without obtaining those health professional's consent meant that the companies had failed to maintain high standards and a breach of the Code was ruled.

The Panel did not consider that the circumstances warranted a ruling of a breach of Clause 2 which was used as a sign of particular censure.

An anonymous complainant who described him/herself as a practising oncologist complained about the arrangements for an advisory board meeting organised jointly by AstraZeneca and Merck Sharp & Dohme. The meeting was held in London on 8 November 2019 to seek advice on new clinically significant data in the treatment of ovarian cancer. The advisory board was part of a strategic collaboration between AstraZeneca and Merck Sharp & Dohme with regard to Lynparza (olaparib). AstraZeneca was the marketing authorisation holder for Lynparza which was indicated in the treatment of ovarian cancer.

COMPLAINT

The complainant stated that he/she was often approached and had attended several advisory boards but the AstraZeneca and Merck Sharp & Dohme alliance advisory board left him/her speechless; in summary it was an interrogation of the worst sort by all.

Firstly, the complainant noted that there was a large number of company staff, with most attendees coming from AstraZeneca. In particular, the complainant noted that there were 6 different AstraZeneca people from different parts of the company, ie sales and marketing, global, (which meant the company parachuted personnel in) medical, market access and there was even an agency representative with a laptop throughout. In short, the advisory board was more of a 'show and tell' with a comprehensive presentation on the clinical data from PAOLA-1 and then an interrogation by pretty much several different departments from AstraZeneca and Merck Sharp & Dohme.

It was not made clear in the meeting invitation that delegates would face interrogation by different people, including a chairperson from AstraZeneca. Normally at advisory boards the chair was a fellow peer, ie a reputable health professional.

The complainant stated that he/she was concerned about the way in which some of the sessions were run. In one session, delegates were split into groups and, using flip charts, were subjected to a humiliation by brain storming. The complainant stated that he/she had never seen this happen at any other advisory board. Normally he/she would expect pharmaceutical companies to understand the advice they were looking for. Usually the chair (a reputable doctor) would have a clear steer and know how to facilitate the discussion. At the meeting in question the delegates were made to work in groups, and then surrounded by staff (a few too many) from both companies and were interrogated. Having people from sales and marketing

and market/pricing for an indication that did not even have a licence granted by the European Medicines Agency (EMA) seemed rather unnecessary.

The complainant stated that his/her greatest concern was that AstraZeneca and Merck Sharp & Dohme made the attending doctors sign a confidentiality contract so that they would keep certain details confidential.

The complainant stated that he/she had not remembered signing a contract for people to take his/her picture during an advisory board. He/she did not consent to that and it was reasonable for advisors to expect privacy. The meeting was not held in a public place, so under GDPR rules one could expect that pictures would not be taken. As it stood, pictures now sat inside somebody's telephone at Merck Sharp & Dohme or AstraZeneca or both. The complainant stated that if that telephone was misplaced his/her privacy would have been breached.

The complainant stated that he/she had never been to any other advisory board where industry personnel took pictures without prior written consent. This was very poor and possibly illegal.

Overall, the complainant stated that this type of poor practice must not be repeated, and (doctors/advisory board doctors) must be told about the full arrangements beforehand. The number of industry personnel should be limited to those who could ask the correct questions and sales/marketing/ and market pricing should not feature at such an early stage.

When writing to AstraZeneca and Merck Sharp & Dohme, the Authority asked each to consider the requirements of Clauses 2, 3.2, 9.1, 12.1 and 23.1 of the Code.

RESPONSE FROM ASTRAZENECA

AstraZeneca explained that the logistics of the advisory board which was entitled 'AstraZeneca and MSD UK: New Treatments in First Line Ovarian Cancer' were planned and led by Merck Sharp and Dohme; AstraZeneca played a supporting role in the arrangements and co-chaired the meeting.

The advisory board was regarded as an essential activity by both Merck Sharp & Dohme and AstraZeneca; it focused on gaining advice into the strengths, limitations and clinical implications of new clinical data from the Phase III PAOLA-1 study and the Phase III PRIMA study, which were presented at the European Society of Medical Oncology meeting in September 2019. The two companies agreed that an advisory board was the most suitable vehicle to obtain this advice, given the complex nature of the disease area and clinical data.

