CASE AUTH/3013/1/18

ASTRAZENECA EMPLOYEE v ASTRAZENECA

Global training and advisory board and provision of incomplete and inaccurate information

An anonymous, non-contactable complainant, who described him/herself as an employee of AstraZeneca UK Limited's marketing company, alleged that although one of AstraZeneca's values was 'we do the right thing', over the last five years the company had become solely focussed on profits ahead of its ethical obligations. Over the last couple of years, the trend had reversed in the UK marketing company and the focus on achieving AstraZeneca's goals through the right means had returned. However, the same was not so for AstraZeneca's global functions.

The complainant stated that as a UK company, and with many employees in the global functions based in the UK, AstraZeneca should comply with the Code for activities led by global. However, this was not so. Global functions did not receive appropriate training on the Code and did not have regular Code case updates as in the UK marketing company. Globally led activities thus usually did not comply with the Code. In particular, the complainant referred to an unspecified global advisory board, held in October 2017, with over 15 external advisors and a similar number of AstraZeneca employees. The UK nominated signatory who was asked to approve the meeting, as UK health professionals were advisors, refused to do so due to the excessive number of people and the view that this was not a genuine advisory board. However, the UK marketing company was put under pressure to approve this and the nominated signatory was told to approve the advisory board by two other staff even though they acknowledged that it was likely to be a breach of the Code.

The detailed response from AstraZeneca is given below.

With regard to the allegations about training, the Panel noted that AstraZeneca distributed training to staff based on their role, location and responsibilities. The Panel noted that although the materials provided by AstraZeneca did not demonstrate comprehensive training on the Code, the company nonetheless trained global staff and provided more detailed training to the nominated signatories. The Panel did not consider that there was evidence to show that on the balance of probabilities, AstraZeneca had not trained relevant global staff as alleged. The Panel therefore ruled no breach of the Code.

With regard to advisory boards, 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. To be considered a legitimate advisory board the choice 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 driven by need and not the invitees' willingness to attend. Invitations to participate should state the purpose of the 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.

AstraZeneca referred to an advisory board meeting, held in Amsterdam in November 2017, which, in the absence of details, it assumed was the one to which the complainant had referred. The Panel noted that the agenda for that advisory board, included in the presentation, started with a welcome coffee and the actual meeting started at 10.30am and ended at 5.30pm; there were breaks for lunch and tea. The meeting was co-chaired by an external speaker and a member of AstraZeneca staff. One of the two speakers in the morning session was from AstraZeneca and the moderators for the afternoon discussion groups were both from AstraZeneca.

The initial invitation described the advisory board as part of AstraZeneca's ongoing commitment to supporting health professionals and patients. The objective of the meeting was to gain expert feedback and insights on the role of selective sodium glucose co-transporter 2 (SGLT2) inhibitors in type 1 diabetes and specifically the Forxiga (dapagliflozin) programme studies (DEPICT-1 and -2). The external speaker was asked to critically evaluate the benefit/risk of dapagliflozin on type 1 diabetics and to provide recommendations for safe and effective use of dapagliflozin in type 1 diabetes.
The UK delegates were emailed 6 published papers as pre-reading 6 days before the meeting.

There were 78 slides to be used during the day. Twenty-eight slides were presented in the first session by an external speaker, one of the investigators of the DEPICT studies. This one-hour session, which focused on the results of the two studies included two periods for discussion. The second session of seventeen slides, presented by an AstraZeneca employee, focused on the safety results of the two studies and lasted for one hour and fifty minutes. In the afternoon the group was split into

two (US and EU/International) and each group, moderated by AstraZeneca, discussed as session 3 (45 mins) the efficacy results. Session 4 (90 minutes) was a discussion of the benefit/risk of dapagliflozin in type 1 diabetes. The day ended with 30 minutes for summary and closing remarks. The short agenda provided included the sub heading 'Group discussion is 80% or more of each allocated session time and includes all participants'.

The Panel queried whether so many slides were needed on the DEPICT outcomes given the prereading included the published studies.

The Panel noted that the advisory board was to help AstraZeneca decide about an application for a new indication in the US and EU. In that regard, seven of the 16 advisors were from the US, eight came variously from five European countries (two from the UK, a doctor and a diabetes specialist nurse) and one advisor was from another country. In addition, there were 12 AstraZeneca staff.

The rationale for the attendance of AstraZeneca staff was provided. The stated business justification was to present and discuss DEPICT data, to critically evaluate benefit/risk of dapagliflozin on type 1 diabetes patients and to provide recommendations for the safe and effective use of dapagliflozin in type 1 diabetes. The business justification in this document was different to the objectives provided to the attendees. This document listed the 12 AstraZeneca staff and the rationale for their attendance. Five of the staff were to watch the first part of the advisory board via a video link and then three would actively participate in the breakout sessions. This was different to the submission from the company which stated that 9 of its staff joined the meeting and three listened in another room. Following a request for further information, the company stated that on the day there were 9 AstraZeneca staff in the room and the three listening in another room joined the main room about half way through the morning session due to a technical problem.

From the list of AstraZeneca attendees, four were assigned to participate in each of the breakout sessions; it was not stated if the other four were to participate in either session or not. The further information confirmed that all 12 AstraZeneca staff participated in the afternoon breakout sessions.

It was not clear to the Panel why AstraZeneca had not described what actually happened at the advisory board in the first instance. It was unacceptable and concerning that details of the arrangements for AstraZeneca attendees were only provided following a request for additional information.

The Panel was concerned about a number of aspects of the advisory board including the number of AstraZeneca attendees which was well outside the UK SOP. However, this did not necessarily mean that the advisory board failed to meet the requirements of the ABPI Code. The Panel was concerned to note, given the compliance difficulties that companies could experience with advisory boards and the high profile given to such in the UK recently, that it appeared that the arrangements for the meeting were only submitted for local review 12 working days before the meeting took place. The Panel was also concerned that the day before the advisory board AstraZeneca made fundamental changes to the arrangements and increased the number of its staff in the meeting room. In the Panel's view, the timescales and last minute changes would put unnecessary pressure on the nominated signatory to approve a meeting for which all of the arrangements should have already been in place; the UK SOP stated that material should be submitted for approval at least 6 weeks before the meeting date.

The Panel noted that no evidence was supplied in relation to the alleged pressure on the UK signatory to certify the meeting. The Panel was concerned as this was a serious allegation and it was vital that signatories were free to decline certifying material if they did not think it met the requirements of the Code. It appeared from AstraZeneca's submission that there was discussion between UK and global. This was particularly concerning given that this was ongoing so close to the date of the advisory board and that advisory boards were high risk area for companies. The Panel queried whether the certification should have been completed before the UK advisors were first approached at the end of September. If the arrangements were not capable of certification, UK health professionals should not have been approached.

The Panel noted that the advisory board which was held outside the UK and involved UK delegates had not been certified. The Panel noted AstraZeneca's submission that this was due to a timing issue rather than because the signatory was concerned with compliance with the Code. The Panel ruled that the failure to certify was in breach of the Code as acknowledged by AstraZeneca.

The Panel noted the complainant alleged that the advisory board was not genuine. No evidence had been provided by the complainant who had not clearly identified the advisory board about which he/she was concerned. As noted above, the Panel was concerned about the advisory board identified by AstraZeneca but did not consider that the complainant had shown, on the balance of probabilities, that the advisory board held on 10 November 2017 failed to meet the requirements of the Code and thus that any payment was inappropriate. Thus, the Panel ruled no breach of the Code.

On balance, the Panel considered that the arrangements for certification and the short time frame increased the pressure on UK certifiers. This and the failure to certify meant that AstraZeneca had failed to maintain high standards and a breach was ruled.

Noting its rulings above 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 and reserved for such use.

ADDENDUM TO SUMMARY

Following completion of this case in April 2018 and its publication on the PMCPA website in May 2018 a letter was received in June 2018 regarding the case and providing further information. It appeared to have come from the original anonymous, non-contactable complainant, who had described him/herself as an employee of AstraZeneca UK Limited.

The letter appeared to provide information which had not been provided by AstraZeneca in its response to the complaint: an email from a senior UK medical department employee outlining options for the advisory board in question. The further information was provided to AstraZeneca for comment including on Case AUTH/2793/9/15 where additional information was provided following the completion of a case.

Detailed comments from the complainant and AstraZeneca are given below.

The PMCPA decided that the original Panel should reconvene to consider the matter in relation to Paragraph 8.2 of the Constitution and Procedure which provided that the Panel might report to the Appeal Board any company whose conduct in relation to the Code, or in relation to a particular case before it, or because it repeatedly breached the Code such that it raised concerns about the company's procedures, warranted consideration by the Appeal Board. Such a report to the Appeal Board might be made notwithstanding the fact that a company had provided an undertaking requested by the Panel. The Panel noted that AstraZeneca had provided the requisite undertaking.

The Panel noted that the author of the letter had provided a copy to the Medicines and Healthcare products Regulatory Agency (MHRA) as the author was concerned there appeared to be no activity and alleging that AstraZeneca was receiving preferential treatment. The PMCPA responded to inform the MHRA that the matter had been followed up with AstraZeneca and would be considered by the Panel shortly. The delay was due to the number of complex cases. AstraZeneca was not receiving any preferential treatment.

