Medicines Australia Code of Conduct Quarterly Report January – March 2013

Medicines Australia Code of Conduct

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 2013. Complaints finalised during this period were in relation to materials or activities conducted under Edition 16 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/

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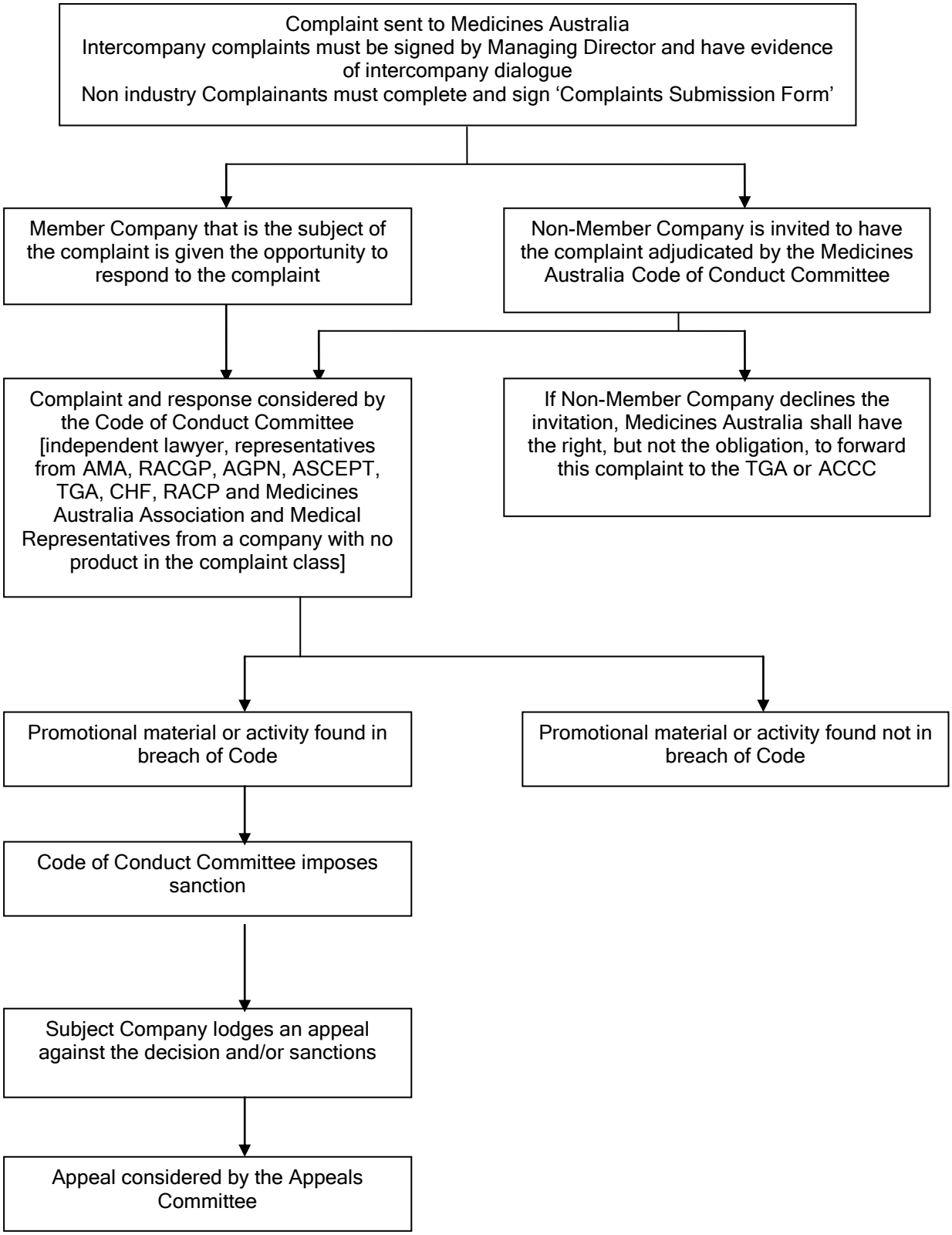
How do I obtain a copy of the Code?

