Medicines Australia Code of Conduct Quarterly Report October - December 2016

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 18 (Effective 16 May 2015).

This report covers all complaints finalised between July and September 2016. Complaints finalised during this period were in relation to materials or activities conducted under Edition 18 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

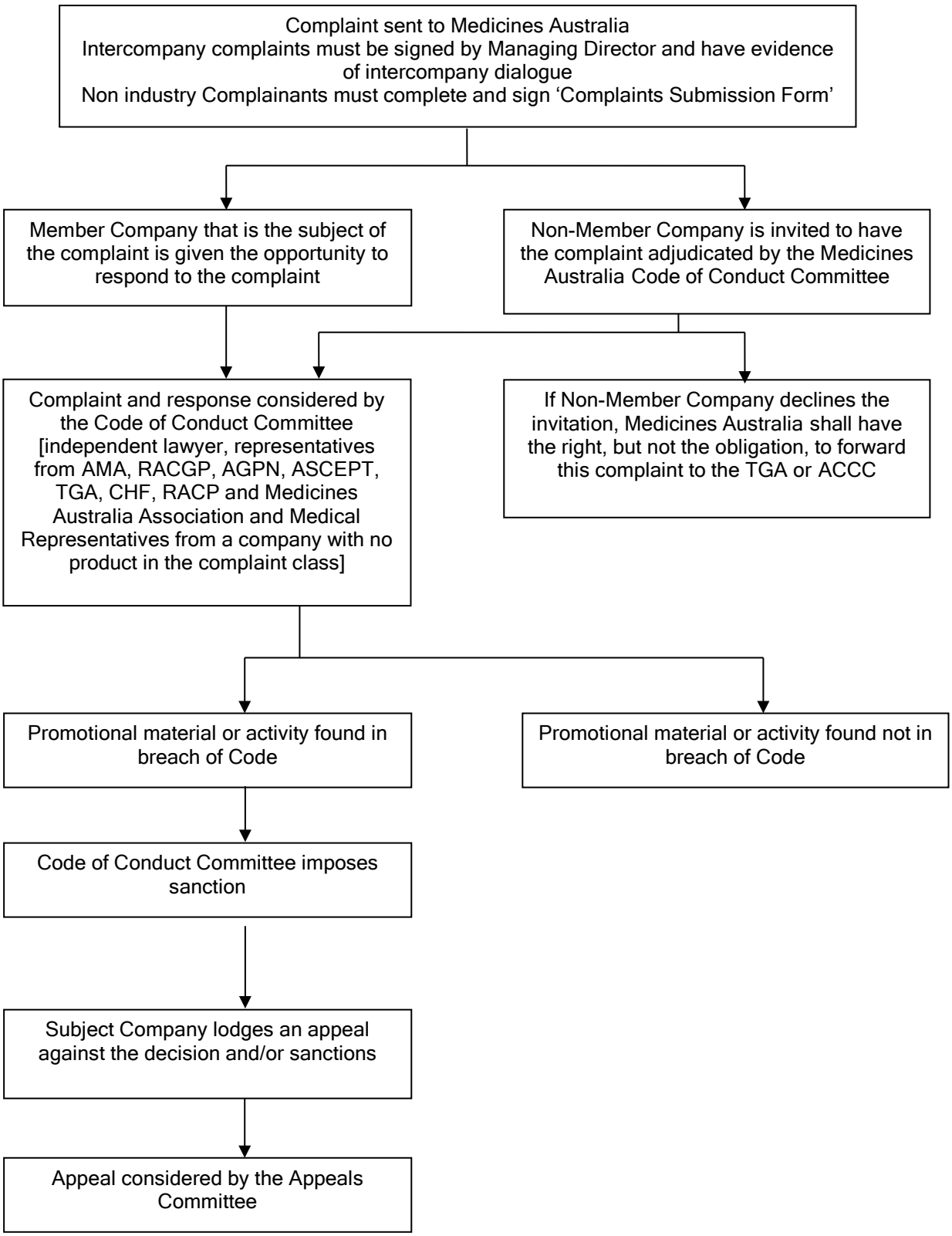
How do I obtain a copy of the Code?