The PAOLA-1 study investigated Lynparza plus Avastin (bevacizumab marketed by Roche) as maintenance therapy in newly diagnosed, advanced ovarian cancer treated with platinum-based chemotherapy plus Avastin. The PRIMA study investigated Zejula (niraparib marketed by GlaxoSmithKline) as a maintenance therapy in newly diagnosed advanced ovarian cancer patients following a response to platinum-based chemotherapy. The data from PAOLA-1 was critically important to both companies because the treatment combination had the potential to become recognised as a standard of care for patients with newly diagnosed advanced ovarian cancer. Insights into the strengths and limitations of the PAOLA-1 data were sought, together with the same on the Phase III results of Lynparza's key competitor, Zejula. The specific objectives of the advisory board were detailed on the meeting agenda (copy provided).

AstraZeneca had three members of staff present for the duration of the day. A fourth individual from AstraZeneca presented the clinical data and departed the meeting at noon. One individual from Merck Sharp & Dohme was present throughout the duration of the meeting. One agency medical writer was present in the meeting room throughout the meeting and a further agency medical writer was present only during the workshop in the afternoon. Two additional Merck Sharp & Dohme representatives were present before the meeting but they took no part in the meeting at any point of the day. AstraZeneca understood that the individuals were present to deal with administrative matters only.

AstraZeneca stated that it was satisfied that the meeting was well organised and that appropriate oversight was provided at all times to ensure compliance with the Code. Both companies collaborated and agreed on the business need, objectives, content and attendees. In accordance with the Working Instruction (copy provided), Merck Sharp & Dohme was the lead company for the meeting and so organised it in line with its standard operating procedures (SOPs). AstraZeneca was the secondary company for the advisory board.

AstraZeneca explained that the two companies operated under an overarching alliance agreement which required both to follow all applicable laws and regulations. In the UK, the Working Instruction specified how alliance activities relating to the review and approval of materials were conducted using a shared system of record (the AstraZeneca system) wherever legally possible. In the case of an advisory board, this meant that the materials should be examined for compliance with the Code by both parties in the AstraZeneca approval system. However, in order to comply with competition law, commercially sensitive documents such as contracts and honoraria could not be shared, and thus it would not be possible for a secondary company to ensure that all documents about an advisory board were compliant.

The companies provided details of the processes used to approve the arrangements for the advisory board in question.

AstraZeneca and Merck Sharp & Dohme were in the process of updating the Working Instruction in order to be more specific the approval of materials in the event that Merck Sharp & Dohme was unable to approve them in the AstraZeneca system. AstraZeneca noted that all materials for which it had oversight were examined to ensure compliance with the Code and it believed high standards had been maintained.

With regard to company attendees at the meeting, AstraZeneca maintained that they were all necessary to meet the objectives of the advisory board and the ratio of industry representatives to external advisors was reasonable. The medical and commercial expertise from the combined AstraZeneca and Merck Sharp & Dohme team was required to interpret the insights provided by the external attendees into forward-looking strategy.

AstraZeneca stated that it was satisfied that the number of attendees was reasonable, proportionate to the purposes of the meeting, and were in line with the requirements of the Code.

Each attendee at the meeting had relevant expertise and a legitimate role to meet the intended objectives of the advisory board. AstraZeneca provided a rationale of marketing and market access personnel attendance at the meeting. Although two members of staff had some sales responsibilities, they fulfilled senior leadership roles (details provided). They were required at the meeting to facilitate one workshop each and were involved throughout to gain relevant

insights for the development of the launch strategy. In addition, one of those members of staff was also required to support discussions on topics related to diagnostics during the meeting.

Therefore, AstraZeneca submitted that the attendance of the individuals present was necessary and reasonable to meet the purposes of the meeting and in line with the requirements of the Code.

AstraZeneca explained that one of the objectives of the meeting was to 'seek advice on the clinical interpretation of olaparib and competitor data in first line advanced ovarian cancer, with a focus on the PAOLA-1 and PRIMA clinical studies'. In order to do this, it was necessary to present data on those studies for appropriate context. This formed a small part of the overall meeting: 23 slides presented were on PAOLA-1 which took 20 minutes, 5 slides formed part of a 95 minutes discussion about PAOLA-1 and 2 slides were presented on olaparib licence and NICE recommendation which formed part of the initial 5 minute presentation. Furthermore, a total of 40 minutes was spent on presentation and 295 minutes on obtaining advice (excluding the opening and closing of the meeting). This demonstrated that rather than a 'show and tell', the overwhelming majority of time was spent on seeking the advice of the experts. This was also shown by the meeting minutes (copy provided).