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/)

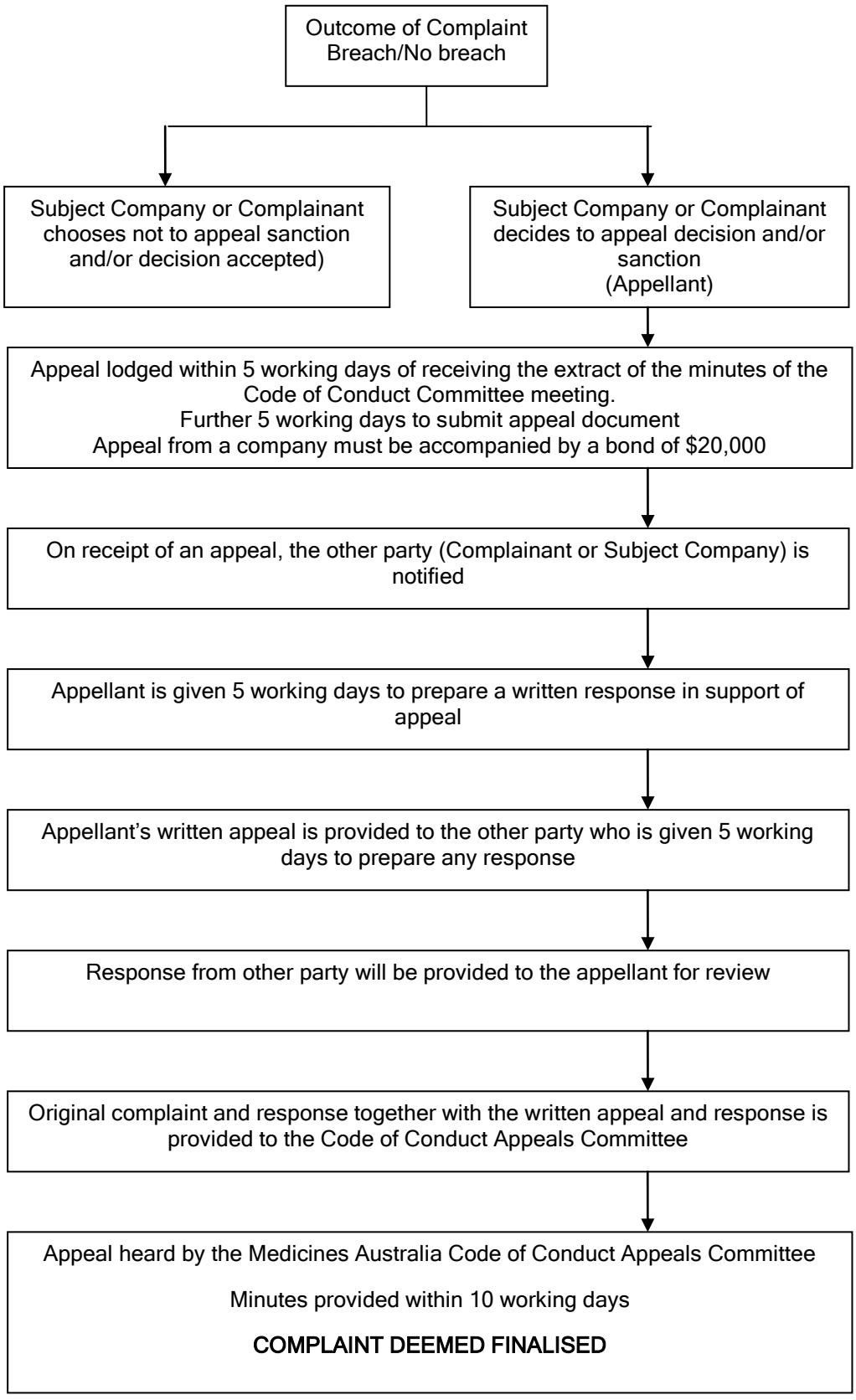
Contents

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 six 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 six 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, AGPN
- 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.

