Medicines Australia Code of Conduct Quarterly Report January – March 2015

The quarterly report of determinations of the Medicines Australia Code of Conduct and Appeals Committees

The Medicines Australia Code of Conduct was introduced in 1960 and is currently operating under Edition 17 (Effective 11 January 2013).

This report covers all complaints finalised between January and March 2015. Complaints finalised during this period were in relation to materials or activities conducted under Edition 17 of the Code.

Quarterly Reports preceding this Report are available from the Medicines Australia website http://medicinesaustralia.com.au/code-of-conduct/code-of-conduct-reports/

How to contact Medicines Australia

Address:
Level 1, 16 Napier Close
DEAKIN ACT 2600

Phone: 02 6122 8500

Fax: 02 6122 8555

Email: secretarycodecommittee@medicinesaustralia.com.au

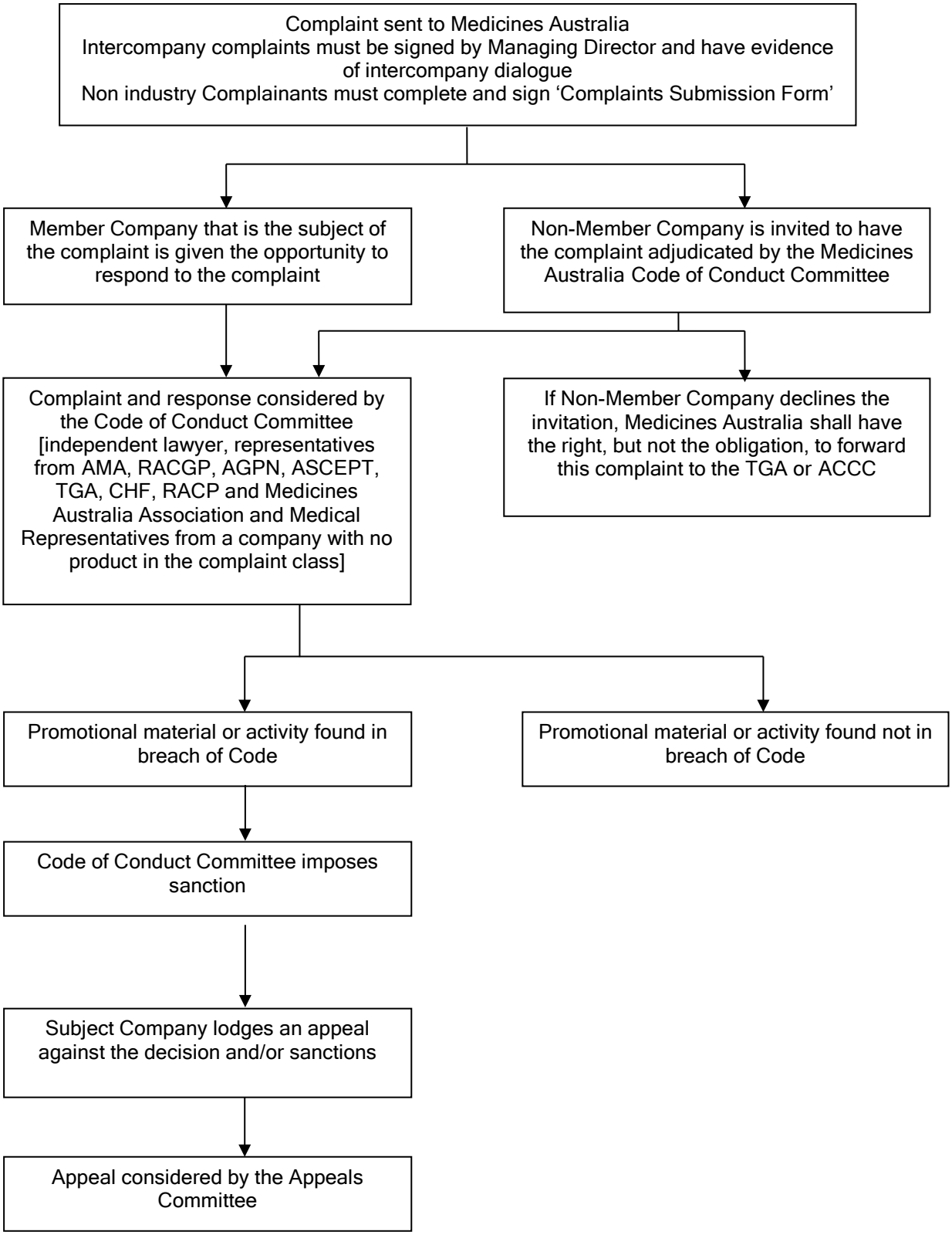
How do I obtain a copy of the Code?

Copies of Edition 17 of the Code (effective from 11 January 2013) are available from Medicines Australia. An order form is available from http://medicinesaustralia.com.au/code-of-conduct/code-of-conduct-current-edition/

The Code of Conduct and the Guidelines that accompany the Code are available from the website (http://medicinesaustralia.com.au/code-of-conduct/code-of-conduct-current-edition/)

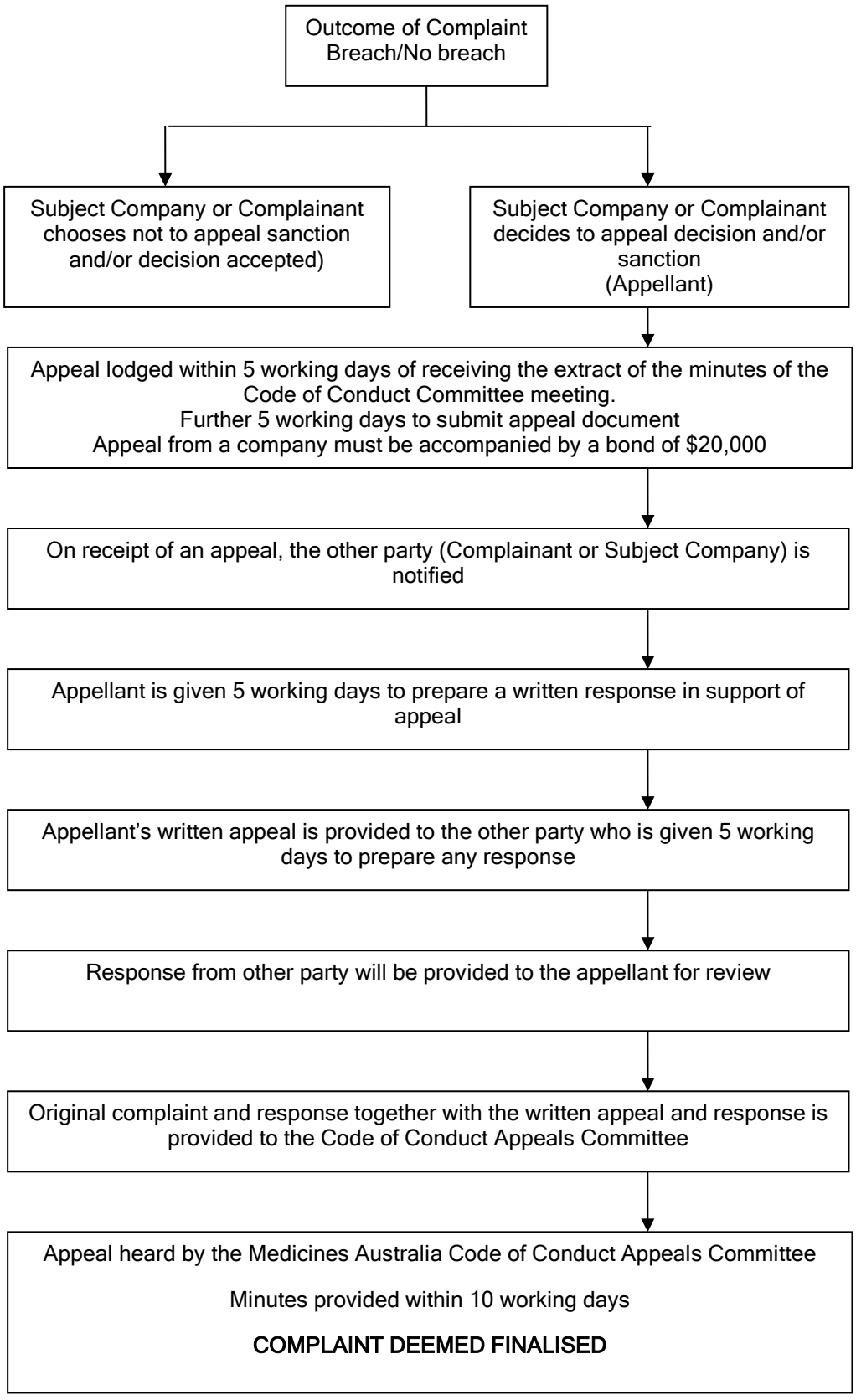
Contents

Medicines Australia Code of Conduct Complaints Handling Process



A complaint is not deemed finalised until the Subject Company has advised Medicines Australia that they will not appeal the outcome of the Code of Conduct Committee decision (following circulation of the Code minutes) or, in the case of an appeal, the minutes of the Appeals Committee meeting have been provided to both parties

Medicines Australia Code of Conduct Appeals Committee Procedures



Committees and Secretariat

The administration of the Code is supervised by the Code of Conduct Committee. The Code of Conduct Committee has the power to make a determination as to a breach of the Code, and impose sanctions. The right of appeal is available to both the Complainant and Subject Company. An appeal is heard by the Appeals Committee which has the power to confirm or overturn the decision and to amend or remove any sanctions.