With respect to the 'workshop' sessions, the advisors were requested to focus on two scenarios in relation to optimising the patient pathway with regard to the two studies under review. This was outlined in the agenda and outputs were included in the meeting minutes (copies provided). As set out above, Merck Sharp & Dohme had sole responsibility for the organisation of the meeting and sent the invitations. AstraZeneca did not have sight of the content of the invitation.

AstraZeneca submitted that workshops in which teams discussed clinical or commercial scenarios were a common and effective means of gaining insight in advisory boards. The minutes from the meeting demonstrated that the outputs from the session were comprehensive, focused and delivered the stated aims. The workshop was clear in its aims and was in line with advice that could legitimately be sought under the Code. Furthermore, the format and objectives presented to the participants at this meeting were aligned with recognised ways of working. AstraZeneca employees who attended the advisory board received no comment to the contrary from attendees at the time. Further, upon interviewing AstraZeneca attendees, there was nothing to suggest that the workshops were conducted in anything other than a professional and appropriate manner.

With regard to the complainant's comment about the chair of the meeting, AstraZeneca noted that it was not a Code requirement for the chair of an advisory board to be a health professional. As stated above, each attendee at the meeting had relevant expertise and a legitimate role to meet the intended objectives of the Advisory Board.

Notwithstanding the points above, both co-chairs were reputable health professionals with appropriate expertise and AstraZeneca did not recognise the complainant's characterisation in any way.

With regard to confidentiality agreements, AstraZeneca stated that it was standard practice across the industry for advisory board attendees to be asked to sign such agreements before receiving any proprietary data which was confidential and commercially sensitive. AstraZeneca did not have access to the contracts produced and issued by Merck Sharp & Dohme so were unable to provide any details.

AstraZeneca stated that nineteen photographs were taken by its employees and the medical writer. Of these, fifteen captured the information on the flip charts; four photographs depicted the general scene of the advisory board and were posted on AstraZeneca's internal collaboration platform which was not accessible to people outside of AstraZeneca. As the purpose of the photograph was not to record the presence of any particular health professionals at the advisory board, the individuals did not ask those present for additional consent on the day. Upon review of these photographs, it did appear that the faces of two health professionals were visible. There was no attempt to hide the fact that the photographs were being taken and no health professionals expressed any reservations about having their photograph taken at the time. To the best of AstraZeneca's knowledge, the photographs were seen by a maximum of around 900 employees before they were removed.

AstraZeneca was comfortable that, to the extent that they contained images of two health professionals present at the meeting, the taking and use of the photographs was justified and proportionate under GDPR on the basis of the company's legitimate interests in keeping relevant members of staff informed. AstraZeneca had also discussed this usage with the Information Commissioner which confirmed that it was acceptable in principle. Given the current complaint, as a precaution, the photographs had been deleted from the internal platform and the telephones of the employee involved.

In summary, AstraZeneca refuted any suggestion that the advisory board in question breached Clauses 2, 3.2, 9.1, 12.1 and 23.1 of the Code. This meeting was regarded as an essential activity by both companies in order to gain advice on the potential impact of newly released evidence for patients with first line ovarian cancer from PAOLA-1. The advice provided by the clinical experts had since enabled a material change in strategic direction for this medicine. The number and purpose of all attendees from both companies was reasonable and proportionate to meet the objectives of the meeting. The balance of 'presentation to insight' throughout the meeting was overwhelmingly favourable to the latter and the professional conduct of the workshop sessions were critical to the delivery of insight gained. As stated above, some photographs were taken in which two health professionals were inadvertently identifiable: although AstraZeneca was comfortable that this did not represent an infringement of GDPR, it had, nonetheless, deleted all copies of these images other than those it had retained for the purposes of this investigation.

AstraZeneca considered that the arrangements and execution of the advisory board were fully compliant with the Code. The company strongly disagreed that the activity had brought discredit upon, or reduced confidence in, the industry. The outputs from this meeting had been crucial to informing both UK and Global strategies to help meet the needs of patients with ovarian cancer.

RESPONSE FROM MERCK SHARP & DOHME

The advisory board was conducted under the framework of the strategic collaboration between Merck Sharp & Dohme and AstraZeneca UK Limited for olaparib which commenced in late 2017.