Copies of Edition 18 of the Code (effective from 16 May 2015) are available from Medicines Australia. An order form is available from https://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/)

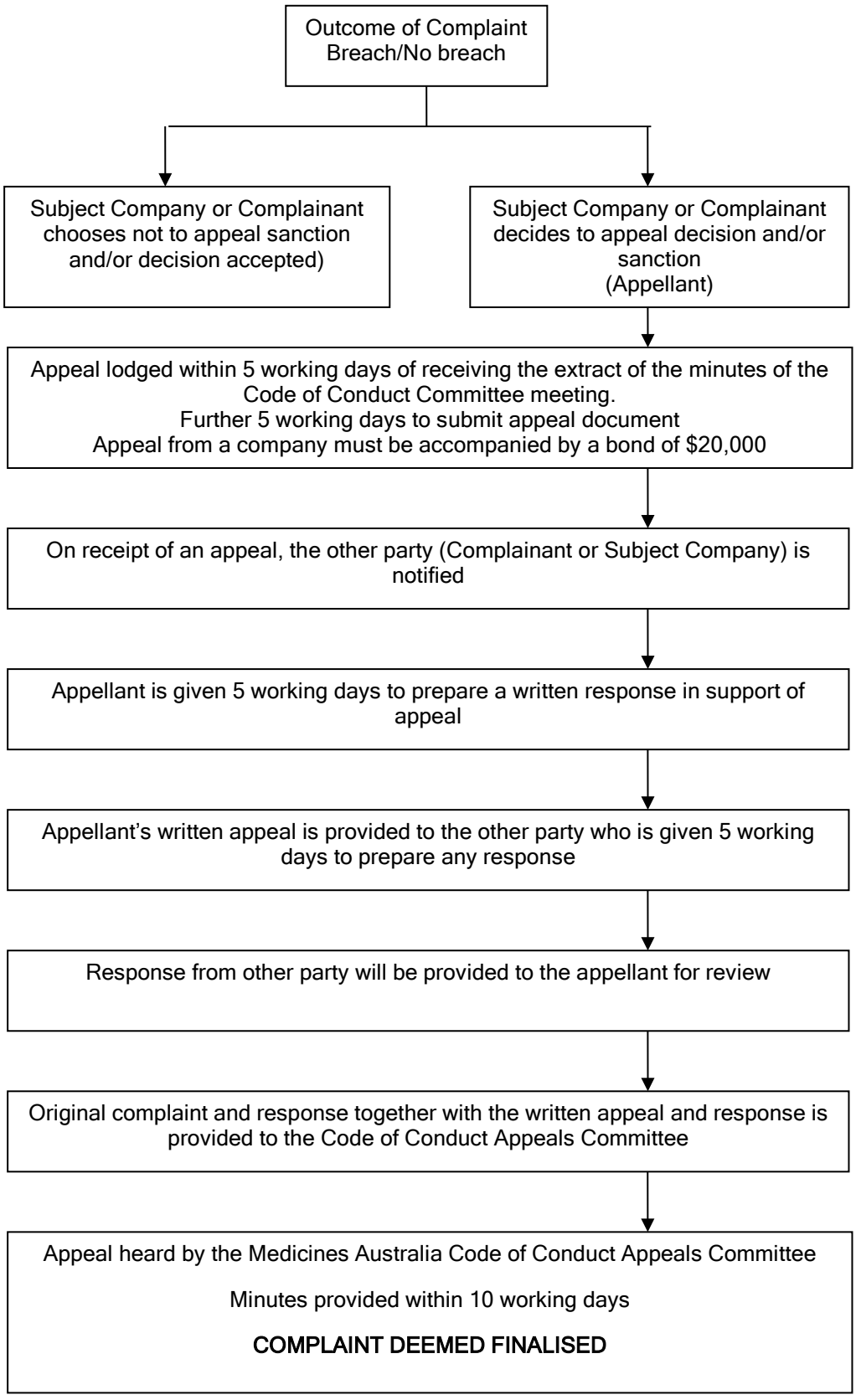
Contents

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 https://medicinesaustralia.com.au/code-of-conduct/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 October – December 2016

No.	Subject Company	Material or Activity	Product	Complainant	Outcomes	Sanction
1138	Sanofi Genzyme	Advertisements	Aubagio and Lemtrada	Biogen Australia	Breach of Sections 1.1, 1,3 and 1.6	Pay a fine of $50,000

1138 – Aubagio and Lemtrada Advertisements

Subject Company: Genzyme Australasia Pty Ltd

Complainant: Biogen Australia Pty Ltd

Product: Aubagio and Lemtrada

Complaint
Biogen alleged that five claims – two in relation to Aubagio and three in relation to Lemtrada – were in breach of the Code. The claims are "Quieting MS" and "Quietly" for Aubagio and "Transformational Therapy", "Transformational dosing" and "Transformational durability" for Lemtrada. The claims appeared either in a product tagline and/or qualifying statements for the taglines in an advertisement for Aubagio in the conference handbook and on a trade display for Aubagio and Lemtrada at the ANZAN meeting in May 2016.