The Panel noted the difficulties for UK companies regarding activities run by global.

The Panel noted the email trail dated 7 and 8 November 2017 provided as additional information which appeared to provide context to the discussions between the UK company and the global company about the arrangements for the advisory board held on 10 November 2017. It was clear that the concerns raised by the UK went beyond just a difference between the UK and global SOPs. Reference was made to advisory boards being in the spotlight in the UK over the last 18 months. The MHRA had questioned the validity of advisory boards and that the UK position was rather sensitive at the moment due to the AstraZeneca cases at the Panel and that it was '… trying to ensure we do not attract an audit'. The senior UK medical department employee stated that the need for the global advisory board was clear and the agenda was reasonable. The ratio of AstraZeneca attendees to health professionals was high. The situation was described as low risk but if a complaint were made it would be marginal as to whether it could be defended from a perceptual perspective. Three options were proposed including option 1 that the extra 5 AstraZeneca attendees watched the first part of the advisory board in a separate room and then participated in the breakout sessions. The email trail went on to state that the senior UK medical department employee wanted to avoid dropping the UK health professionals and also disrupting the plans for the proposed agenda. He/she was happy to go with any of the three options. He/she understood that this was frustrating but 'we do need to be consistent in our approach to implementing the code'.

The Panel considered that it was not clear from the email trail whether the senior UK medical department employee considered that the number of AstraZeneca attendees at the advisory board was in breach of the Code or in breach of the AstraZeneca UK SOP. The email spelt out three options. The Panel noted that the company had decided on option 1 although as included in the report for Case AUTH/3013/1/18 this did not happen due to technical issues.

The Panel considered the email including the context of discussions about the advisory board and the perception of the email. The Panel considered that the reference to self-reporting was a possible reference to the need for AstraZeneca to consider making a voluntary admission about a possible breach of the Code. Clearly it was important that companies followed their SOPs but not doing so was not in itself necessarily a breach of the Code.

The impression of the email was that the UK company had concerns about the arrangements for the advisory board, in particular the number of AstraZeneca attendees. Full details about the number of AstraZeneca attendees had only been provided to the Panel considering the case when it asked for further information.

The Panel noted that clearly there were difficulties with the advisory board and breaches of the Code had been ruled and a number of concerns raised. At that time it was also clear that AstraZeneca had not provided all the information. In relation to AstraZeneca's submission that as the Panel had not asked for the email of 8 November it had not provided the email, the Panel noted that self-regulation relied on companies to provide all relevant material. As the Panel did not know of the existence of the email, it could not request it.

The Panel noted AstraZeneca's submission that the email represented a snapshot of the discussions that had taken place and these were explained in the company's response to Case AUTH/3013/1/18 where it stated 'they presented several options to resolve this, one of which was the option which was eventually settled upon'.

Now having received the email of 8 November the Panel did not consider that this additional information would have made a difference as to whether it thought the advisory board itself was in breach of the Code. The Panel had ruled no breach in this regard based on the complainant not having shown on the balance of probabilities that there was a breach of the Code. However, the new information which provided some insight into the company's compliance culture was a concern as was AstraZeneca's general approach with regard to providing information to the Panel as evidenced by the number of times recently that the company had either not provided all the relevant information or had provided misleading information. This was set out in the Panel's request for further information from AstraZeneca.

Taken as a whole, the Panel considered that AstraZeneca could not clearly demonstrate its stated commitment to self-regulation in the broadest sense. It was concerned that actions might be taken by AstraZeneca so as to '… not attract an audit' rather than ensuring compliance with the Code and its own procedures. The Panel was also concerned that it appeared from the email and other aspects of the complaint that for some staff raising concerns about activities was difficult at AstraZeneca and this contributed to the differences of opinion between UK and Global. However, it decided that, on balance, the material before it, most of which had come to light either during the consideration of the cases or afterwards and had been the subject of a public reprimand, had been addressed and thus on balance a formal report to the Appeal Board was not needed at this stage. The Panel's view was that these examples should be reconsidered if there were further instances of AstraZeneca failing to provide comprehensive information. The Appeal Board would be provided with details of the Panel's further consideration following a similar format to the details provided for cases which concluded at the Panel level.

The Appeal Board received the update to the case report as set out in Paragraph 13.4 of the Constitution and Procedure.

The Appeal Board considered that the additional information in this case raised serious issues including about the provision of incomplete and/ or inaccurate information. The Appeal Board's view was that further consideration should be given to this matter including the possibility of imposing further sanctions under Paragraph 11.1 of the Constitution and Procedure.

The company was advised that the Appeal Board was giving further consideration to this matter including considering imposing additional sanctions and asked to respond in writing, as well as be given the opportunity to attend the Appeal Board when the matter would be considered. AstraZeneca was provided with a copy of the papers.

The detailed comments from AstraZeneca about the possible imposition of further sanctions is given below.

The Appeal Board noted the Panel's rulings of breaches of the Code. The Appeal Board noted that the company had apologised and admitted that it had made errors.

The Appeal Board noted the context in that there had been discussions between AstraZeneca UK and the global company about the arrangements for the advisory board held on 10 November 2017 right up to the meeting taking place. The UK company did not want to certify the meeting due to concerns about the number of AstraZeneca representatives attending. The email at issue dated 8 November 2017 from a senior UK medical department employee was an attempt to overcome this issue. The email included three options in order to enable the advisory board to go ahead. The Appeal Board noted AstraZeneca agreed that the email of 8 November 2017 was poorly worded. The email referred to ensuring the company did not attract an audit and mentioned a self-report to the ABPI if the meeting went ahead as planned. The Appeal Board noted the submission from AstraZeneca that the senior UK medical department employee was new; and that the self-report was in relation to the breach of the company's SOPs and not in relation to the ABPI Code. The Appeal Board considered that the reference to self-report appeared to be in relation to the Code. The Appeal Board noted that the email of 8 November 2017 had been copied to several senior AstraZeneca members and queried why nobody had replied to the email to raise their concerns. AstraZeneca stated that there had been a discussion about the email at the time but there was no written record. Although there was no requirement to self-report, the Appeal Board queried why the company had not self-reported a breach of the Code at this point. This was said by AstraZeneca to be an oversight.

The Appeal Board considered that when submitting a response, companies need not include everything however the company had not provided the relevant source material it used in summarising events. The email of 8 November 2017 was clearly central and relevant to this case and did not appear to be consistent with the summary provided. In the Appeal Board's view to not submit the email was inexplicable. Effective self-regulation required companies to be open and transparent when responding to complaints; they had a duty to disclose all relevant documents and information. When compiling its response to the complaint AstraZeneca stated that it had referred to emails. The Appeal Board was not satisfied with AstraZeneca's submission as to why it had not provided the email dated 8 November when responding to the complaint.

The Appeal Board considered that the email of 8 November 2017 was clearly relevant and should have been provided to the PMCPA as part of AstraZeneca's response. Notwithstanding AstraZeneca's submission that it now had updated its processes, the Appeal Board noted that self-regulation relied, *inter alia*, upon the provision of complete and accurate information from pharmaceutical companies.

The Appeal Board decided that in accordance with Paragraph 11.3 of the Constitution and Procedure, AstraZeneca should be publicly reprimanded for failing to provide complete and accurate information in an open and transparent way.

The Appeal Board was concerned to note that AstraZeneca was also publicly reprimanded in 2016 by the Appeal Board for providing inaccurate information to the Panel (Case AUTH/2793/9/15).

The Appeal Board noted the Panel's comments above regarding AstraZeneca's conduct in responding to complaints. The Appeal Board noted its concerns about AstraZeneca's compliance culture. The Appeal Board gave consideration to the imposition of further sanctions including whether an audit should be required. However, on balance, the Appeal Board decided that no additional action was required.

An anonymous, non-contactable complainant, who described him/herself as an employee of AstraZeneca UK Limited's marketing company, complained about compliance at AstraZeneca. The complainant referred to global activities and referred to an advisory board meeting held in 2017.

COMPLAINT

The complainant alleged that despite stating that one of AstraZeneca's values was 'we do the right thing', over the last five years the company had become solely focussed on profits ahead of its ethical obligations. Over the last couple of years, the trend had reversed in the UK marketing company and the focus on achieving AstraZeneca's goals through the right means had returned. However, the same could not be said for AstraZeneca's global functions.

The complainant stated that as a UK company, and with many of the employees in the global functions based in the UK, AstraZeneca should comply with the Code for activities led by global. However, this was not so. Global functions did not receive appropriate training on the Code and did not have regular Code case updates as in the UK marketing company. Global functions believed that they did have to know or comply with the Code (sic) and only had to follow AstraZeneca global standards which were loosely based on the Code. The complainant understood that all staff working in areas that were covered by the Code should have comprehensive Code training.

Due to this, globally led activities were usually conducted in a manner which was not in line with the requirements in the Code. The complainant was aware of a recent global advisory board, held in October 2017, with over 15 external advisors and a similar number of AstraZeneca employees. This was sent to the UK marketing company for approval as UK health professionals were advisors. The nominated signatory refused to approve this due to the excessive number of people and the view that this was not a genuine advisory board. However, the UK marketing company was put under pressure to approve this and the two other staff (roles named) in the UK told the nominated signatory to approve the advisory board, even though they acknowledged that it was likely to be a breach of the Code.