Committee Member Biographies

Brief biographies for all Code, Appeals and Monitoring Committee members are available on the Medicines Australia website http://medicinesaustralia.com.au/code-ofconduct/committee-membership/

Code of Conduct Committee

Full Members (Voting rights)

- Independent Lawyer (Chairman) selected from a panel of up to 5 trade practices lawyers

Representatives nominated by:

- Australian General Practice Network (AGPN)
- Australian Medical Association (AMA)
- Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists (ASCEPT)
- Consumers Health Forum of Australia (CHF)
- Royal Australasian College of Physicians (RACP)
- Royal Australian College of General Practitioners (RACGP)
- Medicines Australia Association Representatives (maximum 3)
- Medicines Australia Medical/Scientific Directors (maximum 2)

Observers (No voting rights)

- Therapeutic Goods Administration (TGA)
- Medicines Australia member companies' employees (maximum 2)
- Observer nominated by Medicines Australia (maximum 1)

Advisors (No voting rights)

- Secretary, Code of Conduct Committee
- Medicines Australia Chief Executive Officer or delegate
- Medicines Australia officer responsible for Scientific and Technical Affairs

Appeals Committee

Full Members (Voting rights)

- Independent Lawyer (Chairman) selected from a panel of up to 5 trade practices lawyers

Representatives nominated by:

- The College and/or Society associated with the therapeutic class of the product subject to appeal
- The target audience to which the activity was directed eg: AMA, RACGP
- Consumers Health Forum of Australia (CHF)
- Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists (ASCEPT)
- Medicines Australia Association Representatives (maximum 2)
- Medicines Australia Medical/Scientific Director (maximum 1)

Advisors (No voting rights)

- Secretary, Code of Conduct Committee
- Medicines Australia Chief Executive Officer or delegate

Sanctions that can be imposed by the Code of Conduct Committee

Sanctions

If the Code of Conduct Committee finds a breach of the Code it may impose a sanction on the company found in breach. In order to determine an appropriate sanction the Committee will refer to the "Guidelines for determining Code sanctions" which are available on the Medicines Australia website. The following sanctions may be imposed:

Withdrawal of material or activity

Where promotional material or activity is found in breach of the Code the Committee will always require the company to cease use of the item or cease undertaking the activity.

Corrective letter

The Code of Conduct Committee will determine the audience for the letter based on the original distribution of the material found in breach of the Code.

Corrective advertisement

A corrective advertisement must be placed in the same publication as that found in breach of the Code.

Fines (applicable under Edition 17 of the Code)

Breach	Fine
Technical breach Minor breach	Maximum of $100,000
Moderate	Maximum of $150,000
Severe breach	Maximum of $200,000
Severe breach where activities completed Repeat of previous breach	Maximum of $250,000
Cumulative fine for multiple breaches	Maximum of $300,000
Failure to complete corrective action in 30 calendar days Failure to pay a fine in 30 calendar days	Maximum of $50,000
Abuse of the Code (in accordance with Section 25)	Maximum of $200,000

Table of finalised complaints January – March 2015

No.	Subject Company	Material or Activity	Product	Complainant	Outcomes	Sanction
1122	Amgen Australia	Educational Event	Aranesp	Monitoring Committee	No Breach	n/a
1123	Bayer, Merck Sharp & Dohme, Novartis Pharmaceuticals	Advertising	Eylea, Saflutan, Lucentis	Member of the General Public	No Breach	n/a
1124	Bayer Australia	Promotional Material	Xarelto	Pfizer/Bristol-Myers Squibb	Breach of Sections 1.1, 1.2 and 1.3	Pay a fine of $30,000
1125	iNova Pharmaceuticals	Presentation	Duromine	Healthcare Professional	Breach of Section 1.1	Pay a fine of $100,000
1126	Bristol-Myers Squibb Australia	Promotional Material	Sprycel	Novartis Pharmaceuticals	Breach of Sections 1.2 and 1.3	Pay a fine of $45,000

1122 – Amgen Educational Event

Subject Company: Amgen Australia Pty Ltd

Complainant: Monitoring Committee

Product: Aranesp

Complaint
Following its review of Educational Event Reports and subsequent request for clarification, the Medicines Australia Monitoring Committee considered that an event held by Amgen Australia may be in breach of the Code, and therefore has referred the matter to the Code of Conduct Committee for adjudication. The Monitoring Committee were not persuaded that a tour of the company manufacturing facility in Puerto Rico and presentations given to healthcare professions enhanced medical knowledge and the quality use of medicines.

Sections of the Code
The conduct was alleged to be in breach of the following Sections of Edition 17 of the Code:

- 9.1 General Principles
- 9.3 Educational Events
- 9.7 Sponsorship of HCPs to attend educational events

Response
Amgen denied that any breach of the Code has occurred. Amgen responded that only delegates who were attending the American Society of Nephrology (ASN) meeting in Atlanta were invited to attend the meeting in Puerto Rico. Amgen had not sponsored Australian healthcare professionals to attend the ASN meeting.

Amgen's intent in arranging the site visit to Puerto Rico was to provide relevant and appropriate education to Australian healthcare professionals. Amgen argued that a visit to a biotechnology manufacturing facility is medical education that enhances medical knowledge and will improve the quality use of medicines. The decision to provide the site visit was partly driven by expressions of interest from Australian healthcare professionals and was intended to deliver an understanding of manufacturing by experiencing the process first hand. The travel and accommodation provided to delegates was appropriate and consistent with the Code.

Amgen provided the opinions of 10 healthcare professional attendees supporting the educational benefit of the site visit.

Code of Conduct Committee decision
The Committee agreed by unanimous decisions that educational event subject to complaint was in breach of the Sections 9.1, 9.3 and 9.7 of the Code of Conduct.

The Committee agreed by unanimous decision that this was a severe breach of the Code.

Sanction
Having found that the educational event was in breach of the Code, the Committee imposed the following sanctions:

- Pay a fine of $200,000.
- Send a copy of the full reasons for the decision to all healthcare professionals who attended the educational event.

Consideration of the complaint

The Committee expressed considerable concern that Australian healthcare professionals had been flown to Puerto Rico, from Atlanta, to undertake a plant tour and receive presentations about Amgen's biologic product Aranesp.

With regard to the rationale for providing a biologic medicine manufacturing plant tour, the Committee did not accept Amgen's justification that healthcare professionals needed to be assured through first-hand experience of a manufacturing facility that biologic medicines meet appropriate quality standards. The Code Committee agreed with the Monitoring Committee that Australian healthcare professionals are assured of product quality by the Therapeutic Goods Administration's (TGA) evaluation and approval of a product.

The Committee reviewed the presentations by Amgen's Director of Global Biosimilars Policy and an Australian healthcare professional that were provided in Amgen's response to the complaint. The Committee considered that the primary purpose of these presentations and the plant tour were to persuade the attending healthcare professionals to continue to prescribe and recommend Aranesp rather than any biosimilar product. The Committee noted that Amgen had stated in its response that the attending healthcare professionals were "opinion leaders in the nephrology community" who not only prescribed medicines for their patients but also were in influential positions as members of hospital or state formulary committees. Therefore, the Committee was concerned that the plant tour in Puerto Rico may have broader influence on maintaining prescribing of Aranesp than just the individual healthcare professionals who attended.

The Committee referred to Sections 9.1, 9.3 and 9.7 of the Code, which each require that the primary purpose of companies' interactions with healthcare professionals and involvement in educational events must be the enhancement of medical knowledge and the quality use of medicines (QUM). The Committee considered that whilst the presentations provided clinical information about erythropoietin and the treatment of anaemia associated with chronic kidney disease and biosimilar medicines, it was unnecessary for these presentations to be delivered at an educational meeting at a manufacturing facility in Puerto Rico. These presentations could have been given in Australia or in Atlanta where the healthcare professionals attended the ASN meeting. The Committee noted that the cost of the Puerto Rico meeting was over $46,000 for 14 healthcare professionals and included two nights' accommodation and two dinners. The Committee further noted that whilst Amgen had stated that it had not sponsored the healthcare professionals to attend the ASN meeting in Atlanta, it was evident from the testimonial letters that some of the healthcare professionals had also received sponsorship for the ASN conference registration and accommodation in Atlanta for the duration of the conference.

The Committee concluded that there was a lack of balance between the educational purpose of the meeting in Puerto Rico and the travel, accommodation and hospitality provided. The Committee was very concerned that the primary purpose of the meeting was to influence individual healthcare professionals to prescribe

Aranesp and more broadly to influence key decision makers who are members of hospital formulary committees. The Committee considered that the educational meeting would not withstand public and professional scrutiny as is required under section 9.7.1 of the Code.

The Committee reviewed the testimonial letters from 10 healthcare professionals who had attended the event subject to complaint. The Committee was not persuaded by the letters that the educational purpose of the meeting was to enhance medical knowledge and the quality use of medicines. Most of the letters from healthcare professionals emphasised their interest in the manufacturing process for biologic medicines. The Committee reiterated that it considered that it was unnecessary to fly healthcare professionals to Puerto Rico to assure them of the quality of manufacture of medicines supplied in Australia.

The Committee determined by unanimous decisions that the educational meeting held in Puerto Rico was in breach of Sections 9.1, 9.3 and 9.7 of the Code. The Committee also agreed by unanimous decision that it considered that this was a severe breach of the Code because the conduct would not withstand public or professional scrutiny.

Sanction
Having found the educational event to be in breach of the Code, the Committee considered appropriate sanctions. The Committee determined by majority decision that Amgen should be required to pay a fine of $200,000. In relation to taking corrective action, the Committee determined that Amgen should be required to send a copy of the full Code of Conduct Committee reasons for the decision in relation to this complaint to each healthcare professional who had attended the educational event found in breach of the Code.

Appeal
Amgen appealed the Code Committee's decisions as it considered that the Code Committee had based its decisions on a number of errors of fact and assumptions. Amgen argued that a number of irrelevant matters appeared to have influenced the Code Committee's considerations.

Amgen argued that education for prescribers about biologics is legitimate and is supported by Medicines Australia. Experiential learning is commonly used for adult education and other companies have undertaken similar activities involving a visit to a manufacturing facility, which has not been subject to complaint or adverse public opinion. Amgen argued that the hospitality was reasonable given the location and logistics for the event.

Appeals Committee decision
The Appeals Committee agreed by unanimous decision to uphold the appeal and amend the decisions of the Code of Conduct Committee. The Appeals Committee determined that the Amgen educational event was not in breach of the following Sections of the Code of Conduct:

- 9.1 Relationship with Healthcare professionals – General Principles
- 9.3 Educational Events
- 9.7 Sponsorship of Healthcare Professionals to attend educational events

Sanction
As the appeal was upheld and the Code of Conduct Committee's decisions overturned, the sanctions imposed by the Code Committee were removed.

Consideration of the Appeal
The Chairman explained the process for consideration of an appeal. The Appeals Committee must be persuaded that the findings of the Code Committee involved an error on the basis of which the decisions of the Code of Conduct Committee should be set aside or varied.

