CASE AUTH/1950/1/07

FORMER EMPLOYEE v ASTRAZENECA

Promotion of Casodex 150

A former employee of AstraZeneca complained about misleading claims for Casodex 150 (bicalutamide), call rates for representatives and advice on staying within the Code.

The complainant felt that he was being asked to break the law by delivering misleading promotional claims for Casodex and that AstraZeneca was bringing the industry into disrepute which might be a breach of Clause 2 of the Code. Only when the complainant raised his concerns via a formal grievance procedure did AstraZeneca take action in February 2006. AstraZeneca changed the claim for Casodex from 'equivalent to castration' to 'no different to castration in overall survival'. Casodex 150 was, however, up to 36% worse than castration for survival.

Casodex 150mg was indicated for the management of patients with locally advanced, non-metastatic prostate cancer for whom surgical castration or other medical intervention was not considered appropriate or acceptable, ie a second line treatment after a leutinizing hormone releasing hormone (LHRH) analogue; surgical castration was not widely used.

The point about an 'equivalent efficacy to castration' campaign was that if the medicines were equally effective then a decision could be made on first line treatment based on the preferred side effect profile of the treatment. This was a much bigger group of patients and was outside the marketing authorization. AstraZeneca did not consider that patient safety was compromised by the use of the equivalence campaign.

In Iversen *et al* (2000) at a median follow up of 6.3 years, mortality was 56%. The median survival was 63.5 months in the Casodex 150 group and 69.9 months in the castration group. If patients were not informed that Casodex 150 could be up to 36% worse for survival than castration their safety was compromised.

If AstraZeneca was allowed to use the revised claim 'No different to castration in overall survival' it would continue a first line campaign and public health would not be safe guarded.

The Panel considered that the claim 'Equivalent efficacy to castration' was misleading given the statement in the summary of product characteristics (SPC) that 'equivalence of the two treatments [Casodex 150 and castration] could not be concluded statistically'. Thus the Panel ruled a breach of the Code as acknowledged by AstraZeneca.

The Panel noted the complainant's concerns about the revised claim 'No different to castration in overall survival' based on Iversen *et al*. The results from this study were reported in the Casodex 150mg SPC and supported the statement 'At 56% mortality and a mean follow-up of 6.3 years, there was no significant difference between Casodex and castration in survival (hazard ratio = 1.05 [CI 0.81 to 1.36]); however equivalence of the two treatments could not be concluded statistically'. The complainant was concerned that the claim 'No different to castration in overall survival' failed to alert prescribers that patients' survival might be compromised by up to 36%. Equally, however, survival might be improved by up to 19%. The Panel considered that the target audience would appreciate that there were always confidence intervals in statistics. Readers would understand the claim in question to mean that, overall, no meaningful or clinically significant difference in survival had been reported between Casodex 150 and castration which was so. No breach of the Code was ruled. This ruling was upheld on appeal by the complainant.

With regard to call rates, the complainant stated that if a carrot in the form of the AZpiration scheme failed to induce representatives into breaching the Code (Case AUTH/1899/10/06) then a stick in the form of short-term performance measures was threatened.

This was viewed as the first step in a disciplinary process and was a threat which was used, formally and informally, to bully and harass representatives into achieving the frequency of 12 face to face calls. This amounted to harassment to breach the Code.

The complainant noted that the findings in Case AUTH/1899/10/06 regarding frequency of calling referred to this campaign in terms of incentivisation to break the Code. The complainant requested a response concerning the fact that representatives could be put on short-term performance procedures for failing to be incentivised to break the Code in terms of frequency of visits.

The Panel noted that in the previous case, Case AUTH/1899/10/06, it had been ruled that representatives' call rates and incentivisation were in breach of the Code as alleged. In the present case, Case AUTH/1950/1/07, the complainant had asked the Panel to consider the specific allegation that placing representatives on short-term objectives for failing 'to be incentivised to break the Code' in terms of frequency targets was in breach of the Code. This had not been addressed as a discrete issue previously.

The Panel noted the points raised by the complainant and AstraZeneca's comments about the number of representatives on short-term objectives and reasons

given by those leavers who attended exit interviews. In 2004 two members of the entire oncology sales force of 80-85 were on short-term objectives. AstraZeneca's submission that less than 70% of the oncology team had left during 2004/05 was also noted. Taking all the evidence into account the Panel decided that on the balance of probabilities there was insufficient evidence to show a breach of the Code as alleged. The Panel therefore ruled no breach of the Code. This ruling was not appealed.

The complainant stated that during 2004 and the first 6 months of 2005 the oncology team were under extreme pressure to achieve metrics which included (in 2004) 12 face to face calls a year on the main group of target customers. The complainant and others tried to raise their concerns about achieving these metrics and staying within the Code via the union representative.

Concern was raised at all levels of management including hospital area sales manager, national sales manager, human resources, UK director level, the whistleblowing line and the chief executive. Most of this was documented via the union representative; no advice was received.