The complainant stated that there were likely to be a number of other global activities that were in breach of the Code but that AstraZeneca UK was not aware of them. The complainant asked that the PMCPA investigate this in order that the reputation of AstraZeneca and the wider pharmaceutical industry was not tarnished.

When writing to AstraZeneca, attention was drawn to the requirements of Clauses 2, 9.1, 14.2, 16.1, 18.1 and 23.1 of the Code.

RESPONSE

AstraZeneca submitted that it took compliance with all applicable laws and regulations very seriously, including pharmaceutical industry codes of practice. AstraZeneca believed that it had, at all times, addressed the advisory board referred to in the complaint in accordance with the high standards expected of a pharmaceutical company.

AstraZeneca was disappointed that the complainant had brought his/her concerns to the PMCPA rather than raising them internally. AstraZeneca noted that its commitment to ethics included training all staff on induction, and annually thereafter, on its internal escalation processes which also included details of its AZethics line, an externally hosted confidential online and telephone helpline, available 24 hours a day, 7 days a week. Whilst AstraZeneca did not deny the complainant's right to complain to the PMCPA, it was very important to note the reporting system which existed and to reiterate that AstraZeneca made every effort to encourage employees to report concerns and gave them a confidential route to do so. AstraZeneca submitted that it did this, because it was the right thing to do and because it was committed to continuous improvement across its organisation.

AstraZeneca refuted the complainant's general and unsubstantiated allegations about interactions between AstraZeneca's global and UK commercial functions and the general attitude of the global functions to compliance. As recognised in the complaint, 'Do the Right Thing' was one of AstraZeneca's five core values and underpinned all of its decisions. Like any organisation, there would always need to be discussions between colleagues to understand the implications of the underlying legal and regulatory requirements. It was grossly inaccurate to state that such discussions showed a disregard for the Code or a desire to put profit before compliance. The allegations suggested that the complainant did not have full insight into all the relevant and key discussions that took place about the advisory board, and did not have sufficient knowledge and experience of the organisation especially in relation to global processes.

AstraZeneca submitted that the only specific allegation related to an advisory board. Although the complainant did not specify a date, AstraZeneca

believed that the advisory board to which he/she referred was the Global Dapagliflozin T1D Indication Advisory Board held in Amsterdam from 9.30am to 5.30pm on 10 November 2017. AstraZeneca submitted that this advisory board was conducted in a compliant fashion.

Issues to be addressed by the advisory board

AstraZeneca stated that as part of its commitment to science, it had recently conducted the DEPICT-1 and DEPICT-2 studies to investigate the efficacy and safety of the selective sodium-glucose co-transporter 2 (SGLT2) inhibitor, dapagliflozin (Forxiga) in patients with inadequately controlled type 1 diabetes. This was a new area of potential application for this class of product and relied on a mode of action which had not previously been used in type 1 diabetics.

The advisory board was arranged by AstraZeneca's global medical affairs team. Global medical affairs looked to inform AstraZeneca's decision on an application for a potential new indication (US and EU) by gaining insight from key opinion leaders on the benefit/risk profile of Forxiga based on DEPICT-1 and DEPICT-2. The detailed objectives of the meeting were set out in a form for health professionals (copy provided).

The advisory board was a single advisory board required for insight gathering only. It was not part of a series.

Selection and invitation of participants

AstraZeneca selected the participants based upon:

- expertise and experience in the management of type 1 diabetes and its complications;
- experience with SGLT2 inhibitors and/or familiarity with diabetic ketoacidosis;
- the need to represent a diversity of advisor roles across the diabetes therapy area; and
- the need for representation from relevant geographies.

In order to meet the requirements, AstraZeneca selected seventeen potential participants. They were emailed by a global medical leader within global medical affairs in order to ascertain whether they were available (example email provided). A follow-up email invitation was sent by a third party agency based on confirmation of participant availability (copy provided).

Number of health professionals attendees and compensation

AstraZeneca stated that sixteen participants attended the advisory board. Compensation was paid to each in accordance with relevant local guidance and details were provided. It submitted that the compensation paid to the two UK health professionals was reasonable and in accordance with the UK marketing company's fair market value guidance.

Agenda and materials

Copies of the advisory board agenda, the presentations and the participants' pre-reading material were provided. AstraZeneca referred to the audio recording of the advisory board captured by the third party agency for the sole purpose of consolidating a report of the meeting.
The materials associated with this advisory board (agenda, presentations and discussion guide) were examined by a global medical affairs signatory in line with the requirements of the Code for non-promotional activities, and also a host country nominated signatory to ensure local host country regulations were adhered to.

Feedback from participants

There was no feedback form. Whilst AstraZeneca often sought feedback from attendees at its educational and promotional meetings, it was not standard practice to seek feedback from advisory board attendees.

Selection and attendance of AstraZeneca staff

Noting differences between the global and local standard operating procedures (SOPs), a compromise was agreed that only AstraZeneca attendees with a meeting relevant role were to be in the actual meeting room. Colleagues with a secondary requirement were allowed to listen remotely. Nine AstraZeneca staff were in the room along with 2 employees of the third party agency. A further three AstraZeneca staff listened to the advisory board from an adjacent room with a video link, together with a further 2 agency employees. AstraZeneca provided a rationale for attendance of its staff.

Discussions concerning AstraZeneca attendees

Discussions about the differences between the global and UK SOPs for advisory boards took place between global medical affairs and UK marketing company staff, in particular around the more prescriptive limit on the number of internal attendees that ordinarily applied under the UK SOP. Copies of both SOPs were provided. AstraZeneca submitted that neither of the two staff whose roles were mentioned by the complainant considered that the meeting was in breach of the Code. Furthermore, they did not pressurize the UK signatory to certify the meeting arrangements and AstraZeneca had found no evidence to the contrary. Team members confirmed that the one of these roles had made it clear on more than one occasion that AstraZeneca did not expect individuals to sign off any materials if they were not comfortable to do so. The UK nominated signatory confirmed that the two members of staff did not pressurize him/her to certify the meeting arrangements.

The advisory board was designed in line with AstraZeneca's relevant global SOP which AstraZeneca submitted was in accordance with the principles of the ABPI Code. The global SOP required adherence to local requirements including,

where appropriate, the need for local approval of matters relating to the attendance of local health professionals. As two UK health professionals were to attend this advisory board, the global medical affairs team approached local UK marketing company signatories to arrange certification for their attendance. The local UK marketing company signatories reviewed the advisory board and requested that certain changes be made, including in relation to the number/role of attendees: discussions on the changes took place over a number of weeks following the submission of the advisory board for review by the local signatory on 24 October 2017. Eventually, only a request from the UK signatories to change the number of internal attendees present in the meeting in order for the arrangements to be certified under the UK SOP remained under discussion. They presented several options to resolve this, one of which was the option eventually settled upon. Unfortunately, although it was agreed and an amended health professional form submitted by the global medical affairs team for approval on 9 November, they were not able to make a further resubmission of the health professional form before close of business that day owing to additional editorial changes to the form requested by the UK marketing company signatory. As a result, the UK signatory decided that it would not be appropriate to certify the arrangements of the advisory board on the following day (10 November) as the UK health professionals had already travelled and the activity had commenced: to do so would have been viewed as a retrospective certification. The UK signatory did not inform his manager of the lack of certification due to this timing issue until after the advisory board had started. This had been logged as a deviation and would be addressed in accordance with AstraZeneca's standard procedures for dealing with specific deviations.

Training of global personnel

AstraZeneca refuted the complainant's non-specific allegations concerning the level of training of global employees in the requirements of the Code; such allegations appeared to overlook the comprehensive training program in place for all staff across a wide range of topics, including regulatory compliance.

AstraZeneca maintained a web-based software solution to schedule and distribute training to staff based on their role, location and responsibilities. Various topics, including those related to medicines' promotional regulations, were made available to global employees on the network and these interactive modules allowed employees to work through training presentations on their own with trackable progress. An example of one, the training on scientific exchange was provided.

In addition, the global nominated signatories (GNSs) were tasked to train relevant global teams on topics related to the regulation of the promotion of medicines and their assigned therapy areas. Examples of summaries of such trainings were provided. All members of the GNS team were either UK registered pharmacists or registered physicians and they were registered with the Medicines and Healthcare products Regulatory Agency (MHRA) and PMCPA in line with Clause 14.4 of the Code. The majority had had extensive experience working in the medical affairs departments of UK pharmaceutical companies, and so had a deep understanding of the requirements of the Code. In addition, GNSs underwent robust training when they joined the company, and actively took part in various learning initiatives on the job to keep their knowledge up-to-date.

The AstraZeneca team used a variety of techniques to deliver training and these were reviewed regularly to ensure that training was up-to-date and effective. One of the methods used was WebEX for group training, called 'Nom Sig On- Air Sessions'. During these sessions, participants from global and affiliate countries dialled in to receive live audio training and follow visual presentations on their computer screens. The participants interacted with the presenters through the audio function or via webchat, with training sessions recorded to allow for easy make-up for employees who missed the group training or as useful on-demand refresher training. An example of a 'Nom Sig On-Air Session' on running a patient advisory board was provided.