Merck Sharp & Dohme explained that the advisory board held on 8 November 2019 in London was conducted to answer specific clinical questions posed by the publication of two data sets at the European Society for Medical Oncology (ESMO) meeting in Barcelona on 28 September

2019. These were PAOLO-1 and PRIMA, new clinically significant data in the ovarian cancer setting, for Lynparza and niraparib (Tesaro) respectively.

The knowledge gaps that required external expert advice were as follows:

i) Identifying any weaknesses or limitations of new data from a clinical perspective.

ii) Assessing what impact the new data could have on the patient pathway and treatment decisions if the data translated to new licence indications for Lynparza and Zejula in the ovarian cancer setting.

iii) Clarifying the role of breast cancer gene testing and homologous recombination deficiency (HRD) status in any future patient pathway and treatment decision tree.

iv) Evaluating the clinical guidance and considerations when submitting this data set to healthcare technology appraisal (HTAs) bodies, eg National Institute for Health and Care Excellence (NICE) and the Scottish Medicines Consortium (SMC).

The advice obtained was to be used for medical and commercial planning purposes of Lynparza in the ovarian cancer setting. Considering the complexity of the healthcare system in the UK and the clinical nature of the advice being sought, Merck Sharp & Dohme and AstraZeneca both believed that an advisory board was the most appropriate method to do so and that the advice could not be sought through other means.

Merck Sharp & Dohme explained that the strategic collaboration between the two companies required one of them to take the lead for a given activity. For the purpose of this specific advisory board, Merck Sharp & Dohme took the lead.

Merck Sharp & Dohme's responsibilities included:

i) Identifying both the internal company attendees and external advisors.
ii) Inviting the advisors*.
iii) Selecting appropriate external and internal chairpersons.
iv) Liaising with the advisors regarding the logistics of the advisory board eg selection of a suitable date, contracts, honoraria, expenses etc*.
v) Setting the objectives for the advisory board.
vi) Setting the agenda.
vii) Putting together the presentations for the day.
viii) Briefing of the external chair and speaker(s)*.
ix) Contracting a professional medical writer to minute the discussions at the advisory board*.
x) Production of the minutes of the advisory board*.
xi) Payment of honoraria to participants*.

Many of Merck Sharp & Dohme's responsibilities were conducted in consultation with AstraZeneca. Those that were asterisked above were the sole responsibility of Merck Sharp & Dohme. The final materials for the advisory board were examined by both companies, including the objectives, agenda, attendees and final presentations.

The objectives for the advisory board *'New Treatments in First Line Ovarian Cancer Advisory Board',* were set by Merck Sharp & Dohme and agreed with AstraZeneca. These were:

i) Gain insights on current treatment practices in first line advanced ovarian cancer in the UK.
ii) Gain advice on the clinical interpretation of Lynparza and competitor data in first line advanced ovarian cancer, with a focus on PAOLA-1 and PRIMA.
iii) Understand how PAOLA-1 and PRIMA may influence future treatment and testing pathways in the UK.
iv) Gain an understanding of the PAOLA-1 and PRIMA data from a UK market access strategy perspective post-marketing authorisation for olaparib plus bevacizumab following first-line chemotherapy in patients with advanced ovarian cancer.

Merck Sharp & Dohme explained that the principle criteria for the selection of the advisors were that they had to be qualified to provide the advice being sought by Merck Sharp & Dohme and AstraZeneca, ie they were experienced health professionals involved in the treatment and care of patients with ovarian cancer.

The advisors selected included oncologists, gynaecologists, gynaecological oncologists and a genomics expert. As this was a national advisory board, there was representation from across the UK, including health professionals from England, Scotland and Wales. Ten advisors attended the advisory board which allowed adequate time for all of them to participate.

The advisory board was originally planned to have two co-chairs, one from Merck Sharp & Dohme and one of the advisors. The Merck Sharp & Dohme co-chair had to be replaced with an individual from AstraZeneca. Details were provided about the advisor who agreed to be the co-chair who was a world-renowned expert in ovarian cancer with experience of chairing advisory boards for the pharmaceutical industry.

A written agreement with all advisors, put in place before the advisory board took place, set out details of the advice being requested by Merck Sharp & Dohme and listed the objectives of the advisory board. All advisors received an honorarium payment in line with fair market value.