The complainant provided farewell emails and two witness reports from hospital area managers which might give insight into this fear culture which prevented concerns being raised. ABPI complaints forced a change of culture and the medical director had to acknowledge this with an email in November 2005 entitled 'Embracing our People'. The complainant alleged that AstraZeneca ignored the concerns about the Code effectively demeaning the Code and this brought discredit to the pharmaceutical industry in breach of Clause 2.

The Panel noted that in the previous cases breaches of the Code had been ruled. The Panel noted that the allegation now to be considered was wider than that in Case AUTH/1714/5/05 which related specifically to references to the Code in the campaign notes. The Panel considered that the briefing material had been inadequate in relation to the general allegation now before it. The Panel therefore ruled a breach of the Code as acknowledged by AstraZeneca.

The Panel was concerned that AstraZeneca's promotional material was inconsistent with information in the Casodex SPC. It noted that the complaint about call rates and call frequency had been dealt with in previous cases but the complainant had now alleged that those rulings together with those in the above amounted to a breach of Clause 2 of the Code.

Taking all the circumstances into account and bearing in mind its rulings in the previous case, Case AUTH/1899/10/06, the Panel did not accept that the cumulative effect of the Panel's rulings in the above and the previous case were, on balance, sufficient to warrant a breach of Clause 2 which was a sign of particular censure and reserved for such use. The Panel ruled no breach of Clause 2 and this ruling was upheld on appeal by the complainant.

The Medicines and Healthcare products Regulatory Agency (MHRA) forwarded part of a complaint which it had received from an ex-employee of AstraZeneca UK Limited. The complaint, Case AUTH/1899/10/06, concerned, *inter alia*, representative call frequency targets in relation to the promotion of Casodex 150 (bicalutamide). An AstraZeneca oncology sales and marketing booklet showing activity targets was provided together with a company email explaining the call frequency targets for employees. The Panel ruled breaches of the Code (Clauses 9.1, 15.4 and 15.9) and no breach of Clause 2. The complainant appealed the no breach ruling and in the appeal referred to matters in his complaint to the MHRA that had not been referred to the Authority and thus not considered by the Panel. Thus the additional matters in the appeal could not be considered as part of the appeal. The complainant was so informed and subsequently decided to withdrew the appeal and sent a new complaint (Case AUTH/1950/1/07).

1 Misleading claims

COMPLAINT

The complainant alleged that from January 2004 to February 2006 AstraZeneca used a misleading claim when promoting Casodex 150 to urologists, oncologists and their teams (eg detail aid ref 05/15791). AstraZeneca claimed equivalent efficacy to castration whereas the summary of product characteristics (SPC) stated that 'equivalence of the two treatments could not be concluded statistically'.

This situation probably arose as a 'Dear Doctor' letter had been sent to advise of the change to the licence in 2003 when treatment of localised prostate cancer was removed.

Using a study (which failed to demonstrate equivalence between bicalutamide monotherapy and castration with respect to death, progression and treatment failure by rejecting the hypothesis that bicalutamide was at least 25% worse than castration) to say that Casodex 150mg demonstrated equivalent efficacy to castration was misleading. Statistical significance between treatment groups was not demonstrated (Iversen *et al* 2000).

This study was based on the results of combining trials 306 and 307. The Food and Drug Administration (FDA) in the US decided that these trials could not be combined because of positive results in one and negative results in the other. The negative trial (307) was more than twice the size. When put together there was a wash. A non-approvable letter was issued. Did the UK have different statistical methods?

The complainant felt that he was being asked to break the law by delivering misleading promotional claims and that AstraZeneca was bringing the industry into disrepute which might be a breach of Clause 2 of the Code.

Zoladex was £84.14 per 28 days and Casodex 150 was £240 per 28 days. The equivalent efficacy claim from January 2004 to February 2006 could have resulted in patients being inappropriately prescribed Casodex 150.

The study became a basis of Jenkins *et al* (2005).

The complainant noted UK law and MHRA guidance. The complainant alleged a breach of Clause 7.2 of the Code.

The complainant stated that AstraZeneca said no to the following: In the interests of Winning the Right Way do you intend to send out a 'Dear Doctor' letter to counteract over two years of misleading promotional claims?

Only when the complainant raised his concerns via a formal grievance procedure did AstraZeneca take action in February 2006. AstraZeneca changed the efficacy key message 'Equivalent to castration' to 'No different to castration in overall survival'. Although Casodex 150 was up to 36% worse than castration for survival.

Casodex 150mg was indicated for the management of patients with locally advanced, non-metastatic prostate cancer for whom surgical castration or other medical intervention was not considered appropriate or acceptable. Effectively this relegated Casodex 150 to second line treatment after a leutinizing hormone releasing hormone (LHRH) analogue; surgical castration was not widely used.

The point about an 'Equivalent efficacy to castration' campaign was that if the medicines were equally effective then a decision could be made on first line treatment based on the preferred side effect profile of the treatment. This was a much bigger group of patients and was outside the marketing authorization.