AstraZeneca also used multimedia for training, typically videos that were widely available to all employees, not just those involved in the production and review of materials subject to the Code. These videos were mostly about 3 minutes each and provided succinct guidance. They allowed employees to build sufficient knowledge to know when they might be carrying out a regulated activity. An example of a transcript for one of the videos was provided.

Clause 14.2

AstraZeneca was disappointed that the arrangements for the attendance of the UK health professionals at the advisory board were not certified before it commenced, despite the scrutiny that was applied to this advisory board. AstraZeneca acknowledged that it did not meet the requirements of Clause 14.2 but noted that the failure to certify was based on a timing issue rather than a disregard of the requirements of the Code or the activity not being in accordance with the Code.

Clause 16.1

Given the extensive training regime described above, AstraZeneca denied a breach of Clause 16.2, whether generally in relation to the staff within global medical affairs or more specifically with relation to the staff involved in the advisory board.

Clause 18.1

The advisory board was appropriate and the remuneration provided to the health professionals represented a fair market value for their work, in accordance with AstraZeneca's internal guidance on fair market value. AstraZeneca denied any breach of Clause 18.1.

Clause 23.1

AstraZeneca denied any breach of Clause 23.1. In particular, the UK health professionals in question:

- had signed appropriate written contracts in respect of the advisory board;
- were selected based on appropriate criteria in order to enable AstraZeneca to fulfil a legitimate business need;
- were part of an appropriately sized group of health professionals contracted to provide the breadth of advice reflecting the scope of disease, complications of treatment and variation in geography for a global investment decision and
- were paid the fair market value for the services that they provided and were not hired as an inducement to prescribe.

Clause 9.1

Whilst AstraZeneca acknowledged and regretted the breach of Clause 14.2 referred to above, it did not accept that it failed to maintain high standards. The detailed discussions that took place over this one advisory board were a sign of the efforts that the company had made to maintain high standards.

Clause 2

AstraZeneca denied any breach of Clause 2. AstraZeneca believed that it had maintained high standards throughout and that the evidence demonstrated its commitment to upholding the reputation of the industry.

In summary, AstraZeneca stated that the advisory board was carried out for a legitimate business purpose, the arrangements were appropriate including a reasonable number of participants and AstraZeneca staff to achieve the stated business objectives. A difference in opinion based on variation in the UK and global SOPs was appropriately escalated and no pressure was put on the nominated signatory to approve an activity with which he/she was uncomfortable. Nevertheless, AstraZeneca accepted that the arrangements for the advisory board were not certified because the final amended forms were not submitted early enough for the UK signatory to certify them. However, AstraZeneca denied any other breach of the Code.

FURTHER INFORMATION FROM ASTRAZENECA

The Panel requested further information.

With regard to the changes to the arrangements for the advisory board requested by UK signatories, AstraZeneca submitted that during the initial review of travel arrangements for the two UK health professionals invited to attend the advisory board, the only point raised by UK signatories which required further discussion related to the number of AstraZeneca employees invited to attend the meeting and the need to clarify the rationale for their attendance. UK signatories requested that the internal attendee numbers be revised in line with requirements of the local UK SOP for advisory boards. This was in contrast to the global SOP which was not prescriptive regarding specific attendee numbers or ratios, but gave guidance to ensure the number of internal attendees was the minimum required to meet the objectives of the meeting. The ensuing discussion between global medical affairs and the UK focused on how to resolve the conflicting guidance. The compromise reached was to reduce the number of AstraZeneca attendees in the main room where the discussion was taking place during the morning session, with 5 staff members listening in from another room.

Once internal attendee numbers were agreed, the UK signatory requested the following additional changes, which were mostly editorial in nature, before final approval could be granted:

- a correction of an error which marked one of the UK health professional's fee for service as being outside acceptable fair market value limits when in fact it was within the limits;
- a request to attach the biography for one of the UK health professionals;
- a request to correct errors in the flight details for both UK attendees to accurately reflect the travel arrangements;
- a request to clarify job/role descriptions of AstraZeneca attendees and
- a request to clarify the final number of internal attendees.

With regard to the differences between AstraZeneca's letter of response and enclosed rationale for attendance of active AstraZeneca participants, AstraZeneca stated that a final internal preparatory meeting for the advisory board was conducted by global medical affairs on the day before the meeting. At that meeting, those present determined that two members of staff who had been due to listen from the neighbouring room would need to be in the main meeting room in order to answer questions and clarify points as part of the morning discussion. As a result, it was decided that three additional AstraZeneca employees would be present in the room as well. Although this increased the total number of AstraZeneca attendees inside the room to nine, AstraZeneca submitted it needed to exercise a degree of flexibility on this occasion to fulfil the requirements of the advisory board. About half way through the morning session, there was a problem with the listening device which led to the three remaining AstraZeneca participants joining the others in the main room until the end of that session.

Twelve AstraZeneca staff participated to facilitate the needs of the afternoon sessions which were split by region into the US and EU/International sessions. A list of advisors, AstraZeneca attendees and agency staff at each session was provided.

AstraZeneca stated that the welcome coffee was time allocated for coffee to be served outside the meeting room whilst advisors arrived. All twelve AstraZeneca attendees arrived at different times during the welcome coffee. No formal introductions or discussions took place between AstraZeneca staff and the advisors, most of whom used this time to

settle in or catch up with their colleagues or prepare for the meeting.

AstraZeneca stated that emails to ascertain availability to attend the advisory board were sent to one UK health professional on 25 September 2017 and to the other on 3 October 2017. These emails did not constitute formal invitations to attend the advisory board. It was important to clarify that whilst this contact was prior to formal UK signatory involvement, the purpose and nature of this contact was purely to ascertain availability; this communication was appropriate and compliant because it did not contain any substantive content.

The global medical affairs team engaged the UK signatory team to approve attendance of the UK attendees on 24 October 2017, after receiving confirmation of availability to attend. No formal invitation was sent to either UK health professional prior to involvement by UK signatories.

A formal invitation to attend the advisory board was sent to both UK health professionals on 6 November 2017.

A copy of correspondence sent with pre-read materials was provided.

The outcome and recommendations by the advisors were captured by the agency staff. The form containing the details of the information captured was provided. AstraZeneca submitted that this information clearly demonstrated a legitimate need for the advisory board, with relevant content, an appropriate agenda and aligned outputs.

AstraZeneca remained comfortable that the advisory board was entirely appropriate and that it was conducted in compliance with the ABPI Code.

PANEL RULING

The Panel noted that the complainant was anonymous and non-contactable. The Constitution and Procedure for the Prescription Medicines Code of Practice Authority stated that anonymous complaints would be accepted but that like all other complaints, the complainant had the burden of proving his/her complaint on the balance of probabilities. All complaints were judged on the evidence provided by the parties. The Panel noted that the parties' accounts differed; the complainant had provided no evidence to support his/her allegations and could not be contacted for more information.

With regard to the allegations about training staff, the Panel noted that AstraZeneca distributed training to staff based on their role, location and responsibilities. Various topics including those related to medicines' promotional regulations were made available to global employees on the AstraZeneca network allowing them to work through training presentations on their own with trackable progress. The example training for scientific exchange, medical education and sharing off-label information was dated March 2015. Other training for global nominated signatories to use when training relevant global teams was a one-page summary on medicines promotion regulations. There were three versions for the different audiences, medical personnel, marketing personnel and communications personnel. The training for nominated signatories appeared to be more detailed. The screen shot provided dated September 2016 listed 10 training modules with links to AZlearn modules. The patient advisory board training was undated.

The Panel noted that although the materials provided did not demonstrate comprehensive training on the ABPI Code, Clause 16.1 required relevant personnel concerned in any way with the preparation or approval of material or activities covered by the Code to be fully conversant with the Code and the relevant laws and regulations. AstraZeneca provided training to global staff and more detailed training to the nominated signatories who, as required by the supplementary information to Clause 14.1, Suitable Qualifications for Signatories, must have an up-to-date detailed knowledge of the Code. The Panel did not consider that there was evidence to show that on the balance of probabilities, AstraZeneca had not trained relevant global staff as alleged. The Panel therefore ruled no breach of Clause 16.1 of the Code.

Turning to the allegations about the advisory board, 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 the choice 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 driven by need and not the invitees' willingness to attend. Invitations to participate should 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 that the agenda for the advisory board included in the presentation started with a welcome coffee from 9.30am until 10.30am and the actual advisory board started at 10.30am and ended at 5.30pm; there were breaks for lunch and tea. It was held in Amsterdam and was co-chaired by the external speaker and a member of AstraZeneca staff. One of the two speakers in the morning session was from AstraZeneca and the moderators for the afternoon discussion groups were both from AstraZeneca.

The initial invitation to one of the UK participants was provided (dated 25 September 2017). The initial invitation to the other UK participant (dated 29 September 2017) was provided following the Panel's request for further information.

The invitation described the advisory board as part of AstraZeneca's ongoing commitment to supporting health professionals and patients. The objective of the meeting was to gain expert feedback and insights on the role of SGLT2 inhibitors in type 1 diabetes and specifically the DEPICT programme studies.