Fine (applicable under Edition 16 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 $300,000

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Cumulative fine for multiple breaches	Maximum $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 $200,000

Table of finalised complaints January – March 2013

No.	Subject Company	Material or Activity	Product	Complainant	Outcomes	Sanction
1089	Merck Sharp and Dohme	Vytorin Promotional Material	Vytorin	AstraZeneca	Breach of Section 1.1	Pay a fine of $125,000
1090	AstraZeneca	Promotional Material	Nil	Healthcare Professional via the TGA	No breach found	n/a

1089 – Vytorin Promotional Materials

Subject Company: Merck Sharp and Dohme (MSD)

Complainant: AstraZeneca

Product: Vytorin

Complaint
AstraZeneca alleged that MSD has been engaged in promotional activities to increase clinician awareness of an unapproved indication for Vytorin with the intent of encouraging off-label use. The two advertisements subject to this complaint refer to the SHARP study, which was conducted in patients with Chronic Kidney Disease. AstraZeneca argued that the claim "Now with patient outcomes data" constituted promotion of Vytorin for the reduction of cardiovascular events, which is not an approved indication for Vytorin.

AstraZeneca noted that the SHARP study is referred to in the clinical trials section of the Product Information for Vytorin, but alleged that the SHARP study has been used in a promotional manner that is inconsistent with the indicated population for the product. AstraZeneca alleged that MSD GP Sales Representatives had been promoting Vytorin for the reduction of cardiovascular events using the SHARP study.

Sections of the Code
The claim and promotional activities were alleged to be in breach of the following Sections of Edition 16 of the Code:

- Section 1.1 Responsibility
- Section 1.3.1 Unapproved products and indications

Response
MSD rejected that it had promoted an off-label indication for Vytorin. MSD contended that sharing the SHARP data with healthcare professionals reinforces their efforts to lower LDL-C in cardiovascular patients. MSD stated that the SHARP study is a high quality study that had been evaluated by the TGA and included in the Vytorin Product Information. MSD further argued that the promotional claims used in the advertisements are fully supported by the Product Information for Vytorin.

Code of Conduct Committee decision
The Committee unanimously determined that the claim "Now with outcomes data" was in breach of Section 1.1 of the Code of Conduct. The Committee determined by majority decision that there had been no breach of Section 1.3.1 of the Code of Conduct.

Sanction
The Committee agreed by unanimous decision that this was a moderate breach of the Code and imposed the following sanctions:

- Cease using the claim *"Now with patient outcomes data"* in promotion of Vytorin
- Pay a fine of $125,000
- Distribute a corrective letter to the healthcare professionals who are subscribers to the *Australian Doctor* and *Medicine Today* journals where the advertisements were published, as well as to all healthcare professionals who had been detailed by an MSD sales representative using the claim found in breach of the Code.

Consideration of the complaint
The Committee noted the complaint from AstraZeneca centred on the use

of data from the "Study of Heart and Renal Protection" by Baigent C et al., published in *The Lancet* in 2011 (the SHARP Study), which is the reference supporting the claim *"Now with patient outcomes data"*. The Committee further noted that a number of issues had been resolved during intercompany dialogue, including the complaint that two specific advertisements were in breach of the Code. However, two issues relating to MSD's promotion using the SHARP study had not been resolved.