The Chairman invited the Amgen representatives to give their appeal presentation. The following summarises that presentation and discussion with the Appeals Committee.

The Amgen representative noted that a healthcare professional who gave a presentation at the meeting held in Puerto Rico was present to provide a perspective from a participant in the educational event but not to advocate on behalf of Amgen or for its conduct.

Amgen stated that education of healthcare professionals on biologic medicines and biotechnology manufacturing is critical and there is a strong link to quality use of medicines (QUM) outcomes. The TGA is responsible for evaluating products for quality, safety and efficacy but TGA does not provide education on issues that concern biologics such as substitutability and pharmacovigilance.

The education provided at the Amgen event in Puerto Rico was entirely consistent with existing industry standards and benchmarks. Amgen noted that Medicines Australia's *Policy Considerations for Biologics and Biosimilars* recommends educating healthcare professionals on the complexities associated with biologics and biosimilars. Amgen argued that the event was consistent with the Code and with actions of other companies that had held similar plant tours for healthcare professionals in association with educational meetings. Therefore, Amgen considers that the educational event in Puerto Rico would stand up to public and professional scrutiny.

Amgen stated that the Code Committee made errors in its decision making that justify reconsideration of the alleged breach.

In its reasons for decision the Code Committee expressed the view that the primary purpose of the Amgen event was the promotion of Aranesp and gave some weight to that in its decision. However, there is no biosimilar to Aranesp and Amgen has its own biosimilars program. The healthcare professional's presentation in Puerto Rico had referred to other biologics as well as to Aranesp. Amgen argued that it was incorrect to determine that the purpose of the Amgen event was to promote Aranesp. The Code Committee had referred to its consideration that some healthcare professionals who attended the meeting had been sponsored to attend the American Society of Nephrology (ASN) meeting in Atlanta prior to the Amgen educational event. Amgen argued that the ASN meeting was a separate event and reference to this event or sponsorship of healthcare professionals to attend it was irrelevant to consideration of the Amgen educational event in Puerto Rico.

The Code Committee had found that the Amgen event was a serious breach of the Code based on the inability to withstand public or professional

scrutiny. However, there has been no negative commentary about the event from any professional college or society or the media. A number of the attendees work in Western Australia, where they must have prior approval from senior bureaucrats in the Department of Health before receiving sponsorship to attend an educational meeting. The agenda and hospitality are scrutinised before approving the sponsorship. The healthcare professionals' attendance at the Amgen event was approved without question. Further, in its appeal submission Amgen had provided examples of at least five educational events organised by two companies involving similar site visits. Therefore, Amgen considers that the event can withstand public and professional scrutiny and was not in breach of the Code.

Amgen responded to the Code Committee's reasons regarding the location of the Amgen event in Puerto Rico. Amgen argued that the choice of the venue was appropriate. The event in Puerto Rico minimised the cost and participant time in comparison with the alternative of visiting the Amgen manufacturing plant in Ireland. The hotel chosen for accommodating the delegates was close to the airport and had 24 hour security – security is a particular concern in Puerto Rico. Puerto Rico is not in any way a holiday destination and the educational program occupied all of healthcare professionals' time in Puerto Rico except for travel to and from the airport. There was no allowance for free time or leisure activities.

Amgen responded to the Code Committee's opinion that the Amgen meeting did not have medical education and the quality use of medicines as its primary purpose. Amgen stated that experiential learning is a validated approach to delivering effective adult learning that is retained by participants. The complexity of biotech manufacturing requires an experiential approach to learning because the manufacturing steps in producing a biologic are significantly greater than for small molecule medicines; there is a higher need for process controls and trend monitoring.

Amgen described the QUM purpose of the educational event. Amgen argued that the event educated delegates about why it is necessary for healthcare professionals to be clear on which biological they intend to prescribe for a patient and to know which product the patient actually receives. Pharmacovigilance considerations are especially important for biologics and the ability to track the patient and exactly which product was administered is critical. In response to a question from the Committee Amgen explained that these issues were particularly critical for biologics, which are large protein molecules injected into patients. Patients must be monitored for allergic reactions. Minor changes in the manufacturing process can have profound effects on the product, which therefore requires very close controls on manufacturing.

Amgen outlined the cost of the event. The level of hospitality was consistent with the Code, comprising two dinners at less than $100 per person for each and two nights' accommodation. The majority of the cost for the 14 delegates was airfares to and from Puerto Rico. Delegates arrived late one afternoon, had an early morning pick up for the site visit, which finished at 5.30pm, and at 6.30am the following morning returned to the airport. There was no leisure time.

The healthcare professional gave his perspective on the Amgen educational event at which he spoke. He outlined his academic and industry relationships, which included being an Advisory Board member for both innovator and biosimilar companies. In the past, he had attended factory tours organised by three other companies. The purpose of the Amgen factory tour and presentations was to help healthcare professionals understand the issues with pure red cell aplasia and biosimilars and the safeguards employed in manufacturing biologics and biosimilars.

The audience for the presentations in Puerto Rico were Australian nephrologists and Amgen executives from Puerto Rico. The healthcare professional prepared his own presentation, which described the history of the treatment of anaemia in Australia. It was a balanced presentation, which was about not only Aranesp but also discussed outcomes related to other companies' products and biosimilars. The presentation included a criticism of an Aranesp trial, which showed that increasing the dosage interval resulted in more of the product being used.

The healthcare professional described the personal imposition on his time and loss of income from attending the Amgen event. However, whilst the benefit was to gain scientific information from Amgen, it also allowed him to provide research and development feedback directly to Amgen staff about their product and delivery system. The dissemination of information about biologics and biosimilars is important. The Amgen educational event took place in a venue that allowed direct interaction between healthcare professionals and R&D staff, enabling questions to be put to Amgen staff whilst the plant tour was conducted.

Amgen summarised their appeal. Amgen argued that the evidence and data do not support the Code of Conduct Committee's decisions. Amgen considers that education of healthcare professionals on biologics and biotechnology manufacturing is appropriate and has clear QUM outcomes. Prescribers do not receive education from the TGA, nor does the TGA take responsibility for such matters. The education provided would appear to be entirely consistent with existing standards and benchmarks. Amgen believes that the Code Committee made errors in its decision-making. Therefore, the Appeals Committee should uphold the appeal and find that the Amgen educational event had not breached the Code.

An Appeals Committee member asked whether nephrologists have a choice of whether to prescribe Aranesp or an alternative product. Amgen responded that some hospitals provide a choice whereas others do not.

Amgen reiterated the importance of experiential learning and the significant impact on learning of seeing something in real life.

The Chairman thanked the Amgen representatives and the healthcare professional for their presentation and excused them from the meeting to allow the Committee to deliberate on the appeal.

Amgen had argued to the Committee that it was reasonable and appropriate to provide education to healthcare professionals about the challenges of manufacturing of biologics and biosimilars and that this is of

educational value to prescribers of these medicines.

The Appeals Committee accepted that the travel and accommodation provided to the delegates was appropriate to the educational content and purpose. There had been no leisure time provided for at Puerto Rico; the entire duration of the event had been taken up by the educational program and travel to and from Puerto Rico. It appeared to the Appeals Committee that the Code Committee had inappropriately conflated their perception that there was no educational value in the event and its being held in a distant location.

The Appeals Committee discussed whether there was sufficient rationale to justify holding the educational meeting at the Puerto Rico biologics plant. A majority of the Committee accepted that biologic medicines are very complex. As biologic medicines are manufactured using living cells, small changes in the process can have significant impact for patients. A majority of the Appeals Committee accepted that it was beneficial for specialist physicians to be educated about these complex molecules and the differences between biologics and small molecule medicines. A majority of the Committee accepted that it was reasonable to hold the educational meeting at the Puerto Rico plant following the ASN meeting in Atlanta, as the delegates were in relatively close proximity.

The Appeals Committee considered that the Amgen meeting did have educational value for the delegates and the costs were reasonable given the necessity for flights.

The Appeals Committee discussed the Code Committee's opinion expressed in its reasons for decision that the primary purpose of the event was to promote Amgen's product Aranesp. A majority of the Committee accepted that the healthcare professional's presentation was fairly balanced. These members accepted that, as the plant tour was held at Amgen's manufacturing facility, the education about biologic manufacture would have focused on Aranesp. However, this was counterbalanced by the need for education about biologic medicines.

The Appeals Committee noted that Amgen had pointed to several other events held by other companies at their manufacturing facilities outside Australia, which had not been questioned. A minority of the Committee remained concerned that a number of Australian healthcare professionals had been taken to Puerto Rico for a factory tour. Other members of the Committee took into account that the healthcare professionals were already in the US for the ASN meeting.

The Appeals Committee discussed the Code Committee's reasons for finding the educational event in breach of the Code.

The Appeals Committee considered that the Code Committee had erred in its reasoning by finding that Amgen could not justify the educational purpose because the TGA's product evaluation provides assurance of product quality. The Appeals Committee accepted that it was appropriate to educate healthcare professionals about the complex manufacturing process for biologic medicines, which would encourage prescribers to be more aware of potential individual patient reactions to the complex protein molecules.

The Appeals Committee also considered that the Code Committee had erred in its reasoning by finding that the primary purpose of the presentations and plant tour was to persuade healthcare professionals to prescribe and recommend Aranesp rather than a biosimilar product. The Appeals Committee considered that this reasoning could not be sustained on review of the information before the Appeals Committee.

The Appeals Committee considered that the Code Committee had erred by taking into its consideration that some healthcare professionals attending the educational event had been sponsored by Amgen to attend the ASN conference in Atlanta. This information was not relevant to the consideration of whether the educational event held in Puerto Rico was consistent with the Code. The Appeals Committee did not agree with the Code Committee's conclusion that there was a lack of balance between the educational purpose of the meeting and the travel, accommodation and hospitality provided.

The Appeals Committee considered that the Code Committee had erred in its decision that the educational event would not withstand public and professional scrutiny. The Appeals Committee accepted that there was acceptable educational value provided at the educational meeting and, in particular, were persuaded of the value of experiential learning by the healthcare professionals being able to see the manufacturing process first hand and to interact with the personnel responsible for R&D and the manufacturing process. This education would ultimately benefit patients.