The invitation to the external speaker set out the objectives as to critically evaluate the benefit/risk of dapagliflozin on type 1 diabetic patients and to provide recommendations for safe and effective use of dapagliflozin in type 1 diabetes.

The pre-reading consisted of 6 published papers including the 'American Association of Clinical Endocrinologists and American College of Endocrinology Position Statement on the Association of SGLT-2 Inhibitors and Diabetic Ketoacidosis' and the published DEPICT study. It was sent to the UK participants on 4 November 2017. The email of 4 November referred to the recipient already receiving details of how to register for the meeting. The official invitation was sent on 6 November and this asked the participant to register for the meeting.

There were 78 slides to be used during the day. Twenty-eight slides were presented in the first session by an external speaker, one of the investigators of the DEPICT studies. This one-hour session, which focused on the results of the two studies and their clinical interpretation, included two periods for discussion. The second session of seventeen slides, presented by an AstraZeneca employee, focused on the safety results of the two studies and lasted for one hour and fifty minutes. In the afternoon the group was split into two (US and EU/International) and each group, moderated by AstraZeneca, discussed as session 3 (45 mins) the efficacy results, in a 'Focused discussion on efficacy elements including HbA_{1c}, weight and continuous glucose monitoring'. Session 4 (90 minutes) was a discussion of the benefit/risk of dapagliflozin in type 1 diabetes patients in particular 'Guidance on insulin dose reduction, dose response 5mg vs 10mg dapagliflozin, special precautions, patient subgroups, labelling'. The day ended with 30 minutes for summary and closing remarks. The short agenda provided included the sub heading 'Group discussion is 80% or more of each allocated session time and includes all participants'.

The Panel queried whether so many slides were needed on the DEPICT outcomes given the pre-reading included the published studies.

The Panel noted that the advisory board was to help AstraZeneca decide about an application for a new indication in the US and EU. In that regard, seven of the 16 advisors were from the US, eight came variously from five European countries (two from the UK, a doctor and a diabetes specialist nurse) and one advisor was from Israel. In addition, there were 12 AstraZeneca staff.

The rationale for the attendance of AstraZeneca staff was provided. This indicated that the meeting ran from 9.30 until 17.30 whereas the first hour was spent on a welcome coffee with the advisory board starting at 10.30. The stated business justification was to present and discuss DEPICT-1 and -2 data, to critically evaluate benefit/risk of dapagliflozin on type 1 diabetes patients and to provide recommendations for the safe and effective use of dapagliflozin in type 1 diabetes. The business justification in this document was different to the objectives provided to the attendees. This document listed the names of the 12 AstraZeneca staff and their role as well as the rationale for their attendance. Five of the staff were to watch the first part of the advisory board in a separate room on video link and then three would actively participate in the breakout sessions. This was different to the submission from the company which stated that 9 AstraZeneca staff joined the meeting and three listened in another room. The further information from the company stated that on the day there were 9 AstraZeneca staff in the room and the three listening in another room joined the main room about half way through the morning session due to a technical problem.

From the list of AstraZeneca attendees four were assigned to participate in each of the breakout sessions; it was not stated if the other four were to participate in either session or not. The further information confirmed that all 12 AstraZeneca staff participated in the afternoon breakout sessions.

It was not clear to the Panel why AstraZeneca had not described what actually happened at the advisory board in its first letter of response. It was unacceptable and concerning that details of the arrangements for AstraZeneca staff attendees were only provided following a request for additional information.

The AstraZeneca UK marketing company guideline, 'UKMC Advisory Board Standard' stated that an advisory board should generally consist of no more than 10 advisors and that generally no more than 3 AstraZeneca employees might attend. Additional employees might attend only if they could show a legitimate and documented need.

The Panel was concerned about a number of aspects of the advisory board including the number of AstraZeneca attendees which was well outside the UK SOP. However, this did not necessarily mean that the advisory board failed to meet the requirements of the ABPI Code.

The Panel was concerned to note, given the compliance difficulties that companies could experience with advisory boards and the high profile given to such in the UK recently, that it appeared that the arrangements for the meeting were only submitted for local review on 24 October– only 12 working days before the meeting took place. The Panel was also concerned that the day before the advisory board AstraZeneca was making fundamental changes to the arrangements and increasing the number of AstraZeneca staff in the meeting room. In the Panel's view, the timescales and last minute changes would put unnecessary pressure on the nominated signatory to approve a meeting for which all of the arrangements should have already been in place; the UK SOP stated that material should be submitted for approval at least 6 weeks before the meeting date.

The Panel noted that no evidence was supplied in relation to the alleged pressure on the UK signatory to certify the meeting. The Panel was concerned as this was a serious allegation and it was vital that signatories were free to decline certifying material if in their opinion it did not meet the relevant requirements of the Code. It appeared from AstraZeneca's submission that there was discussion between the UK company and the global company. This was particularly concerning given that this was ongoing so close to the date of the advisory board and that advisory boards were high risk area for companies. The Panel queried whether the certification should have been completed before the UK advisors were first approached at the end of September. If the arrangements were not capable of certification, UK health professionals should not have been approached.

The Panel noted that the advisory board which was held outside the UK and involved UK delegates had not been certified. The Panel noted AstraZeneca's submission that this was due to a timing issue rather than because the signatory was concerned with compliance with the Code. The Panel ruled that the failure to certify was a breach of Clause 14.2 of the Code as acknowledged by AstraZeneca.

The Panel noted the complainant alleged that the advisory board was not genuine. No evidence had been provided by the complainant who had not clearly identified the advisory board about which he/she was concerned. As noted above, the Panel was concerned about the advisory board identified by AstraZeneca but did not consider that the complainant had shown, on the balance of probabilities, that the advisory board held on 10 November 2017 failed to meet the requirements of the Code and thus that any payment was inappropriate. Thus, the Panel ruled no breach of Clauses 23.1 and 18.1.

On balance, the Panel considered that the arrangements for certification and the short time frame increased the pressure on UK certifiers. This and the failure to certify meant that AstraZeneca had failed to maintain high standards. The Panel ruled a breach of Clause 9.1 of the Code.

Noting its rulings above 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 and reserved for such use. The Panel therefore ruled no breach of Clause 2.

CASE AUTH/3013/1/18 – ADDENDUM

Following completion of this case in April 2018 and its publication on the PMCPA website in May 2018 a letter was received in June 2018 regarding the case and providing further information. It appeared to have come from the original anonymous, non-contactable complainant, who had described him/herself as an employee of AstraZeneca UK Limited.

The letter appeared to provide information which had not been provided by AstraZeneca in its response to the complaint. The author of the letter referred to an email from a senior UK medical department employee outlining options to deal with the advisory board in question. AstraZeneca referred to 'several options' in its response to the PMCPA but this was not expanded upon nor did the PMCPA question this. The author of the letter stated that one of the options was 'proceed as planned, log this as a breach and consider whether to self report to the ABPI'. The distribution of the email included several senior members of AstraZeneca's UK and Global teams.

The author of the letter referred to AstraZeneca's response to the PMCPA which referred to 'Do the right thing' underpinning all its decisions, however none of the senior people in the email distribution responded to the email to say that proceeding with an advisory board that was considered to be in breach of the Code was unacceptable and not the right thing. It was also noticeable that the senior medical department employee was not concerned about complying with the Code or 'doing the right thing' but rather 'trying to ensure we do not attract an audit' (presumably from the PMCPA).

The author of the letter pointed out that AstraZeneca in its response to the complaint stated that named staff did not believe that the advisory board was in breach of the Code. In the author of the letter's view, the email clearly demonstrated otherwise. In addition, AstraZeneca's failure to disclose the email in response to that case and give complete and accurate information to the PMCPA demonstrated that AstraZeneca did not take self-regulation seriously. Furthermore, that senior employees were already aware of the issues and were happy to proceed without making changes to the advisory board and make a voluntary admission later, meant that it was not appropriate to raise concerns using internal channels, as stated by AstraZeneca in its response.

Given the PMCPA appeared to take a grave view of companies that did not respond in full to complaints, the author of the letter asked the PMCPA to look again at this case as a matter of urgency, stating that '…surely AstraZeneca's conduct is not acceptable?'. There had already been two cases ruled in breach of the Code in 2018 and as long as this unacceptable culture existed, particularly amongst senior employees, then there was likely to be further breaches of the Code.

The matter was taken up with AstraZeneca which was asked to comment on a number of matters including Case AUTH/2793/9/15 where additional information was provided following the completion of a case.

AstraZeneca was advised that on receipt of its response the PMCPA would consider the position. The Appeal Board would have to be informed and this might be by way of a report under Paragraph 8.2 of the Constitution and Procedure.

RESPONSE FROM ASTRAZENECA

AstraZeneca reiterated its firm commitment to compliance with all applicable laws and regulations, pharmaceutical industry codes of practice, including upholding effective self-regulation. It had fully

accepted the breaches of Clauses 9.1 and 14.2 ruled in Case AUTH/3013/1/18 and listed the steps already taken to address the issues raised.