The agenda for the advisory board, other than the introductions and close, consisted of three main components, all specifically designed to address the objectives set out for the advisory board, which were:

i) Presentation and discussion of the relevant clinical data: an overview of the current treatment landscape, the PAOLO-1 study and the PRIMA study.
ii) A workshop session, where the advisors were split into two groups, intended for the advisors to use their expertise to interpret the new data previously presented and discussed, ultimately to design an optimal treatment algorithm should Lynparza and Zejula receive a future marketing authorisation. The workshop format was used to maximise the time for contribution by the advisors.
iii) The market access strategy session was intended to provide advice in relation to any HTA submissions made for Lynparza in respect to the PAOLO-1 study.

    Based on principles to maximise discussion, advice gathering and limit presentations, when conducting advisory boards, due diligence was applied to minimise any presentation time on the agenda.

Merck Sharp & Dohme noted that:

i) Excluding the opening introduction (10 minutes) and the summary and close (10 minutes) – there were three clinical presentations totalling 40 minutes.

ii) Excluding the breaks (30 minutes for lunch and a 5-minute refreshment break) – there was formal discussion time of 295 minutes.

iii) Total presentation and formal discussion time was thus: 335 minutes.

iv) Overall, 12% of the time was allocated to presentation time and 88% to formal discussion.

The agenda was emailed to confirmed advisors ahead of the advisory board. The minutes of the advisory board were consistent with the planned agenda.

The selection of company participants to participate in delivering the advisory board was consistent with Merck Sharp & Dohme's policy for advisory boards. 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.

Details of the 5 company participants in the advisory board were provided. There were two AstraZeneca employees from medical departments, one of whom co-chaired the advisory board. One of these left after the conclusion of the clinical data presentation and discussion session for the PAOLO-1 study and played no further part in the meeting. One senior employee from the AstraZeneca sales and marketing and one senior employee from Merck Sharp and Dohme sales and marketing. Their roles were to facilitate the two workshops on designing the optimal pathway for ovarian cancer patients. One employee from AstraZeneca market access whose role was to facilitate the market access strategy session. As NICE now required that companies submit their oncology HTA submissions ahead of a pending marketing authorisation, with the intention that a reimbursement recommendation could be given concurrently with the granting of a marketing authorisation , it was appropriate and legitimate to seek advice from health professionals on matters relating to the HTA submission for Lynparza at this advisory board before the marketing authorisation being granted.

The original Merck Sharp & Dohme co-chair for the advisory board resigned shortly before it was due to take place and could no longer co-chair the advisory board. This departure also necessitated a deviation from the collaborative agreement in place and meant that items that required examination would not be done using the AstraZeneca joint company approval system but would use Merck Sharp & Dohme's standard approval process. The time constraints for delivery of the advisory board meant there was not enough time to train a new team member on the AstraZeneca approval system.

At the time of the advisory board Merck Sharp & Dohme had a deviation in place for such an eventuality and was working together with AstraZeneca to improve the Work Instruction between the two companies.

A medical writer from a third party agency also attended the advisory board for the sole purpose of providing minutes of the meeting and a second medical writer from the third party agency

attended the workshop session of the advisory board only. As the advisors were split into two workshop groups, two medical writers were required to ensure that the discussion and conclusions of the advisors were captured accordingly. This medical writer left the advisory board room once the workshop session was completed.

On the morning of the advisory board, prior to it starting, there were two further Merck Sharp & Dohme employees present one who was present in order to have sign-in sheets completed, provide the advisors with expense claims information, and to ensure any advisors who had not returned signed agreements completed them prior to the start of the advisory board. The other was from the medical department and was present in order to ensure the external co-chair understood his/her role and had all the information required. This employee left the venue after the advisory board began. He/she waited in the foyer for two late arriving advisors (due to a flight delay) and departed the venue once they had arrived approximately an hour after the advisory board had begun.

Merck Sharp & Dohme explained that the Work Instruction Agreement between the two companies regarding approval of advisory boards required that both companies examined relevant aspects of advisory boards. As advisory boards were non-promotional the agenda, briefings and presentations were examined and not certified by two Merck Sharp & Dohme staff and AstraZeneca staff.