Appeals Committee decision
The Appeals Committee unanimously determined to uphold the appeal and amend the decisions of the Code of Conduct Committee. The Appeals Committee determined that the Amgen educational event was not in breach of the following Sections of the Code of Conduct:

- 9.1 Relationship with Healthcare professionals – General Principles
- 9.3 Educational Events
- 9.7 Sponsorship of Healthcare Professionals to attend educational events

Sanction
As the appeal was upheld and the Code of Conduct Committee's decisions overturned, the sanctions imposed by the Code Committee were removed.

Bond
As the appeal was upheld, the Appeals Committee determined that the appeal bond of $20,000 should be returned to Amgen Australia in full.

1123 – Advertising in non-HCP Publication

Subject Company: Bayer Australia Ltd, Merck Sharp & Dohme (Australia) Pty Ltd and Novartis Pharmaceuticals Australia Pty Ltd

Complainant: A member of the general public

Product: Elyea, Saflutan and Lucentis

Complaint
A member of the general public alleged that advertising by three member companies of prescription

medicine products in the *mivision* magazine are in breach of the Code. The Complainant alleged that this magazine is distributed to optical dispensers who are not classified as healthcare professionals under Edition 17 of the Code. It was alleged that *mivision* is a consumer magazine distributed to the general public that contains prescription medicine advertisements.

Sections of the Code
The advertisements are alleged to be in breach of the following Section of Edition 17 of the Code:

- 13.3 Promotion to the General Public

Response
Each responding company stated that they endeavour to be fully compliant with the Code and do not dispute placing advertisements for prescription medicines in the *mivision* magazine. The companies argued that they have undertaken due diligence by confirming with the Editor of the magazine that it is only distributed to registered healthcare professionals (optometrists and ophthalmologists) before placing their advertisements.

Code of Conduct Committee decision
The Committee agreed by unanimous decision that there had not been a breach of Section 13.3 of the Code of Conduct. As it was determined that no breach had occurred, no sanction was imposed by the Committee

Consideration of the complaint
The Chairman summarised for the Committee that the complaint had been made by a member of the general public, alleging that all three companies have placed advertisements for prescription products in a publication that is also distributed to non-healthcare professionals. No complaint had been made concerning the content of the advertisements.

The complaint relates to the audience for *mivision*. The Complainant alleged that *mivision* is distributed to optical dispensers who are not healthcare professionals. Further, the Complainant argued that advertisements for prescription medicines should not be included in a publication that is distributed to optometrists who are not endorsed by the Optometry Board of Australia to prescribe medicines and therefore should be treated as members of the public.

The Chairman noted that the Code definition of a healthcare professional covers healthcare professionals as described in the Therapeutic Goods Act 1989 (the Act), to whom prescription medicines may be promoted. In their responses, the Subject Companies had noted that the definition of healthcare professionals in the Act includes optometrists and that the Act and the Code do not make a distinction between optometrists who have or have not been endorsed by the Optometry Board. All companies acknowledged that optical dispensers are not healthcare professionals, but *mivision* is not distributed to optical dispensers.

The Committee noted that the publisher of *mivision* had provided advice to the Subject Companies, which was included in their responses to the complaint, stating that the publication was only available to *"…eyecare professionals who work in the Optometry and Ophthalmology professions in Australia and New Zealand. To be eligible to receive a*

subscription to mivision journal you must be either an Optometrist, Ophthalmologist, Ophthalmic Nurse, Orthoptist or an academic with a healthcare qualification. [Optical] Dispensers, [and] non-healthcare professionals…are eligible to receive a free subscription to mivision's e-newsletter…which does not contain any advertising of prescription medication…".

Some members of Committee queried why some classes of healthcare professionals, such as optometrists, should be permitted to receive advertising of prescription medicines, since they are unable to prescribe the products. The Committee agreed, however, that these individuals are included in the definition of healthcare professional as set out in both the Code and the Act. Therefore, it was acceptable for them to be included in the distribution list for a publication that includes advertisements for prescription medicines.

The Committee had no evidence before them that the publication was being distributed to people other than a healthcare professional audience. The Complainant had not provided any evidence that the publication is being distributed to optical dispensers. The Committee agreed, therefore, that the Subject Companies had undertaken due diligence and, based on the information provided by the publisher, it is appropriate for this publication to include advertisements for prescription products. The Committee unanimously agreed that no breach of Section 13.3 of the Code of Conduct had occurred.

Sanction
Having found that no breach of the Code of Conduct had occurred, no sanction was imposed by the Committee.

Appeal
The Complainant continued to argue that *mivision* is a consumer magazine that contained prescription medicine advertisements available to the general public. The Complainant stated that *mivision* is distributed to optical dispensers and orthoptists, who are not registered healthcare professionals to whom prescription medicine advertisements may be directed. The Complainant stated that there have been articles in *mivision* written by optical dispensers and directed to optical dispenser readers.

The Complainant provided two address labels for *mivision* magazine which he stated are addressed to optical dispensers.

Appeal Response
Each company responded that the decision of the Code Committee was correct and should not be varied. All companies stated that they had conducted their due diligence to confirm that *mivision* was only distributed to healthcare professionals before placing any advertisement for prescription medicine in the magazine. The companies stated that they should not be expected to conduct due diligence down to individual subscribers.

Bayer responded that one recipient of the *mivision* magazine identified by the Complainant had received the publication because he was a regular contributor of articles published in the magazine. The other recipient had received the magazine in error, according to the publisher, and has been removed from the distribution list.

MSD stated that the arguments raised by the Complainant in his appeal are irrelevant to any section of the Code of Conduct and appear to be more of a commercial dispute which should be arbitrated though another mechanism or directly between the relevant parties.

Appeals Committee decision
The Appeals Committee agreed by unanimous decision to confirm the decisions of the Code of Conduct Committee. The Appeals Committee determined that the placement of advertisements for Eylea, Lucentis and Saflutan in the *mivision* magazine had not been in breach of Section 13.3 of the Code of Conduct, Promotion to the General Public.

Sanction
As the appeal was not upheld and the Code Committee's decision to find no breach of the Code was confirmed, no sanction was imposed.

Consideration of the Appeal
The Chairman introduced the Appeals Committee members to the Appellant and the company representatives.

Prior to consideration of the appeal, the Chairman called for the declaration of any potential conflicting interests. No potential conflicting interests were declared by the Appeals Committee members.

The Chairman explained the process for consideration of an appeal. The Appeals Committee must be persuaded that the findings of the Code Committee involved an error on the basis of which the decisions of the Code of Conduct Committee should be set aside or varied.

The Chairman invited the Appellant to give his appeal presentation to the Committee. The following summarises that presentation and discussion with the Appeals Committee.

The Appellant noted that in his appeal he had provided a copy of an address label for a person who is an optical dispenser, who receives *mivision*. This is contrary to the claims from the *mivision* publishers that the publication does not go to optical dispensers. The Appellant stated that there is no evidence of cessation of delivery of *mivision* to orthoptists or optical dispensers, except that *mivision* has revised its advertising guidelines (Media Kit).

The Appellant noted that advertising prescription medicines to orthoptists had not been included in his original complaint. Orthoptists were included in his appeal. The Chairman advised that complainants may not expand or embellish their complaint on appeal. An appeal must relate to the decisions of the Code Committee.

The Appellant stated that only 37 percent of optometrists are therapeutically endorsed by the Optometry Board of Australia. The Appellant argued that prescription medicines should not be advertised to optometrists because the majority of optometrists cannot prescribe prescription medicines. The Australian Healthcare Practitioner Regulation Agency (AHPRA) register of optometrists identifies which optometrists are therapeutically endorsed.

The Appellant argued that there is a unique working relationship between optometrists and optical dispensers. There is every chance that the *mivision* magazine will be sighted by an optical dispenser if it is distributed to optometrists, unless the publication is

specifically directed to only be viewed by optometrists. The Appellant stated that some orthoptists receive *mivision* magazine directly and others may view it by reason of their employment by ophthalmologists.

The Appellant noted that in Bayer's response to his complaint it stated that it had extensive discussions with *mivision* regarding its readership prior to placing advertisements in the magazine. The Appellant challenged this assertion, arguing that there had only been a handful of calls and emails. The Appellant also challenged the assertion by the publisher of *mivision* that the magazine is distributed to "medically qualified eye care professionals" because optometrists are not medically qualified.

The Appellant noted that in MSD's response to his complaint it stated that the company was satisfied from its enquiries to *mivision* that the publication did not go to optical dispensers. However, the Appellant had provided a mailing fly sheet addressed to an optical dispenser as evidence that the publication is distributed to optical dispensers. The Appellant stated that due to the Christmas and New Year holiday period, and that the magazine is not issued again until February, he had not been able to obtain fly sheets from other optical dispensers who receive *mivision*. The Appellant argued that if he had more time he would be able to demonstrate that *mivision* is distributed to optical dispensers. The Appellant asked the Appeals Committee to grant him more time to collect more evidence of fly sheets for *mivision* addressed to optical dispensers. The Appeals Committee Chairman advised the Appellant that the evidence to support his complaint should have been available at the time of making his complaint. It is not possible to delay consideration of the complaint whilst the Appellant seeks further evidence to support his allegations.

The Appellant referred to Novartis' response to his complaint, which included a page from the mivision.com.au website, "About Us". The page is dated December 2011, yet it refers to *mivision* circulation data from March 2014, being 7,289 recipients. The Appellant referred to the Media Kit 2013 and Media Kit 2014 published by *mivision*. The Committee Secretary clarified that the Appellant had provided data extracted from these Media Kits in his appeal submission but had not provided copies of them with his submission. The Chairman noted that the subject companies had received the Appellant's appeal submission but had not had the opportunity to review the Media Kits to which the Appellant now referred.

The Appellant noted that the Media Kit 2013 included a statement on page 1 that claims that *mivision* "connects with eye care professionals at all levels (including)… retail staff, optical dispensers, manufacturers and distributors". The Media Kit 2014 does not include this statement. The Media Kit 2013 states that 1,622 optical dispensers received the *mivision* magazine, yet the publisher now claims that optical dispensers are not receiving the magazine.

The Appellant noted that the Media Kit 2014 states that 9,500 people receive the optometry only email *mivision* newsletter and 2,700 people receive the ophthalmology only *mivision* newsletter. The Media Kit does not mention optical dispensers receiving these emailed newsletters.