AstraZeneca acknowledged the PMCPA's concern regarding the completed cases (Case AUTH/3011/1/18, Case AUTH/2793/9/15 and Case AUTH/3013/1/18). The company submitted that it made every effort to respond to the PMCPA in good faith and to the best of its knowledge at the time but recognised the continuing need to review the complexity and efficiency of its ways of working between Global and the UK Marketing Company. Whilst it was extremely disappointed that these incidents occurred, AstraZeneca submitted that the compliance governance framework between the UK Marketing Company and Global teams remained effective.

AstraZeneca referred to its response in Case AUTH/3013/1/18 in which the discussions in relation to the advisory board were outlined:

> 'The local UKMC signatories reviewed the advisory board and requested that certain changes be made, including in relation to the number/role of attendees: discussions on the changes took place over a number of weeks following the submission of the Ad Board for review by the local signatory on 24th of October 2017. Eventually, the one remaining change under discussion was a request from the UK signatories to change the number of internal attendees present in the meeting in order for the arrangements to be certified under the UK SOP. They presented several options to resolve this, one of which was the option which was eventually settled upon.'

AstraZeneca submitted that the email provided by the author of the letter represented a snapshot of these discussions and, in its view, was consistent with the description of them as set out above. In addition, AstraZeneca's further response in Case AUTH/3013/1/18 provided specific information on the acceptance of option 1 as referred to in the email:

> 'The ensuing discussion between the Global Medical Affairs (GMA) team and the UK team focused on how to resolve the conflicting guidance. The compromise reached at this time was to reduce the number of internal AZ attendees in the main room where the discussion was taking place during the morning session, with 5 of the internal attendees listening in from another room.'

Discussion, questioning and challenge were integral parts of reaching the right outcome for all compliance activities under the Code.

AstraZeneca stated that it was important to note that at no point throughout ongoing discussions was the legitimacy of the advisory board called into question: the discussions and opinions were centred around a potential procedural breach of the AstraZeneca UK Marketing Company SOP arising from a conflict with the Global SOP. This email formed part of that on-going discussion and could be misinterpreted when taken out of context. The language was aimed solely for internal dialogue with an audience which was largely aware of the issues and the discussions. AstraZeneca confirmed with its senior UK medical department employee director that he/she was ostensibly referring to the fact that it was technically possible for the global organisation to proceed with the meeting in breach of the UK SOP but, in such an event, it would be necessary to review the question of whether this could then lead to a breach of the Code which would have to be self-reported. The senior UK medical department employee took it that it would be self-evident to the internal audience that this option was to be avoided.

AstraZeneca submitted that in hindsight, the email was vulnerable to misinterpretation by those not involved closely. As a result, AstraZeneca would commit to providing more training to staff on the importance of using clear, unambiguous language in the future to reduce any potential miscommunications. AstraZeneca would continue to support and empower its employees to seek clarity on any concerns they might have.

The email represented a snapshot in time of the discussions held between the AstraZeneca UK Marketing Company and the Global Medical Affairs team prior to the advisory board taking place, which resulted in a suitable resolution being reached for the advisory board to proceed in full compliance with the Code. Therefore, AstraZeneca respectfully believed that the email provided did not provide additional information or change AstraZeneca's position for the Case AUTH/3013/1/18.

AstraZeneca maintained that the advisory board at issue in Case AUTH/3013/1/18 was carried out for a legitimate business purpose and the query raised did not at any stage question the legitimate purpose of the advisory board. Further to the ongoing discussions, the number of proposed AstraZeneca attendees had been satisfactorily resolved, and such resolution allowed AstraZeneca to proceed with the advisory board in good faith. Therefore, a voluntary admission was not considered because the concerns had been satisfactorily addressed and such an admission was not required.

The company stated that it would be reviewing the discrepancy concerning AstraZeneca attendee arrangements internally in line with its processes.

AstraZeneca submitted that the email provided had been taken out of context and did not accurately reflect the full discussions that had taken place. AstraZeneca was concerned that the allegations, based on an isolated email being misrepresented, might be the result of an employee with an intention of harming AstraZeneca's reputation.

In summary, AstraZeneca submitted that the information received by the PMCPA following the completion of Case AUTH/3013/1/18: Global advisory board was appropriately reflected in the initial and follow-up responses provided by AstraZeneca.

REQUEST FROM PMCPA FOR FURTHER INFORMATION

To help the Authority understand this matter, AstraZeneca was asked to address a number of points including other cases where governance was raised by the Panel. These being Case AUTH/2866/8/16 where the Panel referred to concerns about governance of speaker meetings activities, Case AUTH/2746/1/15 where a tweet by global had not been certified and Case AUTH/2969/8/17 where the Panel referred to representative's activities and the need for AstraZeneca to review its processes.

RESPONSE FROM ASTRAZENECA

AstraZeneca stated that it carried out a comprehensive review following receipt of the PMCPA letter and addressed each point including those about other cases where governance was raised by the Panel.

AstraZeneca stated it was fully committed to upholding high standards and compliance with all applicable laws and regulations, pharmaceutical industry codes of practice, including upholding effective self-regulation.

AstraZeneca was disappointed that the cases highlighted occurred and accepted that mistakes were made. However, such errors related to unusual individual facts. In the broader context of its substantial business activities in the UK, reflecting the fact that it was a UK head quartered company, AstraZeneca submitted that they were outliers, which did not reflect the totality of its culture and strong governance framework. In each case, AstraZeneca had reacted by taking measures to ensure that lessons were learnt, processes were strengthened and specific concerns were addressed.

In summary, AstraZeneca stated it had a robust governance framework in place which sought to identify, manage and prevent risks using three distinct lines of defence. Line managers played a critical role as the first line of defence, with a defined duty to promote a strong compliance and risk management culture, whilst ensuring that day to day risks were controlled and monitored on an ongoing basis. The compliance functions provided policy and standard setting, communication and training, advice and assurance as well as monitoring and auditing to ensure that the first line of defence remained fit for purpose and robust. The third line of defence, the internal audit function provided independent advice and assurance to senior management of the effectiveness of risk, first and second lines of defence.

As an organisation, AstraZeneca stated it continuously monitored progress and had continuous improvement initiatives to ensure the robustness of processes and culture of compliance. This was evidenced by the measures AstraZeneca put in place to address failings identified in each of the cases highlighted here and through its standard monitoring and audit processes.

In addition, the AstraZeneca UK Marketing Company had integrated all compliance-related decision making into a cross-functional compliance governance group (Ethics Xceed) in March 2018, comprising compliance, legal, medical, regulatory affairs and finance. The Group's role was to provide advice and guidance to the organisation on issues relating to compliance with the various regulations and provided further evidence of AstraZeneca's commitment to a strong governance culture.

AstraZeneca remained fully committed to maintaining high standards and effective self-regulation. It totally accepted and understood the need for a thorough investigation of the allegations made by the author of the letter dated 18 June 2018 but was concerned that the complainant had made sweeping allegations supported only by an email which had been used and quoted out of context. Although instances of Code-related breaches remain isolated, AstraZeneca was disappointed that any such cases had occurred and continued to strengthen its ways of working and processes to ensure that it continued to remain compliant with the necessary internal and external requirements.

With regard to the PMCPA's identification of six cases, (Cases AUTH/2746/1/15, AUTH/2793/9/15, AUTH/2866/8/16, AUTH/2969/8/17, AUTH/3011/1/18 and AUTH/3013/1/18) involving both AstraZeneca UK Marketing Company and the Global company over a period of some four years, AstraZeneca submitted it had provided full responses to all of the completed cases and demonstrated that these cases did not reflect a pattern, but were based on specific individual circumstance. Furthermore, it had shown that not only had it carefully considered the Panel's recommendations, it had taken all necessary action to address these and to effect changes to prevent recurrence. In the circumstances described, AstraZeneca respectfully suggested that a referral to the Appeal Board under Paragraph 8.2 of the Constitution and Procedure was neither merited nor appropriate.

FURTHER CONSIDERATION BY THE PANEL

The PMCPA decided that the original Panel should reconvene to consider the matter in relation to Paragraph 8.2 of the Constitution and Procedure which provided that the Panel might report to the Appeal Board any company whose conduct in relation to the Code, or in relation to a new particular case before it, or because it repeatedly breached the Code such that it raised concerns about the company's procedures, warranted consideration by the Appeal Board. Such a report to the Appeal Board might be made notwithstanding the fact that a company had provided an undertaking requested by the Panel. The Panel noted that AstraZeneca had provided the requisite undertaking.

The Panel noted that the author of the letter had provided a copy to the Medicines and Healthcare products Regulatory Agency (MHRA) as the author was concerned there appeared to be no activity and alleging that AstraZeneca was receiving preferential treatment. The PMCPA responded to inform the MHRA that the matter had been followed up with AstraZeneca and would be considered by the Panel shortly. The delay was due to the number of

complex cases. AstraZeneca was not receiving any preferential treatment.

The Panel noted the difficulties for UK companies regarding activities run by global.