The Committee noted that the SHARP Study is extensively referenced in the Clinical Trials section of the Vytorin Product Information. The Committee accepted that the SHARP Study was a well-designed, multi-national, randomised, double-blind trial in more than 9,000 patients, with follow up for at least four years. Trial participants all had advanced chronic kidney disease (CKD) and were randomised to receive ezetimibe 10mg plus simvastatin 20mg daily or simvastatin 20mg alone or placebo. The primary endpoint was major atherosclerotic events, defined as the combination of non-fatal, myocardial infarction, coronary death, non-haemorrhagic stroke or any arterial revascularisation procedure.

The Committee discussed at length whether information contained in the Clinical Trial section of an approved Product Information document can be discussed with healthcare professionals, and whether doing so would be promotional or could be done in a manner which was educational or informational. Further, the Committee discussed whether the proactive communication of such information may then constitute promotion of an unapproved indication.

The Committee agreed that, when used appropriately, data from the Clinical Trials section can be used to provide educational messages to healthcare professionals. However, the fact that information is included in the Product Information does not necessarily mean that its provision to healthcare professionals will not be in breach of the Code, such as where a claim is based on that information and it is not consistent with the approved indications, this could be considered promotion of an unapproved indication. The Committee agreed that companies have the responsibility to update their Product Information documents through application to the TGA to reflect new data and emerging evidence.

The Committee considered that in the two Vytorin advertisements, which had given rise to the dispute between the companies, the claim *"Now with patient outcomes data"* implied that the outcomes data from the SHARP Study were applicable to all patients who met the indications for Vytorin, which is not correct. The outcome data from the SHARP Study is only applicable to the study population - people with chronic kidney disease - and cannot be generalised to all patients with hypercholesterolemia. The Committee noted that hyperlipidemia was not an entry criteria for the SHARP Study, although it was also noted that the baseline mean LDL-C exceeded current best-practice treatment targets for high-risk patients (<2.0mmol/l) The entire study population may therefore not have aligned with the approved indications for Vytorin.

The Committee agreed that although there was a qualifying statement associated with the claim, which stated the outcomes and primary endpoint of

the SHARP Study, this did not limit the outcomes data claim to CKD patients. It was not clear to a reader that the outcomes data was only in the CKD patient group. Although the "Now with outcomes data" claim was not immediately below the reduction in LDL-C claims, it was in the same visual frame and therefore would be linked with the cholesterol lowering claims. The Committee was unanimously of the view that the claim "Now with outcomes data" as used in the advertisements would have amounted to a breach of section 1.1 of the Code because the manner in which the SHARP Study was used in the Vytorin promotional pieces through the claim "Now with outcomes data" was not balanced or fully supported by the Vytorin Product Information.

Against this backdrop, the Committee considered what was the substantive issue before it, which related to the ongoing use of the SHARP Study by MSD and the claim "Now with patient outcomes data".

The Committee noted that AstraZeneca had alleged that MSD was utilising the outcomes data claim in a broader promotional campaign for Vytorin and had submitted selected IMS GP Promotional Monitor extracts to support this. The Committee did not find the IMS Monitor extracts particularly persuasive as evidence of what had been said by MSD representatives. However, the Committee accepted that the SHARP outcomes data claim for Vytorin used in the print advertisement was likely to have been used by medical representatives when detailing GPs and specialists, and noted that the MSD position was that it considered it could make similar claims on an ongoing basis.

The Committee considered that the use of the claim "Now with patient outcomes data" is not in accordance with Section 1.1, as it uses the SHARP Study in a manner that over-steps its proper usage, and generalises and links its outcomes to a broader patient population. The qualification and context of the patient population of the SHARP Study is a necessary part of any statement about its outcomes, and is not achieved by merely foot-noting such aspects. Accordingly, such claim should not be used.