The Appellant referred to circulation statistics for *mivision* between September 2012 and September 2014, which ranged between 7,289 and 6,893. The Appellant queried why it was that if *mivision* no longer was distributed to optical dispensers, the circulation had not decreased by approximately 1,600?

The Appellant noted that the *mivision* magazine includes some 10 to 15 pages relating to frame styles for spectacles. He questioned whether this information would be of interest to ophthalmologists and optometrists, inferring that these pages were directed to optical dispensers.

The Chairman invited the companies to make their responses to the appeal, noting that it would assist the Committee if each company did not repeat arguments made by another company and confine their remarks to matters that have not been covered.

Bayer Australia presented their response to the appeal.

Bayer summarised the complaint, which alleged that Bayer had placed advertisements in *mivision*, which was in breach of Code section 13.3 because *mivision* is available to optometrists who are not endorsed by the Optometry Board of Australia to prescribe and use therapeutic drugs and that these practitioners are 'consumers' for the purposes of the Code; and secondly that *mivision* is distributed to optical dispensers. The Code Committee unanimously found that Bayer had not breached the Code. Bayer noted that Code section 13.3 refers to promotion to the general public, which is wider than to consumers.

Bayer highlighted that the Code sets a high threshold for an appeal to be upheld. An appellant must show that the Code Committee made an error of judgement on the basis of which they should be set aside or varied. The Appeals Committee would need to find that the *mivision* magazine was distributed to the general public. Bayer is fully aware that companies are prohibited from promoting a prescription medicine to the general public, which is not something the company would wilfully do.

The allegation that orthoptists are not healthcare professionals should be dismissed by the Appeals Committee. The Code definition of healthcare professionals, which are people who in their professional activities may prescribe, dispense, recommend, supply or administer a prescription medicine, includes orthoptists. Optometrists and ophthalmologists are healthcare professionals according to the Code definition.

Bayer noted that the regulations for each Australian State vary with regard to definition of a healthcare professional. For example, the *Poisons Act 1964 (WA)* permits a prescribed class of healthcare professional to possess, use, supply, sell or prescribe a prescription medicine. The *Poisons Regulations 1965* (*WA*) state that an endorsed optometrist is a prescribed healthcare professional. The *Health (Drugs and Poisons) Regulation 1996* (*Qld*) state that an orthoptist may obtain, possess and administer a restricted drug. Therefore, optometrists and orthoptists are healthcare professionals as defined by the Code of Conduct.

Bayer stated that optical dispensers are not healthcare professionals as defined by the Code. Optical

dispensers cannot administer or purchase prescription medicines. Bayer asserted that there is no evidence that it had placed advertisements in *mivision* so as to influence prescribing of Eylea by optical dispensers.

Bayer does not have access to the distribution lists for *mivision* magazine. A company must be able to rely on information provided by a publisher. If the publishers have misrepresented who are subscribers to *mivision*, this should be taken up with the publisher.

Bayer understands that the hard copy *mivision* magazine contains prescription medicine advertising, whereas the *mivision* e-newsletter, which is distributed to optical dispensers, does not include advertisements for prescription medicines.

Bayer asserted that the Appellant has changed his definition of who is considered to be a healthcare professional. Bayer referred to a letter from the Appellant dated 21 January 2013, which stated that the Appellant considered optical dispensers to be health professionals who may receive prescription medicine advertisements. At that time the Appellant had been seeking advertising by Bayer for his publication, which "goes to is subscribed optometrists, ophthalmologists, optical dispensers, orthoptists and their suppliers. It is not a publication that can be accessed by members of the general public." Bayer argued that the Appellant at that time had accepted that optical dispensers may receive a publication that included advertisements for prescription medicines.

Bayer responded to the Appellant's argument that *mivision* had been received by an optical dispenser whose address label was provided by the Appellant. Bayer noted that the recipient wrote articles published in *mivision*, so it was reasonable for him to receive the publication. This is not evidence that *mivision* is distributed widely to optical dispensers. With regard to the second optical dispenser whose *mivision* address fly sheet had been submitted by the Appellant, Bayer stated that *mivision* has removed that person from the distribution of the magazine.

An Appeals Committee member asked Bayer if they have received a breakdown of their subscribers. Bayer responded that it had not received that information. The Chairman asked Bayer if they had any comment on the circulation statistics for *mivision* reported by the Appellant. Bayer responded that it could not comment as it does not have access to the statistics quoted by the Appellant. Bayer advised that they understand that *mivision* is available as a printed magazine, an online website, an emailed newsletter and an open online version of the magazine. Bayer has limited its placement of advertisements to the print magazine as it was informed by the publisher that the magazine is only distributed to healthcare professionals who may receive prescription medicine advertising.

The Chairman invited MSD to give their response to the appeal.

MSD stated that Bayer's presentation was representative of MSD's position. MSD maintains that it has not breached section 13.3 of the Code. The finding of no breach was a unanimous decision of the Code Committee.

MSD has acted in good faith in placing advertisements in *mivision* magazine. It had reviewed the *mivision* website information regarding who may subscribe to the magazine and had a conversation with the publisher. The website states that the magazine is only distributed to optometrists, ophthalmologists, ophthalmic nurses, orthoptists and academics with a healthcare qualification. *mivision* publishers had informed MSD that the magazine was distributed only to healthcare professionals. MSD had made reasonable enquiries about whether the magazine was directed to healthcare professionals.

The Chairman asked when MSD had made these enquiries to *mivision*. MSD responded that this had been in 2014 but the MSD representative was not aware of the precise date. Advertisements for its product Saflutan had only been placed in *mivision* in 2014.

Bayer advised the Committee that it had placed its first advertisement in *mivision* print magazine in September 2012. It had received confirmation from *mivision* in August 2012 that the distribution of *mivision* was to health professionals. Bayer had decided not to continue to advertise in the Appellant's journal in April 2013 and had again sought and received confirmation from *mivision* publishers that the magazine was distributed only to health professionals. This had been reconfirmed in October 2014 when Bayer received the complaint from the Appellant. Bayer therefore had undertaken due diligence.

MSD stated that although optical dispensers work closely with optometrists and may see the *mivision* magazine received by an optometrist, a company cannot be held responsible for what an optometrist or other subscriber does with *mivision* or other health professional journals containing advertisements for prescription medicines.

The Chairman invited Novartis to give their response to the appeal.

Novartis stated that it agreed with the positions put by Bayer and MSD. Novartis considered that the Code Committee's decision should not be changed.

An Appeals Committee member asked whether the companies have at present withdrawn their advertisements from *mivision*. Novartis advised that it has, at present, ceased to advertise its product in *mivision*. Bayer responded that it would not be appropriate or relevant to the complaint to discuss its plans for advertising its products.

The Chairman invited the Appellant to make any closing remarks, particularly with respect to the definition of a healthcare professional on which there appeared to be quite different views between the Appellant and the companies. The Chairman also asked the Appellant to comment on whether the statistics he quoted related to the print magazine as well as the online version.

The Appellant responded that figure he had quoted of 1,622 optical dispensers related to the print magazine. He stated that in the companies' responses to his complaint they had relied on the word of the publishers of *mivision*.

The Appellant reiterated that orthoptists are not healthcare professionals and referred to a

specialist ophthalmologist who shared this view.

Bayer noted that healthcare professionals are permitted to receive prescription medicine advertising. The Code definition of healthcare professionals takes a broad perspective, referring to "any other persons who in the course of their professional activities may prescribe, dispense, recommend, supply or administer a Product." The Code does not make any distinction between registered optometrists and therapeutically endorsed optometrists. With regard to the individual optical dispenser who writes articles for *mivision* and received the magazine, an Appeals Committee member noted that it would be normal practice to give contributors a copy of the publication.

The Chairman advised the Appellant that if his complaint is based on one or two optical dispensers receiving *mivision* magazine, that is not sufficient to find the companies in breach of the Code. The Appellant stated that he is sure that he could obtain evidence of many optical dispensers receiving *mivision* if he was given more time. The Chairman advised that the Code requires a complainant to make out their complaint. If the evidence is not available, the Code and Appeals Committee have to proceed on the evidence that is before them.

The Appellant agreed to table the print versions of the Media Kits 2013 and 2014 for the Committee. Bayer stated that as the companies had not had the opportunity to review this information, it would be concerned at the level of interpretation and weight that the Appeals Committee might place on these documents. The Chairman agreed that each party should have all the material available to the Appeals Committee.

The Chairman thanked the Appellant and company representatives for their presentations and excused them from the meeting to allow the Committee to deliberate on the appeal.

The Appeals Committee agreed to deal with the appeal by working from the Code Committee's reasons for its decision and the evidence that was before the Code Committee, with the addition of any material that is acceptable as new evidence.

The Appeals Committee unanimously agreed to reject the extension of the scope of the complaint to include orthoptists. The Appeals Committee reviews the decisions of the Code Committee. Orthoptists had not been included in the original complaint considered by the Code Committee. However, there remained the question of whether *mivision* magazine was distributed to optical dispensers, which all companies had accepted were not healthcare professionals.

The Appeals Committee discussed the two Media Kits 2013 and 2014 tabled by the Appellant. These documents had not been submitted with the original complaint or with the appeal submission. The three subject companies had not had the opportunity to review them. The issue therefore arose as to how the Appeals Committee should treat the material in the Media Kits and the Appellant's summary of data from the Media Kit 2013 in his appeal.

The Committee decided in its discretion to not receive the Media Kits or the distribution figures contained in them for reasons of procedural fairness and because the figures

referred to by the Appellant appeared to conflict with information provided by *mivision* to the companies. As referenced in the Code of Conduct Committee's reasons for decision, *mivision* had unequivocally stated to each subject company that *mivision* is not distributed to optical dispensers. While the Code does permit the Appeals Committee to consider new evidence, the Media Kits did not appear to meet the requisite definition. Even if they did, the Appeals Committee, having not heard from the companies in relation to the Media Kit 2013, was not able to resolve this conflict. It follows that the Appellant had not made out his case that the Code Committee had erred in making its decision to find no breach of the Code by any of the companies. The Appeals Committee, however, asked the Secretariat to provide the Media Kits 2013 and 2014 to each company as they were tabled at the meeting.