The Panel noted the email trail dated 7 and 8 November 2017 provided as additional information which appeared to provide context to the discussions between the UK company and the global company about the arrangements for the advisory board held on 10 November 2017. It was clear that the concerns raised by the UK went beyond just a difference between the UK and global SOPs. Reference was made to advisory boards being in the spotlight in the UK over the last 18 months, ever since the Astellas case. The MHRA had questioned the validity of advisory boards and that the UK position was rather sensitive at the moment due to the AstraZeneca cases at the Panel and that it was '… trying to ensure we do not attract an audit'. The senior UK medical department employee stated that the need for the global advisory board was clear and the agenda was reasonable. The ratio of AstraZeneca attendees to health professionals was high. The situation was described as low risk but if a complaint were made it would be marginal as to whether it could be defended from a perceptual perspective. Three options were proposed these being firstly that the extra 5 AstraZeneca attendees watched the first part of the advisory board in a separate room via a video link and then participated in the breakout sessions. Secondly to minimise the risk, reduce the number of AstraZeneca attendees to 8 (the ratio of just above 2:1 would still be inconsistent with the UK SOP). And thirdly to proceed as planned and capture it in the UK as a breach and then it could be discussed with the relevant UK team as to whether a self-report to the ABPI was needed. The email trail went on to state that the senior UK medical department employee wanted to avoid dropping the UK health professionals and also disrupting the plans for the proposed agenda. He/she was happy to go with any of the three options. He/she understood that this was frustrating but 'we do need to be consistent in our approach to implementing the code'. The email concluded that he/she would be working with the team to look at current SOPs to ensure that they continue to be compliant but were clear and not arduous to implement.

The Panel considered that it was not clear from the email trail whether the senior UK medical department employee considered that the number of AstraZeneca attendees at the advisory board was in breach of the Code or in breach of the AstraZeneca UK SOP. The email spelt out three options. The Panel noted that the company had decided on option 1 although as included in the report for Case AUTH/3013/1/18 this did not happen due to technical issues.

The Panel considered the email including the context of discussions about the advisory board and the perception of the email. The Panel considered that the reference to self-reporting was a possible reference to the need for AstraZeneca to consider making a voluntary admission about a possible breach of the Code. Clearly it was important that companies followed their SOPs but not doing so was not in itself necessarily a breach of the Code.

The impression of the email was that the UK company had concerns about the arrangements for the advisory board, in particular the number of AstraZeneca attendees. Full details about the number of AstraZeneca attendees had only been provided to the Panel considering the case when it asked for further information.

The Panel noted that clearly there were difficulties with the advisory board and breaches of the Code had been ruled and a number of concerns raised. At that time it was also clear that AstraZeneca had not provided all the information. In relation to AstraZeneca's submission that as the Panel had not asked for the email of 8 November it had not provided the email, the Panel noted that self-regulation relied on companies to provide all relevant material. As the Panel did not know of the existence of the email, it could not request it.

The Panel noted AstraZeneca's submission that the email represented a snapshot of the discussions that had taken place and these were explained in the company's response to Case AUTH/3013/1/18 where it stated 'they presented several options to resolve this, one of which was the option which was eventually settled upon'.

Now having received the email of 8 November the Panel did not consider that this additional information would have made a difference as to whether it thought the advisory board itself was in breach of the Code. The Panel had ruled no breach in this regard based on the complainant not having shown on the balance of probabilities that there was a breach of the Code. However, the new information which provided some insight into the company's compliance culture was a concern as was AstraZeneca's general approach with regard to providing information to the Panel as evidenced by the number of times over the last couple of years that the company had either not provided all the relevant information or had provided misleading information. This was set out in the Panel's request for further information from AstraZeneca.

Taken as a whole, the Panel considered that AstraZeneca could not clearly demonstrate its stated commitment to self-regulation in the broadest sense. It was concerned that actions might be taken by AstraZeneca so as to '… not attract an audit' rather than ensuring compliance with the Code and its own procedures. The Panel was also concerned that it appeared from the email and other aspects of the complaint that for some staff raising concerns about activities was difficult at AstraZeneca and this contributed to the differences of opinion between UK and Global. However, it decided that, on balance, the material before it, most of which had come to light either during the consideration of the cases or afterwards and had been the subject of a public reprimand, had been addressed and thus on balance a formal report to the Appeal Board was not needed at this stage. The Panel's view was that these examples should be reconsidered if there

were further instances of AstraZeneca failing to provide comprehensive information. The Appeal Board would be provided with details of the Panel's further consideration following a similar format to the details provided for cases which concluded at the Panel level.

APPEAL BOARD CONSIDERATION OF CASE REPORT

As the case completed at the Panel level the Appeal Board was provided with certain papers (the case report, Panel minutes, update to the case report, letter from the anonymous non-contactable complainant providing the email at issue dated 18 June 2018, and the correspondence with the MHRA. (Paragraph 4.1 of the Constitution and Procedure).

The Appeal Board considered that the additional information in this case raised serious issues including about the provision of incomplete and/or inaccurate information. The Appeal Board's view was that further consideration should be given to this matter including the possibility of imposing further sanctions under Paragraph 11.1 of the Constitution and Procedure.

AstraZeneca was advised that the Appeal Board was giving further consideration to this matter including considering imposing additional sanctions and asked to respond in writing, as well as be given the opportunity to attend the Appeal Board when the matter would be considered. AstraZeneca was provided with a copy of the papers.

COMMENTS FROM ASTRAZENECA

AstraZeneca submitted that in order for it to appropriately be represented it wanted more information on those specific matters which were of concern to the Appeal Board and which would be considered in that regard it noted that the Panel had made reference to Case AUTH/2793/9/15.

RESPONSE FROM THE PMCPA

The PMCPA advised AstraZeneca that the matters of concern to the Appeal Board were set out in its decision. The issues were set out in the Panel's consideration of the additional information. Various letters from the PMCPA and AstraZeneca's response referred to other cases:

Case AUTH/2538/10/12, Case AUTH/2746/1/15, Case AUTH/2793/9/15, Case AUTH/2866/8/16
Case AUTH/2969/8/17 and Case AUTH/3011/1/18.

COMMENTS FROM ASTRAZENECA

AstraZeneca submitted that it strongly disagreed with the Panel's characterisation of it. However, whilst it was disappointed by the Panel's consideration and the decision of the Appeal Board, it remained fully committed to the Code and the principle of self-regulation. AstraZeneca therefore welcomed the opportunity to discuss these issues with the Appeal Board.

Background

AstraZeneca set out the background including that in June 2018, the PMCPA received a further letter, attaching an email from a senior UK medical department employee describing available options in relation to the advisory board meeting, which had not been provided by AstraZeneca in its response to the original complaint. AstraZeneca submitted its detailed response above.

AstraZeneca noted that it had received no further correspondence or decision from the PMCPA until 10 May 2019, over 9 months later. The Panel's consideration concluded that the additional information would not have made a difference as to whether the advisory board was in breach of the Code and did not alter its previous ruling. However, as a result of the email from a senior UK medical department employee, the Panel raised various concerns in relation to AstraZeneca's compliance culture and the company's approach to the provision of information to the PMCPA.

AstraZeneca noted that the Panel had raised the following concerns:

- The UK company appeared to have concerns in relation to the arrangements for the advisory board organised by Global, in particular the number of AstraZeneca attendees. However full details about the number of AstraZeneca attendees had been provided to the Panel only when it requested further information.
- AstraZeneca's reason for not disclosing the email from a senior UK medical department employee of 8 November 2017 was that this had not been requested. However, self-regulation relied on companies to provide all relevant material; as the Panel had not been aware of the email it could not request disclosure.
- The Panel considered that the new information (ie the email of 8 November 2017), provided some insight into the company's compliance culture and was a concern.
- The Panel expressed concern in relation to AstraZeneca's general approach with regard to providing information to the Panel as evidenced by the number of times over the past couple of years that the company had either not provided all relevant information or had provided misleading information.
- Overall, the Panel considered that AstraZeneca could not clearly demonstrate its stated commitment to self-regulation in the broadest sense. It was concerned that actions might be taken so as not to attract an audit, rather than ensuring compliance with the Code and its own procedures. The Panel was also concerned that for some staff, raising concerns about activities was difficult at AstraZeneca and this contributed to differences of opinion between AstraZeneca UK and Global.

After considering the totality of the evidence, the Panel concluded that these matters had been addressed and that, on balance a formal report to the Appeal Board was not needed at this stage.

AstraZeneca's response to the Appeal Board's concerns

AstraZeneca submitted that the characterisation of its compliance culture and approach to the PMCPA was fundamentally incorrect. AstraZeneca would therefore demonstrate its commitment to a robust culture of compliance and respect for the Code both within the UK Marketing Company (UKMC) and across the Global organisation and address the specific issues that the Panel had highlighted.

AstraZeneca submitted that the matters identified by the Panel were not indicative of wider or systematic issues. One of five of AstraZeneca's core values was 'Do the Right Thing' and this underpinned how it conducted its activities and every decision that it made.

As a preliminary matter AstraZeneca reiterated that throughout Case AUTH/3013/1/18, the legitimacy and the business need for the advisory board itself was not in doubt and was not therefore, considered a breach of the Code. The advisory board was important to provide AstraZeneca key advice on Type 1 Diabetes, in addition, AstraZeneca had accepted the breaches associated with this case and as disclosed previously, had taken steps to address these as a UK and Global organisation.

AstraZeneca submitted that the PMCPA had stated that it had withheld information in two ways: firstly, by failing to provide the email dated 8 November 2017, and secondly, by having failed to disclose that technical issues had meant that the agreed arrangements for the advisory board had not been implemented in practice. AstraZeneca's detailed response to these matters was set out in its letter of 22 August 2018.