The Committee then discussed at length whether the use of the "Now with outcomes data" claim was in breach of Section 1.3.1 of the Code - unapproved products and indications. Some Committee members considered that use of the "Now with outcomes data" claim in association with the "statin-reduced LDL-C" and "LDL-C reductions through dual inhibition" claims implied that Vytorin was indicated for reducing cardiovascular outcomes. As highlighted by the submissions made by both companies, this complaint raised some issues of significance; first as to what sort of messaging might amount to promotion, and second as to whether if such messaging could be promotional, whether it was in this case. The majority of the Committee did not consider that on the material before it the use of the outcomes data claim was promoting Vytorin for the reduction of cardiovascular or atherosclerotic events, either generally or in the population the subject of the SHARP Study.

The Committee considered the first issue, and noted the tension between the desire (and the need) to communicate information about a product to medical professionals, but where such information might relate to

an unapproved indication, to do so in a manner which could not be regarded as promotional. As revealed in the MSD response, a tension which was not made lesser where the information was included in the Product Information. The submissions made highlighted in the Committee's view that where information is being proactively communicated to healthcare professionals, as opposed to provided in response to requests, that such dialogs provide a promotional context and that companies must therefore be very careful with the relevant messages.

In relation to the second issue, the majority view of the Committee was that the use of the SHARP Study outcomes data as demonstrated in the material before it, was not use in a manner that implied Vytorin was indicated for the patient population the subject of the SHARP Study and accordingly did not constitute off-label promotion of Vytorin. The Committee determined by majority decision that the conduct was not in breach of Section 1.3.1 of the Code.

One Committee member raised a concern regarding the issues that had been resolved during intercompany dialogue and the possibility that the Code requirement for intercompany dialogue could be used as a way to obfuscate a company's responsibility to comply with the Code. The Committee member was concerned that the relevant Vytorin advertisements were in breach of the Code, but the Committee did not have the opportunity to adjudicate on the advertisements in their entirety as many of the breaches had been resolved during the intercompany dialogue process. The Committee member was strongly of the view that if the alleged breaches in their entirety had been considered by the Committee, the breach and sanctions may have been more significant, and it was undesirable that clear breaches of the Code go unsanctioned. The Committee unanimously agreed that the intercompany dialogue provisions are valuable, however it was suggested that Medicines Australia consider refinements to the process during the next review of the Code of Conduct to ensure that the process is not used to avoid penalties imposed by the Code.

Sanction

The Committee reviewed the definitions of severe, moderate and minor breaches of the Code. It agreed by unanimous decision that the complained of claims in respect of Vytorin constituted a moderate breach of the Code of Conduct as the conduct did not have any safety implications for patients, but may have an effect on how the medical profession will prescribe the product, and may continue to do so if not addressed.

The Committee agreed by unanimous decision that MSD must:

- cease using the claim *"Now with outcomes data"* and not use the claim again in the same or similar form.
- pay a fine of $125,000.
- distribute a corrective letter to the healthcare professionals who are subscribers to *The Australian Doctor* and *Medicine Today* journals, where the Vytorin advertisements were published, as well as to all healthcare professionals who had been detailed by an MSD sales representative using the claim found in breach of the Code.

1090 – Clear Out Cholesterol Campaign

Subject Company: AstraZeneca

Complainant: Healthcare professional via the TGA

Product: Nil

Complaint
Dr Peter Horsfall lodged a complaint to the Therapeutic Goods Administration (TGA) regarding activities conducted by AstraZeneca. The TGA had assisted Dr Horsfall in formulating the complaint before referring it to Medicines Australia for adjudication.

Dr Horsfall alleged that AstraZeneca had conducted an inappropriate disease education activity that had consequences in terms of influencing prescribing patterns for statins in the Australian community. The campaign included a television advertisement with the message "clear out cholesterol – go back to your doctor". The advertisement featured a former Special Forces diver.