Biogen alleged that the claims were not balanced, accurate or correct; not consistent with the approved Product Information; and are misleading. In addition, in relation to the claims for Lemtrada that include the word "transformational", Biogen alleged that these claims were unqualified superlatives and hanging comparatives which were imprecise, unbalanced and unable to be substantiated.

Sections of the Code
The claims were alleged to be in breach of the following Sections of Edition 18 of the Code:

- 1.1 Responsibility
- 1.3 False or Misleading Claims
- 1.6 Unqualified Superlatives
- 1.8 Comparative Statements

Response
Sanofi Genzyme denied that the claims for Aubagio and Lemtrada were in breach of the Code of Conduct. It argued that the claims were balanced, had been appropriately qualified and were able to be substantiated. In its response, Sanofi Genzyme rejected Biogen's rationale for its complaints. Sanofi Genzyme argued that Biogen had treated individual words within the claims as separate claims and had selectively interpreted their meaning in terms of their compliance with the Code.

Sanofi Genzyme responded that the claims and associated qualifying statements were consistent with the Code requirements and demonstrated balance with respect to efficacy and safety, were fair and accurate, were not misleading by error or omission, and were referenced to peer-reviewed international high impact journals.

Sanofi Genzyme further argued that the claims contained words used commonly in a medical context and, contrary to Biogen's allegations, that these words can be clearly defined, substantiated and supported by the medical literature. Nevertheless, without admission of breaching the Code and in the interest of resolving Biogen's complaints, Sanofi Genzyme had made amendments to future promotional materials containing these claims to strengthen the qualifying statements and include additional references.

Code of Conduct Committee decision
The Committee reviewed the complaint and found as follows:

Complaint 1 – "Quieting MS"
1.1 – Majority No Breach
1.3 – Majority No Breach

Complaint 2 – "Quietly"
1.1 – Unanimous Breach
1.3 – Unanimous Breach

Complaint 3 – "Transformational Therapy"
1.1 – Unanimous Breach
1.3 – Unanimous Breach
1.6 – Unanimous Breach

Complaint 4 – "Transformational Dosing"
1.1 – Majority No Breach
1.3 – Majority No Breach
1.8 – Majority No Breach

Complaint 5 – "Transformational Durability"
1.1 – Majority Breach
1.3 – Majority Breach
1.8 – Majority No Breach

Sanction
As several breaches had been found, the Committee determined that the claims found in breach must be withdrawn from use and must not be used again in the same or similar form in any future materials. The Committee also imposed a fine of $50,000.

Consideration of the complaint
The Committee noted that the complaint related to claims for two products – "Quieting MS *Quietly*" for Aubagio and three claims for

Lemtrada that used the word "Transformational". The Committee also noted that it was a matter of dispute between the companies as to whether the claim "Quieting MS *Quietly*" was one claim or two. The words "Quieting MS" had appeared in a bold, non-italic font and "*Quietly*" had appeared in an italic, regular font which visually suggested the separation of "*Quietly*" from "Quieting MS". The Committee further noted that during inter-company dialogue Sanofi Genzyme had stated that the claim "Quieting MS" related to efficacy data for Aubagio and "Quietly" referred to safety and tolerability data. The Committee determined to consider the complaint as set out in the submission from Biogen, considering "Quieting MS" and "*Quietly*" separately.

Complaint 1: "Quieting MS"

The majority of the Committee members were of the opinion that the term "quieting" was relatively well understood in the medical community in relation to non-curable diseases where treatments can dampen or reduce the symptoms of a disease. It was noted that Aubagio may only be prescribed by specialist neurologists. The majority of the Committee members agreed that it would be unlikely for a healthcare professional to interpret "quieting" to mean that Multiple Sclerosis (MS) would be cured by Aubagio; only that the symptoms of the disease may be reduced. These Committee members considered that the claim was not misleading and could be adequately substantiated as it is effective in reducing the symptoms of MS.