Merck Sharp & Dohme submitted that the advisory board was attended by 5 company staff and 10 external advisors. Merck Sharp & Dohme submitted that this was appropriate and aligned with its SOP and the PMCPA's guidance on advisory boards. All the company participants had defined roles at the advisory board. Additional agency staff attended to take the minutes and assist with the scribing of the pathways, that were developed by the advisors in the workshops.

This advisory board had an external and internal chair. The external chair was a highly experienced oncologist with a world-renowned reputation. The internal chair also had a background in clinical oncology and was a trained senior pharmacist. Both chairs participated in the advisory board.

The agenda demonstrated that most of the advisory board was allocated to advice seeking and discussion. The presentation themselves focused on the topic of the advisory board only.

There were no company participants at the advisory board with a role in sales. The two marketeers present had clearly defined roles and the advice being sought was relevant to their future development of the launch strategy.

The advisory board had key clinical questions that both companies were seeking advice on. The opinion that was being sought was to establish a national picture. The change in format when discussing the patient pathway in ovarian cancer from a desktop-based meeting to that of a workshop encouraged inclusivity of opinion, allowing some health professionals who might find the desktop format of advisory boards intimidating the opportunity to contribute. By interviewing the Merck Sharp & Dohme attendee and examining the minutes of the advisory board, Merck Sharp & Dohme found no evidence that this format was intimidating or aggressive in nature. No participant raised any concerns before, during or after the advisory board.

It was not the policy of Merck Sharp & Dohme to take photographs during advisory boards and it was not mentioned in the signed contracts of the advisors that photographs would be taken.

Photographs were taken after the advisory board of the flip charts to create the minutes by the medical writer.

Four further photographs were taken during the advisory board (see response from AstraZeneca for the reason behind these photographs being taken and their use) which had now been destroyed.

Merck Sharp & Dohme contended that, overall, the intention of the advisory board was legitimate, in accordance with the Code, and conducted in a way to obtain advice from the health professionals in attendance to achieve the clear set objectives of the advisory board.

The advisory board was held for legitimate reasons with a genuine knowledge gap and the ratio of presentation to discussion maximised the opportunity to gain advice from the advisors.

Merck Sharp & Dohme strongly denied that there was any promotion during the advisory board. The meeting was carried out according to the objectives set out in the contract for the meeting. All participants (internal and external) that attended the advisory board had clearly defined roles.

The presentation of data outside of licence was limited to that relevant to meet the objectives of the meeting and therefore did not represent either promotion outside of licence or disguised promotion. Merck Sharp & Dohme submitted that Clauses 23.1, 12.1 and 3.2 were not breached.

Merck Sharp & Dohme had high standards and took any complaint received very seriously. The company considered that the way in which the advisory board was developed and held was in accordance with the Code, in house SOPs and PMCPA guidance on advisory boards.

The company personnel present were appropriate in number and had a legitimate reason for being present. The outputs sought from the advisors, including the use of breakout groups, was both appropriate and acceptable.

Given the legitimacy of the advisory board in terms of genuine knowledge gaps and the conduct to maximise contribution of the appropriately selected advisors, Merck Sharp & Dohme denied the alleged breach of Clause 9.1 that high standards had not been maintained.

Whilst the company was concerned that the complainants experience in the advisory board was negative, and he/she was compelled to complain to the PMCPA, it considered that the intent, planning and conduct of the advisory board was to the highest standard possible. For these, and the other reasons outlined above, Merck Sharp & Dohme denied that it had brought discredit upon the industry in breach of Clause 2.

In response to a request for further information, Merck Sharp & Dohme provided a copy of the email invites sent to attendees and confirmed that no pre-reading was issued to the attendees prior to the meeting.

PANEL RULING

The Panel noted that the parties' accounts differed. The Panel noted the difficulty in dealing with complaints based on one party's word against the other; it was often impossible, in such circumstances, to determine precisely what had happened. Paragraph 2.2 of the Constitution

and Procedure stated that a complainant had the burden of proving their complaint on the balance of probabilities. The Panel noted, however, that a high degree of dissatisfaction was usually required before an individual health professional was moved to submit a formal complaint. The letter of complaint, although dated the day after the advisory board meeting, was not received by the PMCPA until early in January 2020.