Sections of the Code
The television advertisement was alleged to be in breach of the following Sections of Edition 16 of the Code:

- Section 12.7 Disease education activities in any media
  - Section 12.7.2
  - Section 12.7.3
  - Section 12.7.4
  - Section 12.7.6

Response
AstraZeneca disagreed that the Clear Out Cholesterol campaign breached the Code of Conduct. AstraZeneca contended that the campaign was designed to build disease awareness in a target group of high cardiovascular risk patients who have ceased taking their prescribed cholesterol-lowering therapy. The purpose of the campaign was to address a quality use of medicines issue in patients already prescribed a lipid-lowering therapy by a doctor.

AstraZeneca argued that the campaign was in line with the Australian guidelines for primary and secondary prevention of cardiovascular disease, and the health messages provided by health consumer organisations such as the National Heart Foundation and the National Stroke Foundation of Australia.

Code of Conduct Committee decision
The Committee agreed unanimously that Section 12.7.2 did not apply to this complaint and therefore did not make a ruling on this Section. The Committee agreed by majority decision that there was no breach of Sections 12.7.3, 12.7.4 or 12.7.6.

Sanction
As no breach was found, no sanction was imposed by the Committee.

Consideration of the complaint
The Chairman advised the Committee that the complaint was initially made to the Therapeutic Goods Administration (TGA), and was forwarded to Medicines Australia following consultation with the healthcare professional complainant. The Committee noted that in its communication with the complainant the TGA had identified sections of the Code of Conduct that had potentially been breached.

The Committee discussed the media and regulatory environment at the time the campaign was initiated. The Food

and Drug Administration (FDA) in the United States of America had issued a safety communication relating to all statins. This communication received extensive coverage in Australian media, prompting an escalation in adverse event reporting related to statins. The Committee acknowledged that AZ and other companies producing products in the same class had contacted healthcare professionals regarding this safety communication. The Committee also noted that several key stakeholders had released communications urging patients to continue statin therapy unless otherwise advised by their healthcare professional.

The Committee discussed the content of the FDA safety communication and noted that it advised a potential worsening of diabetes, and cognitive issues. The FDA communication also noted that the cognitive changes associated with statin use were not common and did not lead to a clinically significant cognitive decline.

The Committee accepted that statin use in Australia is high. The Committee also acknowledged that coverage in the Australian media of the FDA communication was intense, and was followed by a marked drop-off in statin use. The Committee agreed that the general public should be made aware of the safety concerns.

The Committee noted that the AstraZeneca 'Clear Out Cholesterol' campaign did not mention any specific product or therapeutic class, but referred to "cholesterol-lowering medication". The Committee agreed that the key message of the campaign was for patients who had been prescribed a cholesterol-lowering medication, but had ceased taking it, to consult their healthcare professional.

It was noted that at the top of the patient questionnaire it was stated "If you stopped ...".

The Committee considered the imagery used in the campaign. The Committee noted that the campaign used the consistent image of a scuba diver, identified as David Apps a former Australian and British Special Forces officer. One Committee member was of the opinion that the imagery was potentially misleading as it could lead patients to believe that if they took their cholesterol-lowering medicine, in spite of having a high risk of heart attack or stroke, they could be qualified or re-certified to scuba dive. The Committee member noted that cardiovascular risk could exclude a person from achieving that qualification. Further, the Committee member felt that the materials were alarmist and sensationalist.

The Committee agreed that the title of the campaign – 'clear out cholesterol', and specifically the use of this wording in the associated website URL, potentially could be misleading. The Committee agreed that the use of "clear out" could suggest that treatment will reduce or 'clear out' plaque build-up in arteries, which is not the case. Cholesterol-lowering treatments have been shown to stabilise plaque but not to reduce or clear it. The Committee noted that the campaign materials referred to exercise and diet in addition to use of medication. The Committee agreed by majority that overall the messages and information contained in the materials and television advertisement were sufficiently balanced.

The Committee noted that the call to action in the campaign was directing patients who had ceased taking their cholesterol-lowering medication to

return to their healthcare professional. The patient group targeted by the campaign had already been diagnosed by their healthcare professional as being at high enough risk to require cholesterol-lowering therapy.