The Appeals Committee discussed the Appellant's request for further time in which to try to obtain address fly sheets from optical dispensers who receive *mivision* magazine. The Appeals Committee determined that, as was explained earlier to the Appellant, the request could not be considered by the Appeals Committee.

The Appeals Committee discussed the Code Committee's reasons for its decision. The Appeals Committee determined that there was no basis on which to find that the Code Committee had made an error in its decision. No evidence had been provided to that Committee that *mivision* was being distributed to optical dispensers. The Appeals Committee therefore determined not to uphold the appeal.

The Appeals Committee agreed by unanimous decision to confirm the decisions of the Code of Conduct Committee. The Appeals Committee determined that the placement of advertisements for Eylea, Lucentis and Saflutan in the *mivision* magazine had not been in breach of Section 13.3 of the Code of Conduct.

Sanction

As the appeal was not upheld and the Code Committee's decision to find no breach of the Code was confirmed, no sanction was imposed.

1124 – Xarelto Promotional Material

Subject Company: Bayer Australia Limited

Complainant: Pfizer Australia and Bristol-Myers Squibb Australia

Product: Xarelto

Complaint

Bristol-Myers Squibb and Pfizer alleged that the claim "One less is more" for Xarelto has the potential to mislead clinicians and negatively influence patient outcomes. They alleged that the claim is not balanced, accurate, or fully supported by the Product Information, literature, data on file or an appropriate industry source.

Sections of the Code

The material was alleged to be in breach of the following Sections of Edition 17 of the Code:

- 1.1 Responsibility
- 1.2 Substantiating Date
- 1.3 False or Misleading Claims
- 1.8 Comparative Statements

Response
Bayer strongly rejected the allegation that the material would mislead clinicians or negatively influence patient outcomes. Bayer argued that BMS and Pfizer have misconstrued the promotional material. Bayer stated that the claim is fully supported by the literature. Bayer further argued that the claim is not comparative and does not claim superior efficacy or safety of once-daily medicines. The claim is adequately qualified, substantiated, does not mislead, and is fully compliant with the Code.

Code of Conduct Committee decision
The Committee agreed by unanimous decision that the claim was in breach of sections 1.1, 1.2 and 1.3 of the Code of Conduct. The Committee also agreed by unanimous decision that the claim was not in breach of Section 1.8 of the Code of Conduct.

Sanction
The Committee agreed by unanimous decisions that the claim must not be used again in the same or in a similar form and imposed a fine of $30,000.

Consideration of the complaint
The Chairman summarised the complaint for the Committee, noting that the substance of the complaint is that the referenced study does not adequately substantiate the claim *"One less is more"*. The Chairman noted that Bayer had responded to the complaint stating that the claim was not about Xarelto being superior or having greater efficacy. Bayer had argued that the claim was only that a one tablet a day regimen results in better compliance than twice daily regimens, and therefore the referenced study is sufficient to support the claim.

The Committee reviewed the referenced study – *Impact of Daily Dosing Frequency on Adherence to Chronic Medications Among Nonvalvuar Atrial Fibrillation Patients* (Laliberte et al (2012) (Laliberte Study). The Committee noted that the Laliberte Study was a retrospective cohort analysis of a health insurance claims database. Subjects were adult patients newly initiated on once-daily or twice daily oral antidiabetic or antihypertensive medications. The Committee noted that the study population did not include patients prescribed Xarelto, but was conducted in patients with nonvalvular atrial fibrillation (NVAF), which is one indication for Xarelto.

The Committee discussed the claim *"One less is more"* and the associated qualifying statement and study description. The qualifying statement was *"once daily-dosing is associated with improved patient compliance vs. twice-daily dosing in NVAF"* and the Laliberte study was described as: *"A retrospective cohort study assessing adherence rates to once- vs. twice-daily dosing regimens of chronic medications (for diabetes or hypertension) in >10,000 patients with NVAF demonstrated that once-daily dosing was associated with a 26% higher likelihood of adherence vs. twice daily dosing"*. The claim, the qualifying statement and the study description were referenced to the Laliberte Study. The Committee agreed that the placement and font size of the qualifiers appeared to be compliant with the Code of Conduct.

The Committee agreed that this complaint pivoted on whether the Laliberte Study was appropriate and sufficient to support the claim. The Committee noted that the study design, which compared adherence to

once daily and twice daily regimens based on the frequency of refilling prescriptions, did not investigate other factors that will influence compliance and adherence such as the time of day the medicine should be taken and whether the medicine must be taken with food, before food or on an empty stomach. In particular, the Committee noted that the study authors had warned against extrapolating results from this study to adherence to other chronic medications for atrial fibrillation. Specifically, the Laliberte Study authors noted, *"It is important to take note that the current study on adherence to antihypertensive and antidiabetic drugs only allowed indirect conclusions to be drawn regarding AF patents' adherence to other chronic medications".* The Committee concluded that Bayer had selected the Laliberte study because it had studied patients with NVAF, one of the indications for Xarelto. However, the Committee agreed that the study results could not be extrapolated to other chronic medications. Therefore, the Committee unanimously agreed that the study was not adequate as the sole reference to substantiate the claim subject to complaint. The Committee agreed unanimously that the claim had not been adequately substantiated and was therefore misleading and was in breach of Sections 1.1, 1.2 and 1.3 of the Code of Conduct.

The Committee discussed whether the claim "*One less is more*" was a comparative claim. The Committee noted that whilst the claim could, on first reading, suggest that it was comparative, the qualifying statement specifically communicated that the claim related to improved patient compliance; it did not suggest any claim for better efficacy or safety. The Committee agreed unanimously that the claim was not in breach of Section 1.8 of the Code.

Sanction
Having found that the claim was in breach of Sections 1.1, 1.2 and 1.3 of the Code, the Committee discussed an appropriate sanction. The Committee considered that this advertisement constituted a moderate breach of the Code of Conduct, as there was the potential for it to influence prescribing of the product.

The Committee agreed unanimously that the advertisement should be withdrawn from use, and that the claim *"One less is more"* should not be used in the same or similar form in the future. Additionally, the Committee imposed a fine of $30,000.

1125 – Duromine Presentation

Subject Company: iNova Pharmaceuticals (Australia) Pty Ltd

Complainant: Healthcare professional

Product: Duromine

Complaint
The healthcare professional complainant had attended an educational meeting in August 2014 at which an International Guest Speaker gave a presentation about management of obesity. The Complainant alleged that iNova had breached the Code by:

- Presenting inappropriate information regarding the off-label use of Duromine (i.e. that it is safe to use this product for longer than 6 months), which can lead to patient harm
- Lack of substantiating data for the off-label use of Duromine

- Making misleading claims by suggesting to the GP audience that long term use of Duromine (10-15 years) is safe, even though the study conducted and cited by the Guest Speaker was not a safety study

Sections of the Code
The presentation/educational meeting was alleged to be in breach of the following Sections of Edition 17 of the Code:

- 1.1 Responsibility
- 1.2 Substantiating Data
- 1.3 False or Misleading Claims

Response
iNova denied that the company had breached any section of the Code. iNova stated that it had briefed the Guest Speaker about the company's responsibilities under the Code of Conduct.

iNova stated that the Guest Speaker had discussed the cardiovascular safety of Duromine in response to a question at the educational meeting. iNova denied that the Guest Speaker had downplayed the cardiovascular risks of Duromine. Further iNova responded that the Guest Speaker had not suggested that long-term use of Duromine was safe. iNova argued that the Guest Speaker had informed participants at the commencement of the meeting that the material he would present were his own opinions based on his clinical experience and were not those of the sponsor, iNova.

Code of Conduct Committee decision
The Committee agreed by majority decision that the educational event was in breach of Section 1.1 of the Code of Conduct. The Committee also agreed by majority decision that there had been no breach of Sections 1.2 or 1.3 of the Code of Conduct.

Sanction
The Committee agreed by majority decision that iNova must send a corrective letter to each healthcare professional who attended any of the capital city educational events it had organised, advising them that the International Guest Speakers' presentation had related to a product that was not approved in Australia and that Duromine should only be prescribed for short-term use in accordance with the approved Product Information. This letter must be approved by the Code of Conduct Committee before it is issued. In addition, the Committee imposed a fine of $100,000.

Consideration of the complaint
The Chairman summarised the complaint for the Committee, noting that the complaint centred on a presentation given on 12 August 2014 where an International Guest Speaker, presented his study of the long-term use (up to 7 years) of phentermine hydrochloride. This presentation was one of a series of capital city educational meetings organised by iNova, which followed the National Obesity Forum 2014 that iNova had also sponsored. The Chairman noted that phentermine hydrochloride (immediate release) is not available in Australia, however phentermine resin (controlled release) is marketed in Australia by iNova under the brand name Duromine. Duromine is approved in Australia for short-term use.

The healthcare professional Complainant had provided a précis of the presentation given by the Guest Speaker, which included that the Guest Speaker had advised attendees

of the dose equivalence between phentermine hydrochloride and Duromine. iNova had stated in its response to the complaint that the Guest Speaker had started his presentation with a statement that the content of his presentation was his own opinion based on his clinical experience. iNova had not provided the Committee with a copy of the slides the Guest Speaker presented at the meeting or with a copy of the invitation to this educational meeting. However, the Committee noted that the presentation would not provide evidence of what the Guest Speaker had said beyond his formal presentation or in response to impromptu questions from attendees.

The majority of the Committee were concerned that iNova had organised a series of educational meetings with a presentation about a product that is not registered in Australia. The majority of the Committee considered that the purpose of these meetings was to encourage discussion about the off-label use of Duromine. The Committee agreed that this posed a serious safety risk for patients because Duromine is only indicated for short term use – the approved Duromine Product Information states that a defined course of treatment should not exceed three months. The Guest Speakers' study, presented by him at the meetings, included patients with a treatment duration of a minimum of 12 weeks to a maximum of 12 years.