The Panel noted from the companies' submissions that the advisory board, entitled 'AstraZeneca and MSD UK: New Treatments in First Line Ovarian Cancer', was planned and led by Merck Sharp and Dohme whilst AstraZeneca played a supporting role in the arrangements and co-chaired the meeting. Both companies collaborated and agreed on the business need, objectives, content and attendees. Merck Sharp & Dohme was solely responsible for inviting attendees and liaising with them regarding the logistics, eg contracts, honoraria, expenses; briefing the external chair and speakers; and contracting a professional medical writer to minute the discussions. According to both companies, the advisory board focused on gaining advice on the strengths, limitations and clinical implications of new clinical data from the Phase III PAOLA-1 study and the Phase III PRIMA study which were presented at the European Society for Medical Oncology (ESMO) meeting in Barcelona on in September 2019. The Panel noted Merck Sharp & Dohme's submission that the advice obtained was to be used for medical and commercial planning purposes of Lynparza in the ovarian cancer setting.

The Panel noted that it was acceptable for companies to pay health professionals and others for relevant advice. Nonetheless, the arrangements for such meetings had to comply with the Code, particularly Clause 23. To be considered a legitimate advisory board, amongst other things, the agenda should allow adequate time for discussion and feedback from the participants should be the main focus with only a small proportion of the time should be spent on company presentations.

The Panel considered that the invitation sent to possible attendees in June did not include much detail about the agenda and what would be expected from attendees. The Merck Sharp & Dohme sample advisor contract, which appeared to be dated October 2019, included more information about expectations and the objectives for the advisory board. These included reviewing the data and outlining and obtaining feedback on the UK commercial and HTA strategy following marketing authorization. The Panel had no information from the complainant as to whether he/she signed a contract.

The Panel noted the complainant's concern that the advisory board was a 'show and tell' with a comprehensive presentation on PAOLA-1. The Panel noted AstraZeneca's submission that, in order to seek advice on the clinical interpretation of olaparib and competitor data in first line advanced ovarian cancer, with a focus on the PAOLA-1 and PRIMA clinical studies, it was necessary to present data on those studies for appropriate context. According to AstraZeneca, 23 slides were presented on PAOLA-1 which took 20 minutes, 5 slides formed part of a 95 minute discussion about PAOLA-1 and 2 slides were presented on olaparib licence and NICE recommendation which formed part of the initial 5 minute presentation. The Panel noted that, according to both companies and the agenda, a total of 40 minutes was spent on presentations and 295 minutes on obtaining advice (excluding the opening and closing of the meeting). The Panel noted that no pre-reading was sent to attendees. The Panel queried why the data presented was not sent as pre-reading, however, on the information provided, there was no evidence to suggest that there had not been adequate time for discussion at the advisory board meeting. The Panel noted from the minutes of the meeting that the meeting appeared to deliver the stated aims.

The Panel noted the complainant's concern about the number and type of company attendees present at the advisory board including sales, marketing, global, medical and market access. The complainant was particularly concerned with the presence of sales and marketing staff when an unlicensed indication was being discussed. The Panel noted that the attendance of medical and commercial staff at an advisory board was not necessarily unacceptable nor when such an advisory board was about an unlicensed medicine or indication provided that their presence complied with the requirements of the Code.

The Panel noted AstraZeneca's submission that the medical and commercial expertise from the combined AstraZeneca and Merck Sharp & Dohme team was required to interpret the insights provided by the external attendees.

Although the Panel had some concerns, it did not consider that the complainant had shown, on the balance of probabilities, that the advisory board was disguised promotion or that the presence of commercial staff at the advisory board meant that an unlicensed indication had been promoted. The Panel ruled no breach of Clauses 12.1 and 3.2.

The Panel disagreed with Merk Sharp & Dohme's submission that the advisory board was attended by 5 company staff and the ratio of company staff to advisors did not exceed 1:2 at any point. The Panel noted that whilst ten advisors from across the UK attended the advisory board, AstraZeneca had three members of staff present for the duration of the day. A fourth individual from AstraZeneca presented the clinical data and departed the meeting at noon. One individual from Merck Sharp & Dohme was present throughout the duration of the meeting. The Panel noted that company attendees included those attending on behalf of the company and noted that one agency medical writer was present in the meeting room throughout the meeting and a further agency medical writer was present only during the workshop in the afternoon. It thus appeared that there were six company staff present at one point. The Panel noted that two additional Merck Sharp & Dohme representatives were present before the meeting to deal with administrative matters and, according to the companies, took no part in the meeting at any point of the day. The Panel noted the companies' submission that each attendee had relevant expertise and a legitimate role to meet the intended objectives of the advisory board. AstraZeneca provided a rationale for marketing and market access personnel attendance at the meeting and noted that, although two members of staff had some sales responsibilities, they fulfilled senior leadership roles which included, overall, responsibility for brand strategy and marketing for their respective franchises.