A minority of the Committee, however, were concerned that "quieting" was not something that could be quantified or measured in a medical or clinical sense. Further, some of these Committee members considered that "Quieting MS Quietly" should be considered as a single claim as it was difficult to interpret the individual elements except in their overall context. The Committee noted that there was a qualifying statement below the claim. It referred to "a significant and consistent reduction in multiple measures of disease activity…" and "its most common adverse events were transient and rarely required treatment discontinuation". A minority of Committee members considered that this qualification was quite general and did not specify which measures of disease activity may be reduced or which side effects were transient and not a significant problem for patients and therefore did not adequately explain or justify the claim. These Committee members considered that that the claim "Quieting MS Quietly" may be interpreted as to mean the silencing or cure of symptoms associated with MS, which cannot be substantiated.

The Committee agreed by majority decision that the claim "Quieting MS" was not in breach of Sections 1.1 or 1.3 of the Code.

Complaint 2: "Quietly"

The Committee discussed the claim "Quietly" both separately and in association with the image of a smiling woman holding her finger to her mouth making a "shhhh" motion.

The Committee noted that the claim was referenced to the Approved Product Information and two published studies that had included safety and tolerability data. The Committee noted that there were potentially serious side effects to Aubagio which were common or very common, including elevated liver enzymes. The Committee considered that by simply referring to the most common adverse events in the qualifying statement, the claim does not communicate sufficient information about the potentially serious adverse effects, some of which require ongoing monitoring. The Committee considered that the claim downplays the potentially serious side effects of the product. The Committee also considered that the term "quietly" did not have a clear meaning or interpretation from a medical or clinical sense. The Committee concluded that the claim, therefore, was not balanced and was misleading.

The Committee discussed the image associated with the claim. The Committee agreed unanimously that the imagery further supported its conclusion that the claim was not balanced and was misleading. The imagery reinforced the impression that side effects were not of concern as they had been "silenced" or didn't create any "noise". The imagery contributed to the lack of balance and misleading nature of the claim.

The Committee agreed by unanimous decision that the claim "Quietly" was in breach of Sections 1.1 and 1.3 of the Code of Conduct.

In considering the claims the Committee noted that Sanofi Genzyme had provided anonymous comments from members of its Advisory Boards in relation to both the Lemtrada and Aubagio claims. This was a select group of healthcare professionals who worked closely with the company rather than randomly selected, representative sample of doctors or

neurologists. The Committee unanimously agreed that these comments did not assist it in considering whether the claims subject to complaint were compliant with the Code.

Lemtrada claims

The Committee decided to review the claims in a different order to that presented in the complaint. The Committee reviewed the claims for "Transformational dosing" and "Transformational durability" before considering the overarching claim for "Transformational therapy" because the dosing and durability claims were presented as qualifying statements or claims that supported "Transformational therapy".

Complaint 4: "Transformational dosing"

The Committee acknowledged that the once yearly dosing regimen for Lemtrada is a significant change from other MS treatments that must be taken daily. Specifically, when compared to competitor products, which require more frequent doses, it is a significant advance. A majority of the Committee considered that the claim was able to be supported by the Product Information, was sufficiently explained by the description of the dosing regimen that followed the claim and would not mislead healthcare professionals.

A minority of the Committee members, however, were of the opinion that the use of the superlative "transformational" in this claim overstated the benefit and made too strong a claim that could not be substantiated. No evidence had been provided to substantiate that the dosing schedule was "transformational" for patients. Further, the treatment requires a daily infusion for 5 consecutive days in the first year and 3 consecutive days 12 months later, which would need to be administered in a hospital or day clinic. Although Lemtrada is currently the only once-yearly therapy for MS, there are other medicines that are administered once a year for other incurable diseases. These Committee members considered that the convenience of once yearly dosing may be beneficial, but a claim for "transformational dosing" requires more than simply a less frequent dosing regimen.

The Committee agreed by majority decision that the claim "Transformational dosing" was not in breach of Sections 1.1 or 1.3 of the Code.