The Committee noted that in its response, iNova stated that it had briefed the Guest Speaker on the regulatory requirements in Australia and the obligation for compliance with the Medicines Australia Code of Conduct. However, no evidence was supplied by iNova to support that such a briefing had occurred or its actual content. Further, a disclaimer given at the start of a presentation will not avoid a potential breach of the Code of Conduct, nor absolve iNova of its responsibilities as the sponsor of the Guest Speakers' speaking engagements. The Committee accepted that the Guest Speakers' presentation at the National Obesity Forum 2014, which was organised by an independent steering group of Australian healthcare professionals, was sufficiently independent to allow the exchange of clinical and scientific information, including the Guest Speakers' study. However, the Committee considered that in organising the capital city road show, iNova was fully responsible for the content of these events.

The Committee agreed by majority decision that the educational meeting was focused on a product that is not available in Australia and encouraged doctors to prescribe Duromine for long-term use, for which it is not approved.

The Committee determined by majority decision that the educational event constituted a breach of Section 1.1 of the Code of Conduct because it promoted use of Duromine that was not supported by the Product Information. The Committee also agreed by majority decision that there had been no breach of Sections 1.2 or 1.3 of the Code of Conduct.

Sanction

Having found that the educational event was in breach of Section 1.1 of the Code, the Committee discussed an appropriate sanction.

The Committee considered that this activity constituted a severe breach of the Code of Conduct, as there were potential safety implications for patients and the activity had the

potential to have a major effect on how the medical profession would prescribe the product. The Committee agreed by majority decision that iNova must send a corrective letter to each healthcare professional who attended any of the capital city educational events it had organised. The corrective letter must advise them that the Guest Speakers' presentation had related to a product that was not approved in Australia and that Duromine should only be prescribed for short-term use in accordance with the approved Product Information. The Code of Conduct Committee must approve this letter before it is issued. In addition, the Committee imposed a fine of $100,000.

1126 – Sprycel Promotional Material

Subject Company: Bristol-Myers Squibb Australia Pty Ltd

Complainant: Novartis Pharmaceuticals Australia Pty Ltd

Product: Sprycel

Complaint
Novartis alleged that two items of promotional material for Sprycel – one for specialist haematologists and the other for pharmacists – were in breach of the Code of Conduct. Novartis alleged that a number of statements in these items made false and misleading claims, were unable to be adequately substantiated, promoted an unapproved indication and, in relation to one statement, had the potential to bring the industry into disrepute. Novartis asserted that the promotional material had the potential to have a negative effect on patient safety.

Sections of the Code
The materials were alleged to be in breach of the following Sections of Edition 17 of the Code:

- 1.1 Responsibility
- 1.2 Substantiating Date
- 1.3 False or Misleading Claims
- 1.4 Unapproved Products and Indications
- 9.14 Discredit to and Reduction of Confidence in the Industry

Response
BMS strongly denied that the materials breached any section of the Code of Conduct. BMS asserted that both pieces included safety messages related to Sprycel and reinforced to physicians the need for monitoring. Furthermore, BMS noted that there was no mention of other products in either piece and no comparisons between Sprycel and another product had been made.

BMS contended that Novartis had restated a number of complaints that had been resolved during the intercompany dialogue, which gave a misleading impression to the Code Committee of the scope of the complaint. Further, BMS contended that Novartis had been unwilling to accept solutions proposed during intercompany dialogue and had demanded that BMS issue a corrective letter. BMS requested the Committee to consider whether Novartis had abused the Code.

Code of Conduct Committee decisions
Complaints relating to the promotional material for specialists, titled "*How do patient comorbidities influence your TKI selection?*":

Complaint 1 - Statement "*Sprycel has been shown to lower blood glucose*

and some patients have discontinued hypoglycaemic medication, including insulin"
The Committee determined by majority decisions that the statement was not in breach of the following Sections of the Code of Conduct:

- 1.2 Substantiating data
- 1.3 False or Misleading Claims
- 1.4 Unapproved Products and Indications

The Committee determined by unanimous decision that the statement was not in breach of the following Sections of the Code of Conduct:

- 9.14 Discredit to and Reduction of Confidence in the Industry

Complaint 2 – Statement "*In the DASISION study…Sprycel's safety profile was similar for patients with and without baseline diabetes*"
The Committee determined by majority decisions that the statement was not in breach of the following Sections of the Code of Conduct:

- 1.2 Substantiating Data
- 1.3 False and Misleading Claims

Complaint 5 – Statement "*Sprycel's overall safety profile was similar in patients with and without diabetes mellitus, hepatobiliary disease, hyperlipidaemia and CVD*"
The Committee determined by majority decision that the statement was not in breach of the following Section of the Code of Conduct:

- 1.3 False or Misleading Claims

Complaint 6 – Statement "*A subanalysis of DASISION demonstrated no substantial effects of baseline cardiovascular conditions, other comorbidities, or use of baseline medications on the side-effects of Sprycel*"
The Committee determined by unanimous decision that the statement was in breach of the following Section of the Code of Conduct:

- 1.3 False or Misleading Claims

Complaint 8 – Statement "*Simple dosing (one pill, once daily) helps to maximize adherence…*"
The Committee determined by unanimous decision that the statement was in breach of the following Section of the Code of Conduct:

- 1.3 False or Misleading Claims

Complaint 9 – Statement "*Increased treatment restrictions and associated difficulty may affect adherence to TKI therapy*"
The Committee determined by unanimous decision that the statement was not in breach of the following Section of the Code of Conduct:

- 1.2 Substantiating Data

Complaint relating to the promotional material for pharmacists, titled "*Pharmacists play a critical role in the management of CML*"

Complaint 14 – Statement "Simple dosing (one pill, once daily) helps to maximize adherence…"
The Committee agreed by unanimous decisions that the statement was in breach of the following Sections of the Code of Conduct:

- 1.2 Substantiating Data
- 1.3 False or Misleading Claims

The Committee agreed that the breach in relation to Complaint 6 was a minor to moderate breach of the Code and the two breaches in relation to Complaints 8 and 14 were minor breaches of the Code.

Sanction
Having found that the two items of promotional material were in breach of the Code, the Committee imposed the following sanctions:

- Withdraw both items of promotional material from use and do not use the statements found in breach of the Code again in the same or similar form.
- Pay a fine of $45,000

No corrective letter was imposed by the Code Committee.

Abuse of the Code

The Committee determined that, on this occasion, Novartis should not be asked to respond to the allegation that it was potentially in breach of Section 25 of the Code.

Consideration of the complaint

The Committee noted that 14 separate complaints were described in Novartis' complaint submission, which stated in the conclusion that complaints 1, 2, 5, 6, 8, 9 and 14 had not been resolved. The Committee therefore did not consider complaints 3, 4, 7, 10, 11, 12 or 13.

Complaints 1, 2, 5, 6, 8 and 9 related to statements in promotional material for specialists titled "*How do patient comorbidities influence your TKI selection?*"

Complaint 1 - Statement "*Sprycel has been shown to lower blood glucose and some patients have discontinued hypoglycaemic medication, including insulin*"

Novartis had primarily alleged that this statement promoted Sprycel for an unapproved indication, to treat diabetes by lowering blood glucose, and was in breach of Section 1.4 of the Code. The Code Committee noted that Novartis had omitted the words "In some reports" from the start of the statement as it appeared in the material. Thus, the statement was limited to "some reports".

The Committee reviewed the cited references to support the statement. The article by Agostino et al (2010) was a retrospective analysis of 78 patients who had been treated with tyrosine kinase inhibitors (TKI). Eight of these patients had received dasatinib (Sprycel), but only one of these patients was a diabetic. This patient had been taking three oral antidiabetic medicines which was reduced to two (a metformin combination product) whilst treated with dasatinib. Two other references were single case reports (Breccia et al (2008) and Ono et al (2012)) about two patients who had reduced their insulin requirements or discontinued insulin treatment whilst being treated with dasatinib for CML.

The Committee also noted that the Sprycel Product Information does not mention effects on blood glucose levels or recommend monitoring diabetic patients for changes in hypoglycaemic medicine requirements.

The majority of the Committee did not agree with the allegation that the statement was promoting Sprycel for the treatment of diabetes. These members considered that it would be very unlikely that a specialist haematologist, to whom the promotional material was directed, would start treating diabetic patients or managing their CML patients' diabetes by choosing Sprycel. Some Committee members thought that the statement could highlight to physicians that they should be aware of Sprycel's potential effect on blood glucose in their CML patients.

A minority of the Committee were concerned that the statement relied on just three patients in the cited references and the hypoglycaemic effect had not been mentioned in the

Product Information. These members were concerned that the statement made a claim beyond the approved use of Sprycel.

In a majority decision, the Committee found that the statement was not in breach of Section 1.4 of the Code.

Some Committee members were concerned that the statement had overreached the substantiating data. Whilst there is some evidence that Sprycel and some other TKIs may lower blood glucose, as already noted the statement relies on just two case reports and one retrospective analysis of eight patients, only one of whom had diabetes. However, the majority of members considered that there was some evidence to support the statement and the statement was limited in its interpretation by the words "In some reports". In a majority decision, the Committee determined that the statement was not in breach of Section 1.2 of the Code.

Having found in majority decisions that the statement was not in breach of Sections 1.2 or 1.4, the Committee determined in a majority decision that the statement was not false or misleading and was not in breach of Section 1.3 of the Code. Having found that the statement was not in breach of any Code provision, the Committee determined in a unanimous decision that the statement would not bring the industry into disrepute and was not in breach of Section 9.14.

Complaint 2 – Statement "*In the DASISION study…Sprycel's safety profile was similar for patients with and without baseline diabetes*"

This statement appeared immediately below the statement subject to complaint 1 in the promotional material.

The Committee reviewed the cited references to support this statement. Khoury et al (2010) was an oral presentation at the American Society of Hematology (ASH) 2010 Annual Meeting. It reported a retrospective sub-analysis of the DASISION clinical trial. The Committee noted that the DASISION trial evidently did not exclude patients with diabetes. Table 5 on page 19 of the Khoury et al presentation provided data on drug-related adverse effects in dasatinib-treated and imatinib-treated patients with or without diabetes. Regrettably, this study did not include any statistical analysis, so the Committee was unable to assess if any differences between patients with or without diabetes were statistically significant. However, 33 percent of patients with diabetes reported the adverse effect 'fluid retention' whereas only 18 percent of patients without diabetes reported fluid retention. Clearly more dasatinib-treated patients with diabetes experienced fluid retention compared with dasatinib-treated patients without diabetes.