AstraZeneca submitted that they were required at the meeting to facilitate workshops (one each) and were involved throughout to gain relevant insights for the development of the launch strategy. In addition, one of those members of staff was also required to support discussions on topics related to diagnostics during the meeting. The Panel noted that whilst the number of company staff was on the limits of acceptability, one AstraZeneca employee left the advisory board meeting after the conclusion of the clinical data presentation and discussion session for the PAOLO-1 study and played no further part in the meeting and the second agency staff member only attended one of the two workshop sessions to ensure that the discussion and conclusions of the advisors were captured accordingly and left once the workshop session was completed. The Panel did not consider that the complainant had shown, on the balance of probabilities, that the number or types of company attendees were unacceptable as alleged and no breach of Clause 9.1 was ruled in this regard.

The Panel noted the complainant's concern that the chairperson was an AstraZeneca employee whereas usually the chair of an advisory board would be a reputable health professional. The Panel noted that it was not necessarily unacceptable for a company employee to act as the chair of an advisory board provided that the way in which it was done complied with the requirements of the Code. The Panel noted that the advisory board at issue had an external and internal chair, both of whom were to participate in the advisory board. According to the companies, the external chair was a highly experienced oncologist with a world-renowned reputation. The internal chair was an AstraZeneca employee who had a background in clinical oncology and was a trained senior pharmacist. The Panel did not consider that the complainant had shown, on the balance of probabilities, that having the meeting co-chaired with an employee of AstraZeneca was unacceptable *per se* or that the meeting was inappropriately facilitated as alleged and no breach of Clause 23.1 was ruled.

The Panel noted the complainant's concern that the advisory board was an interrogation of the worst sort. He/she also highlighted the way in which the afternoon sessions were run. The purpose of any advisory board would be to obtain advice and feedback. The Panel noted AstraZeneca's submission that workshops to discuss clinical or commercial scenarios were a common and effective means of gaining insight at advisory boards. The Panel appreciated that attendees might not feel comfortable in that type of setting, however, this did not mean that a workshop type session was, in itself, unacceptable. The Panel noted AstraZeneca's submission that the workshop was clear in its aims and was in line with advice that could legitimately be sought and that AstraZeneca employees received no comment to the contrary from attendees at the time. AstraZeneca further submitted that there was nothing to suggest that the workshops were conducted in anything other than a professional and appropriate manner. The Panel was concerned that the complainant felt interrogated as well as humiliated by the workshops but did not consider that the complainant had shown, on the balance of probabilities, that either the way of obtaining feedback or the workshop sessions were inappropriate and no breach of Clause 9.1 was ruled in this regard.

The Panel considered that it was standard practice for companies to ask health professionals and others to sign confidentiality agreements particularly before sharing data. It was not a breach of the Code for a company to ask an attendee at an advisory board to sign a confidentiality agreement. The Panel noted that the confidentiality agreements were part of the arrangements run by Merck Sharp & Dohme. The Panel did not consider that the complainant had established that Merck Sharp & Dohme asking the attendees to sign confidentiality agreements, meant that the companies had failed to maintain high standards and no breach of Clause 9.1 was ruled.

The Panel noted Merck Sharp & Dohme's submission that it was not its policy to take photographs during advisory boards and it was not mentioned in the signed contracts of the advisors that photographs would be taken. The Panel noted AstraZeneca's submission regarding the photographs, which included the faces of two health professionals, and that Astra Zeneca submitted that no health professional expressed any reservations about having his/her photograph taken at the time. AstraZeneca submitted that the photographs were deleted when it received notification of the complaint. The Panel considered that by taking photographs which identified individual health professionals and posting them, albeit on AstraZeneca's internal system, without obtaining those health professional's consent meant that the companies had failed to maintain high standards and a breach of Clause 9.1 was ruled.

The Panel did not consider that the circumstances warranted a ruling of a breach of Clause 2 which was used as a sign of particular censure.

Complaint received **2 January 2020**

Cases completed **6 July 2020 and 10 July 2020**