The Committee discussed whether the claim was a hanging comparative. The Committee noted that the claim "transformational dosing" is explained by the description of the dosing schedule that immediately followed the claim. A majority of the Committee considered that the intended meaning of the claim was sufficiently clear and accepted that no other MS treatment was dosed in the same manner. In a majority decision the Committee concluded that the claims was not in breach of Section 1.8 of the Code.

Complaint 5: "Transformational Durability"

The Committee discussed the claim "transformational durability" and noted that while the referenced data were statistically significant, supporting five year durability of Lemtrada's effects for at least sixty percent of patients, they were not of adequate quality to support the claim. Specifically, the Committee noted that the referenced studies were two conference posters that referred to two studies, but these were not peer-reviewed, published papers.

Further, the Committee considered that whilst a statistically significant proportion of patients in these studies had not required further treatment with Lemtrada at 5 years after their initial treatment, there was still a reasonable proportion of patients, up to forty percent of patients, who did require further treatments. The supporting references refer to the "durability" of efficacy and "durable" reduction of MRI activity over 5 years, but the Committee did not agree that this warranted a claim of "transformational durability". The "transformational" nature of the durable efficacy had not been adequately substantiated and therefore the claim was not balanced and was misleading.

A minority of the Committee members considered that the claim could be substantiated by the referenced studies and that the durability of effect was a significant change.

The Committee agreed by majority decision that the claim "transformational durability" was in breach of Sections 1.1 and 1.3 of the Code because it was misleading, could not be adequately substantiated and was not accurate or balanced.

The Committee discussed whether the claim "transformational durability" could be considered comparative, and agreed that the claim was referring to the durability of effectiveness extending to five years and would not be construed by a reader as being a

comparison to other products generally or to a specific product used to treat MS. A minority of the Committee that disagreed with this assessment and considered that the claim was a hanging comparative that claimed general superiority without specifying the basis for the comparison.

The Committee agreed by majority decision that the claim was not in breach of Section 1.8 of the Code.

Complaint 3: "Transformational Therapy"
Having considered the "transformational dosing" and "transformational durability" claims, the Committee then considered the "Transformational therapy" claim.

The Committee noted that the word "unique" had been used in the studies used to substantiate the claims and the word "revolutionary" had reportedly been used by the Chief Executive of NICE in the UK. The Committee however, were of the opinion that the use of "transformational therapy" in relation to the product was overstating the advance and was misleading. Having found that the claim "transformational durability", which was one of the claims qualifying the overarching claim for "transformational therapy", could not be adequately substantiated and was misleading, the Committee considered that "transformational therapy" was also misleading, could not be adequately substantiated and was not balanced. Further, the Committee considered that a significant claim that a therapy is "transformational" requires more than an improved dosing schedule and durable efficacy. Whilst the claim "transformational dosing" had not been found in breach of the Code and the Committee had agreed that an annual dose given in two consecutive years was a significant change in the treatment of MS, this was insufficient to support a claim that the therapy itself was "transformational".

The Committee also considered the claim in the context of the image of a man in the surf carrying a body/surf board. The Committee understood that not all MS patients would experience sufficient benefit from Lemtrada that would enable them to go surfing or participate in strenuous activities. The Committee considered that the imagery reinforced the "transformational" claims to give the impression that the therapy may transform MS patients' lives, which could not be adequately substantiated. The Committee acknowledged that Lemtrada may provide an improvement in managing the symptoms of MS for some patients and that the yearly dosing may be convenient for some patients, but this was not sufficient to claim "transformational therapy".

In relation to whether "transformational therapy" is an unqualified superlative, as the Committee had determined that the claim for the medicine being "transformational" could not be adequately substantiated with regard to a clinical outcome, the Committee unanimously agreed that the claim was an unqualified superlative and was in breach of Section 1.6 of the Code

The Committee agreed by unanimous decisions that the claim "Transformational therapy" was in breach of Sections 1.1, 1.3 and 1.6 of the Code.

Sanction
The Committee discussed the severity of the breaches and determined by unanimous decision that they constituted a moderate breach of the Code of Conduct.

The Committee determined unanimously that the claims found in breach of the Code must not be used again in the same or similar format in any future materials. Any materials containing the claims found in breach of the Code must be withdrawn from further use or distribution. The Committee also agreed by majority decision that Sanofi Genzyme should pay a fine of $50,000.