Some Committee members were concerned that the statement identified in complaint 2 relied on the broad concluding statement from the Khoury et al (2010) presentation. The conclusion that "baseline co-morbidities appeared to have no substantial impact on the overall safety and efficacy of dasatinib or imatinib as first-line treatment for CML-CP" did not take into account the more detailed data analysis where some differences were shown. One member commented that the statement in the promotional material was somewhat ambiguous – it could be interpreted that Sprycel's safety profile was similar

to imatinib's in patients with and without diabetes, or that Sprycel's safety profile was similar between patients with and without diabetes.

The majority of the Committee accepted that overall there was not a great deal of difference in safety of dasatinib in patients with and without diabetes except for fluid retention. These Committee members noted that there are no specific precautions in the Sprycel Product Information that would suggest that diabetic patients experience more adverse effects from dasatinib than non-diabetic patients.

The Committee noted that complaint 2 was not discussed during the intercompany meeting, which suggested that Novartis had accepted BMS' substantiation for the statement, as BMS had argued in its response to the complaint.

The Committee also referred to Hochhaus and Kantarjian (2013), which is a literature review of dasatinib in CML. This paper supported the statement subject to complaint, although, in relation to this statement, it cited Khoury et al (2010) and two other abstracts from the ASH 2010 Annual Meeting rather than published, peer-reviewed articles.

Following this detailed discussion of the complaint, the Committee concluded in majority decisions that, on balance, the statement was able to be adequately substantiated and was not false or misleading. The Committee found no breach of Sections 1.2 or 1.3.

Complaint 5 – Statement "*Sprycel's overall safety profile was similar in patients with and without diabetes mellitus, hepatobiliary disease, hyperlipidaemia and CVD*" and

Complaint 6 – Statement "*A subanalysis of DASISION demonstrated no substantial effects of baseline cardiovascular conditions, other comorbidities, or use of baseline medications on the side-effects of Sprycel*"

The statement subject to complaint 5 is similar to complaint 2, but the statement also refers to hepatobiliary disease, hyperlipidaemia and CVD (cardiovascular disease). The statement subject to complaint 6 is a direct quote from Hochhaus and Kantarjian (2013).

The Committee reviewed the supporting references for the statements, which were the same references reviewed in relation to complaint 2 with an additional abstract by Saglio et al (2010) presented at the ASH 2010 Annual Meeting. Tables 6 and 7 on slides 20 and 21 in the Khoury et al (2010) oral presentation included data relating to adverse effects in dasatinib-treated patients with or without baseline hepatobiliary disease and with or without baseline hyperlipidaemia. Once again, the proportion of patients experiencing adverse effects in each subgroup is given, but there was no statistical analysis. There were considerably more patients in the 'no hepatobiliary disease' subgroup than the 'hepatobiliary disease' subgroup. In addition, there were considerably more patients in the 'no hyperlipidaemia' subgroup than the 'hyperlipidaemia' subgroup. In the absence of any statistical analysis, this makes these data difficult to evaluate.

The Committee reviewed the Saglio et al (2010) abstract, which was a retrospective subgroup analysis of safety and efficacy in DASISION trial

subjects with a cardiovascular pre-existing condition and without any pre-existing cardiovascular condition. Saglio et al concluded that although fluid retention and cardiac adverse effects were more common in patients with a baseline cardiovascular condition, overall, the authors stated, the data showed no substantial impact of baseline cardiovascular conditions on the general safety of dasatinib (or imatinib) in DASISION trial subjects.

The Committee noted that the Sprycel Product Information includes a section on *Cardiac Adverse Reactions*, which states that adverse cardiac reactions were more frequent in patients (in the DASISION trial) with cardiac risk factors or a previous history of cardiac disease. The Product Information recommends careful monitoring and evaluation of patients with a history of cardiac disease.

The Committee noted that the statements in complaints 5 and 6 are specific to "In the DASISION study". Statement 5 is a compilation of the broad conclusions from Khoury et al (2010) and Saglio et al (2010) and Statement 6 is a direct quote from Hochhaus and Kantarjian (2010).

Committee members were concerned that the Saglio et al subgroup analysis made a broad brushstroke conclusion from the data and seemed to have ignored the detailed results of their retrospective subgroup analyses, particularly with respect to increased fluid retention, superficial oedema and cardiac adverse effects. Committee members were concerned that the Saglio et al study had identified higher rates of superficial oedema and pleural effusion in dasatinib-treated patients with a baseline cardiovascular condition, yet the overall conclusion was that there was no substantial impact on adverse effects from baseline cardiovascular conditions. The conclusion appears to conflict with the data presented in the abstract.

As previously noted, the Hochhaus and Kantarjian (2013) literature review, from which the statement in complaint 6 is directly quoted, references Khoury et al (2010), Saglio et al (2010) and Guilot et al (2010), which are three abstracts presented by the DASISION study group at the ASH 2010 Annual Meeting. The statement in the Hochhaus and Kantarjian paper did not refer to the higher rates of fluid retention and superficial oedema found by Saglio et al (2010) and only reflected the broad, general conclusion from that abstract. The Committee also was concerned that statement 6, whilst it was a quote, contradicted the precautions in the Sprycel Product Information about cardiac adverse reactions and fluid retention. The Committee also noted that the Product Information states that patients with uncontrolled or significant cardiovascular disease were not included in clinical studies. It would not be clear to a haematologist that patients with more significant baseline cardiovascular disease were excluded from the DASISION study and that the subanalysis referred to in statement 6 might not apply to such patients. The Committee concluded that the statement subject to complaint 6 was misleading.

Following this detailed review and lengthy discussion of the supporting evidence, the majority of the Committee accepted that the leading statement subject to complaint 5 was consistent with and reflected the conclusions of the DASISION study group's retrospective subgroup analyses and was not misleading. However, the statement subject to

complaint 6 was determined to be misleading by a unanimous decision.

In a majority decision, the Committee determined that the statement in complaint 5 was not false or misleading and was not in breach of Section 1.3 of the Code of Conduct.

In a unanimous decision, the Committee determined that the statement in complaint 6 was in breach of Section 1.3 of the Code.

Complaint 8 – Statement "*Simple dosing (one pill, once daily) helps to maximize adherence…*"

The Committee noted that this quotation is from Osterberg and Blaschke (2005), which is a general article on adherence to medication; it is not specific to Sprycel, TKIs or the treatment of CML. The Committee also reviewed the Hirji et al (2013) paper, which included an investigation of treatment adherence in CML patients treated with TKIs. In the Hirji et al study there was no statistically significant difference in non-adherence between dasatinib compared to imatinib and nilotinib patients, noting that nilotinib is taken twice daily.

Whilst it is generally accepted that more simple dosing regimens will improve adherence, in the case of Sprycel there is insufficient evidence that its 'one pill, once daily' regimen results in better adherence. The Committee considered that taking the statement subject to complaint 8 out of context could potentially mislead clinicians to think that it related specifically to Sprycel, particularly by the inclusion of "(one pill, once daily)".

The Committee determined by unanimous decision that the statement was in breach of the Section 1.3 of the Code of Conduct.

Complaint 9 – Statement "*Increased treatment restrictions and associated difficulty may affect adherence to TKI therapy*"

As noted in relation to complaint 8, the Hirji et al (2013) study investigated adherence to treatment with TKIs in CML. The statement subject to complaint 9 was an adapted quotation from the paper. The Committee considered that the statement was factual, directly relevant to TKI treatment for CML and could be substantiated.

The Committee determined by unanimous decision that the statement was not in breach of Section 1.2 of the Code.

Complaint 14 related to a statement in promotional material for pharmacists titled "*Pharmacists play a critical role in the management of CML*"

Complaint 14 – Statement "Simple dosing (one pill, once daily) helps to maximize adherence…"

The Committee noted that this statement was identical to the statement subject to complaint 8. However, in this material the statement appeared under the heading "Sprycel offers simple dosing" and dot point "One tablet once daily with no fasting or ECG requirements". This context increased the likelihood that a pharmacist would be misled to think that the statement subject to complaint was a quote from a paper that specifically had investigated adherence to Sprycel, which it did not. The Committee considered that the statement could not be substantiated with respect to adherence to Sprycel.

The Committee determined by unanimous decisions that the statement was in breach of Sections 1.2 and 1.3 of the Code.

Sanction

Having found that three statements subject to complaint were in breach of the Code, the Committee discussed the severity of the breaches. The Committee agreed that the breach in relation to Complaint 6 was a minor to moderate breach of the Code. The statement was misleading and may have an effect on how healthcare professionals prescribe Sprycel. The Committee did not raise concerns about patient safety. The two breaches in relation to Complaints 8 and 14 were minor breaches of the Code.

The Committee agreed unanimously that the promotional materials containing the statements found in breach of the Code should be withdrawn from use. The statements found in breach should not be used again in the same or similar form. Additionally, the Committee imposed a fine of $45,000.

The Committee discussed whether a corrective letter was required. It noted that the promotional material for physicians had been withdrawn from use in October 2014. The Committee determined that no corrective letter should be imposed.

Abuse of the Code

The Committee discussed BMS' allegation that Novartis had abused the Code process, misled the Committee by including matters in its complaint submission that had been resolved in intercompany dialogue and insufficiently explaining which parts of the complaint required the Code Committee's consideration. BMS also alleged that Novartis' insistence on a corrective letter undermined the ability to resolve matters through intercompany dialogue.

The Committee agreed that the intercompany dialogue could have been more constructive.

Novartis could have made it clearer to the Committee which issues had been fully resolved and which not, or only included those issues which remained in dispute. The Committee was also concerned by the lack of detail in Novartis' complaint submission. This submission only very briefly stated the nature of each complaint and relied on the Code Committee referring to intercompany correspondence and intercompany meeting minutes to elaborate on the basis for the complaints. Further, the Committee undertook a detailed examination of each supporting reference, identifying the data, content and issues relevant to each complaint. This analysis and explanation of the detailed rationale for each alleged breach should have been presented by Novartis in its complaint.

In spite of these criticisms of the complaint and intercompany dialogue, the Committee did not consider that the issues rose to the level of a frivolous or vexatious complaint. The Committee determined that on this occasion Novartis should not be asked to respond to the allegation that it was potentially in breach of Section 25 of the Code. However, the Committee cautioned that Novartis should carefully consider the Committee's concerns regarding this complaint.