The Committee discussed the method chosen by AstraZeneca to target this group. Some Committee members were concerned that by conducting a wide-ranging campaign, AstraZeneca was potentially encouraging members of the general public who were not taking a cholesterol-lowering medicine to see their healthcare professional and ask for a prescription. These Committee members felt that a campaign initiated through healthcare professionals would have been preferred. However, the Committee agreed that this would be a more difficult strategy to deliver as the target group are unlikely to present to their healthcare professional.

The Committee agreed that this type of communication does not necessarily fall under the Code as a disease education campaign. The Code refers specifically to communication of educational messages that relate to a disease, and that such education activities must encompass all aspects of the disease. The AstraZeneca communication campaign addresses a specific target audience within a disease state, rather than a disease state as a whole. The Committee agreed that whilst some people may be misled in some way by the campaign, they are referred back to a healthcare professional who then makes the prescribing decision.

In discussing whether any breach had occurred, the Committee referred to the sections of the Code. The Committee noted that section 12.7.2 of Edition 16 of the Code states *"a disease education activity may make reference to the availability of different treatment options… but this should not be of such a nature than individual would be encouraged to seek a prescription for a prescription only product"*. The Committee agreed that in the context of the 'Clear Out Cholesterol' campaign, Section 12.7.2 did not apply as the campaign was not about a disease state, but targeting a specific patient population who had been prescribed a class of medicine and had stopped taking it. Therefore the Committee agreed unanimously that Section 12.7.2 was not appropriately applicable to the campaign subject to complaint.

Section 12.7.3 states "*The emphasis of the disease education activity should be on the condition and its recognition rather than on the treatment options*. *The appropriate treatment for an individual patient is for the healthcare professional to decide in consultation with the patient*." Some Committee members considered that, similarly to Section 12.7.2, this section did not apply to the activity subject to complaint. However, other members noted that the campaign materials stated that "there are different cholesterol-lowering medications available" and directed patients to talk to their doctor. Therefore, the Committee determined by majority decision that there was no breach of Section 12.7.3.

The Committee discussed Section 12.7.4, with particular reference to the requirement that a disease awareness activity must not be alarmist. As previously noted, one Committee member was of the opinion that the campaign was alarmist. However, other Committee members accepted that there is some need for dramatisation in this sort of

communication in order to convince patients to respond to the call to action. It was noted that the consequences of high cholesterol resulting in cardiovascular mortality and stroke are significant public health issues. The Committee determined by majority decision that there was no breach of Section 12.7.4.

In considering Section 12.7.6, one Committee member considered that it was not sufficiently clear to a member of the general public that the diver passing through a narrow passage and pushing rocks out of the way was a visual analogy, and therefore was misleading as to the effect of cholesterol-lowering medicines. The member also considered the advertisement was misleading with regard to suggesting that people at risk of heart attack or stroke could go scuba diving if they were taking a cholesterol-lowering medication. The Committee noted that the "clear out cholesterol" message and tagline and the visual analogy of the diver could potentially be misleading and reiterated the recommendation that these be reviewed. However, a majority of the Committee agreed that on balance the television advertisement and other materials conveyed the message to return to see your healthcare professional if you have stopped taking a prescribed cholesterol-lowering medication. The Committee agreed by majority decision that the advertisement and materials did not breach section 12.7.6.

The Committee noted that the Sections relevant to the complaint had been identified by the TGA in its communication with the complainant. One Committee member expressed concern that the Committee was not provided with the complainant's original complaint, only the TGA's interpretation of the issues and relevant Sections of the Code and an email from the complainant in response to the TGA. The Committee considered that this type of campaign might have been considered under other sections of the Code. The Committee noted that the use of the Independent Facilitator as provided by Medicines Australia might have resulted in a differently formulated complaint encompassing other Code provisions.

Sanction
As no breach was found, no sanctions were imposed by the Committee.