AstraZeneca submitted that in relation to the first issue, the Panel appeared to have misconstrued its comment that this email was not provided because it had not been requested. To be clear, AstraZeneca had never suggested that the email was not provided because this specific email was not requested but rather that AstraZeneca did not provide any emails because the PMCPA had asked it to provide details of the internal discussions that took place. Therefore, AstraZeneca had summarised the relevant discussions (verbal and written) in a manner which properly reflected the totality of those discussions. The complainant shared one email from the totality of the discussion and it had been positioned in a manner that was inconsistent with the context of the discussions; considering this email in isolation gave an incorrect impression of the overall email correspondence and created a misleading representation of AstraZeneca's culture. The Panel had effectively confirmed this where it noted that now having received the email of 8 November it did not consider that this additional information would have made a difference as to whether it thought the advisory board itself was in breach of the Code. Furthermore, AstraZeneca submitted that it would significantly increase the already substantial burden on companies and the PMCPA if companies were required to disclose all correspondence, even tangentially related to a complaint, in every case. AstraZeneca submitted that with respect to the second issue, it acknowledged that it was unfortunate that it was not able to disclose in its original response that the option that had been agreed between the UKMC and the Global teams could not be implemented on the day of the advisory board. As explained previously, this was not provided to the internal complaint management team as part of the original investigation. It was only as part of the second stage of the complaint [March 2018] that a member of the Global medical team recalled the internal meeting the day before the advisory board and technical issues on the day of the advisory board. AstraZeneca submitted that it had taken preventative actions to ensure full initial disclosure.

AstraZeneca submitted that as soon as its investigating team became aware that the advisory board had not been conducted in accordance with the agreed plan, due to the technical issues that occurred on the morning of the advisory board, this was passed on to the PMCPA in its submission of 15 March 2018. This indicated AstraZeneca's commitment to openness and transparency with the PMCPA rather than any systematic attempt to withhold information.

Finally, AstraZeneca submitted that whilst the Panel did not explain its particular concerns in relation to Case AUTH2793/9/15 and Case AUTH/3011/1/18, delayed disclosure in these cases resulted from the particular facts of those matters and did not reflect a deficiency in AstraZeneca's culture or approach. Case AUTH/2793/9/15 related to a leavepiece about how to create a clinical system search to identify patients suitable for treatment with Forxiga (dapagliflozin). Following a complaint, AstraZeneca provided information about the search arrangements, including details (which could not be verified by AstraZeneca) provided by the agency contracted by AstraZeneca for this work. The information provided by the agency turned out to be incorrect. While AstraZeneca accepted responsibility for the error of its agency, it strongly resisted any conclusion that this case demonstrated any deficiency in company culture in relation to disclosure of information during the self-regulation process.

AstraZeneca submitted that Case AUTH/3011/1/18, related to a press release issued in November 2017. In this case AstraZeneca did not fail to disclose information but rather acted in good faith to present its understanding that the applicable financial regulations prevented it from removing the press release from its website. AstraZeneca offered a solution that it thought would meet the needs of the Code and the financial regulations. When this solution was turned down by the PMCPA, it took external legal advice to determine if there was any way to satisfy both the financial regulations and Code requirements. It was determined this could be done by modifying and not removing the press release provided that the modifications did not have any financial implications. AstraZeneca then worked with its legal team to find an edit that would meet both sets of regulations. AstraZeneca contended this demonstrated its flexibility and willingness to find

solutions to meet the various regulations it operated under and underlined its value of doing the right thing. At the consideration of this matter the AstraZeneca representatives fully accepted the breaches of Clauses 14.2 and 9.1 ruled and remained disappointed that the arrangements were not certified, despite the scrutiny applied to the advisory board. Reassurance had been provided to the UK signatory team and confirmation on internal reporting routes. The UK had run a 'Speak Up' campaign during its regional compliance week. The global Advisory Board SOP had been revised, and training provided. Case AUTH/3013/1/18 was published and shared with all relevant staff. The UK Advisory Board SOP was currently being reviewed to ensure alignment with Global. Management of the investigation process had been strengthened and a clearer process for investigating cases involving both UK and Global had been agreed.

With regard to the non-disclosure of a senior UK medical department employee's email, AstraZeneca noted that the PMCPA had requested comprehensive details about the advisory board at issue and asked what internal discussions had taken place about the number of staff attending. The PMCPA had also requested specific documents as part of the initial complaint, but not email correspondence. AstraZeneca provided a summary of the discussions in the initial response to the complaint, as requested. The PMCPA had not objected to the summary. Following disclosure of the email by the complainant and additional context provided by AstraZeneca, the PMCPA found that the email did not alter its original ruling.

AstraZeneca submitted that the information provided in its initial response with regard to the number of AstraZeneca attendees was made in good faith. Upon further questioning, additional information was provided when Global colleagues recalled the precise arrangements on the day of the advisory board.

AstraZeneca accepted that the email was poorly worded but submitted that it was directed to an informed audience. The comment regarding audit referred to the fact that advisory boards were a sensitive area. The overall intent behind the email was to uphold compliance.

AstraZeneca submitted that the signatory did raise his/her concerns with senior medical and compliance colleagues.

In summary AstraZeneca submitted that the advisory board at issue was legitimate and the initial failure to provide accurate information concerning attendees was not deliberate or intentional. AstraZeneca's response was an appropriate summary of the totality of discussions as requested by the PMCPA. The email of 8 November 2017 was poorly worded but was not intended to suggest any disregard for the Code or for company procedures. It did not reflect a poor compliance culture. Actions had been taken to address these failings and to improve ways of working. The discussions that took place actually showed that individuals were free to raise concerns as a normal part of AstraZeneca's processes and culture. The additional cases identified by the PMCPA had their own particular facts and unique root-causes. Appropriate corrective and preventative actions (CAPAs) had been implemented.

APPEAL BOARD CONSIDERATION

The Appeal Board noted the Panel's rulings of breaches of Clauses 9.1 and 14.2 of the Code. The Appeal Board noted that the company had apologised and admitted that it had made errors.

The Appeal Board noted the context in that there had been discussions between AstraZeneca UK and the global company about the arrangements for the advisory board held on 10 November 2017 right up to the meeting taking place. The UK company did not want to certify the meeting due to concerns about the number of AstraZeneca representatives attending. The email at issue dated 8 November 2017 from the senior UK medical department employee was an attempt to overcome this issue. The email included three options in order to enable the advisory board to go ahead. The Appeal Board noted AstraZeneca agreed that the email of 8 November 2017 was poorly worded. The email referred to ensuring the company did not attract an audit and mentioned a self-report to the ABPI if the meeting went ahead as planned. The Appeal Board noted the submission from AstraZeneca that the senior UK medical department employee was new and that the self-report was in relation to the breach of the company's SOPs and not in relation to the ABPI Code. The Appeal Board considered that the reference to self-report appeared to be in relation to the Code. The Appeal Board noted that the email of 8 November 2017 had been copied to several senior AstraZeneca members of staff including some who represented the company at the Appeal Board meeting. The Appeal Board queried why nobody had replied to the email to raise their concerns. AstraZeneca stated that there had been a discussion about the email at the time but there was no written record. Although there was no requirement to self-report, the Appeal Board queried why the company had not self-reported a breach of Clause 14.2 at this point. AstraZeneca stated that this had been an oversight by the company.

The Appeal Board considered that when submitting a response, companies need not include everything however the company had not provided the relevant source material it used in summarising events. The email of 8 November 2017 was clearly central and relevant to this case and did not appear to be consistent with the summary provided. In the Appeal Board's view to not submit the email was inexplicable. Effective self-regulation required companies to be open and transparent when responding to complaints; they had a duty to disclose all relevant documents and information. When compiling its response to the complaint the representatives from AstraZeneca stated that they had referred to emails. The Appeal Board was not satisfied with AstraZeneca's submission as to why it had not provided the email dated 8 November when responding to the complaint.

The Appeal Board considered that the email of 8 November 2017 was clearly relevant and

should have been provided to the PMCPA as part of AstraZeneca's response. Notwithstanding AstraZeneca's submission that it now had updated its processes, the Appeal Board noted that self-regulation relied, *inter alia*, upon the provision of complete and accurate information from pharmaceutical companies. The Appeal Board decided that in accordance with Paragraph 11.3 of the Constitution and Procedure, AstraZeneca should be publicly reprimanded for failing to provide complete and accurate information in an open and transparent way.

The Appeal Board was concerned to note that AstraZeneca was also publicly reprimanded in 2016 by the Appeal Board for providing inaccurate information to the Panel (Case AUTH/2793/9/15).

The Appeal Board noted the Panel's comments above regarding AstraZeneca's conduct in responding to complaints. The Appeal Board noted its concerns about AstraZeneca's compliance culture. The Appeal Board gave consideration to the imposition of further sanctions including whether an audit should be required. However, on balance, the Appeal Board decided that no additional action was required.

Complaint received	**22 January 2018**
Undertaking received	**10 April 2018**
Panel reconvened	**2 May 2019**
Appeal Board consideration	**11 July 2019**
Case completed	**11 July 2019**
Updated case report Including addendum published	**3 February 2020**