AstraZeneca did not consider that patient safety was compromised by the use of the equivalence campaign.

In Iversen *et al*, quoted by AstraZeneca, at a median follow up of 6.3 years, mortality was 56%. The median survival was 63.5 months in the Casodex 150 group and 69.9 months in the castration group. If patients were not informed that Casodex 150 could be up to 36% worse for survival than castration their safety was compromised.

The complainant stated that if AstraZeneca was allowed to use the revised claim 'No different to castration in overall survival' it would continue a first line campaign and the MHRA and ABPI would not be safeguarding public health.

The equivalence campaign (with the might of AstraZeneca's resources behind it) ran for over two years and many patients were inappropriately on Casodex 150. It should now be made clear to urologists, oncologists and their teams that their patients' survival could be compromised by up to 36%. If patients were not informed that Casodex 150 could be worse for survival than castration their safety was compromised.

RESPONSE

AstraZeneca submitted that the matter had been dealt with appropriately in correspondence with the MHRA.

It was first raised internally with AstraZeneca by the complainant with the medical director at the end of 2005 and formed the basis of his grievance. At a grievance hearing in January 2006 the complainant was able to expand on the points raised and to provide evidence to support his claims. This specific point (the promotional claim that survival with Casodex was equivalent to that with castration) of the formal grievance procedure was upheld and the complainant was thanked for bringing it to AstraZeneca's attention. On 17 February 2006 AstraZeneca initiated a recall of all promotional material that bore the claim and new material was produced to more accurately reflect the reference publication and the Casodex 150 SPC.

The grievance procedure was concluded in January 2006 and the complainant left AstraZeneca in summer 2006. AstraZeneca received a complaint via the MHRA on the same issue relating to claims for Casodex 150 on 5 October 2006. AstraZeneca informed the MHRA of the corrective action taken as well as the justification for not issuing a 'Dear Doctor' letter. The MHRA was also given a copy of a Casodex 150 sales aid prepared in March 2006 that bore a revised claim. The assertion that Casodex was up to 36% worse than castration for survival was not an accurate reflection of the data and was based on an inaccurate interpretation of the 95% confidence interval associated with the result. The hazard ratio for survival was 1.05 (95% CI of 0.81-1.36). The 95% confidence limit indicated that the range in which the true value might lie was somewhere between Casodex being up to 19% better or up to 36% worse than castration. Overall, AstraZeneca concluded only that no statistically significant difference was found between the two treatments.

The MHRA upheld the complaint but determined that no further action would be taken against AstraZeneca. The outcome was published on the MHRA website.

As an indication of AstraZeneca's commitment to the Code and the Medicines Act it restated that this matter was dealt with immediately after the complainant brought it to AstraZeneca's attention. AstraZeneca accepted a breach of Clause 7.2.

AstraZeneca noted that the promotion of Casodex 150 for a first line indication for prostate cancer was consistent with the SPC. Casodex 150 was indicated for immediate use alone or as adjuvant to surgery or radiotherapy for the treatment of locally advanced prostate cancer, in addition to being indicated for the management of patients with locally advanced, non-metastatic prostate cancer for whom surgical castration or other medical intervention was not considered appropriate or acceptable.

PANEL RULING

The Panel noted that its role related to matters covered

by the Code. The complaint had been considered by the MHRA which was responsible for administering UK law on behalf of the health ministers.

The Panel considered that the claim 'Equivalent efficacy to castration' was misleading given the statement in the SPC that 'equivalence of the two treatments [Casodex 150 and castration] could not be concluded statistically'. Thus the Panel ruled a breach of Clause 7.2 as acknowledged by AstraZeneca.

The Panel noted the complainant's concerns about the revised claim 'No different to castration in overall survival' based on Iversen *et al*. The results from this study were reported in the Casodex 150mg SPC and supported the statement 'At 56% mortality and a mean follow-up of 6.3 years, there was no significant difference between Casodex and castration in survival (hazard ratio = 1.05 [CI 0.81 to 1.36]); however equivalence of the two treatments could not be concluded statistically'. The complainant was concerned that the claim 'No different to castration in overall survival' failed to alert prescribers that patients' survival might be compromised by up to 36%. Equally, however, survival might be improved by up to 19%. The Panel considered that the target audience would appreciate that there were always confidence intervals in statistics. Readers would understand the claim in question to mean that, overall, no meaningful or clinically significant difference in survival had been reported between Casodex 150 and castration which was so. No breach of Clause 7.2 was ruled. This ruling was appealed by the complainant.

The Panel noted that Casodex 150 was indicated first line either alone or as adjuvant therapy in patients with locally advanced prostate cancer. In patients with locally advanced, non-metastatic prostate cancer it could be used in those for whom surgical castration or other medical intervention was not considered appropriate or acceptable.

AstraZeneca needed to be clear when promoting Casodex first line but such promotion was not necessarily outside the marketing authorization.

APPEAL BY THE COMPLAINANT

The complainant appealed the ruling of no breach of Clause 7.2 with regard to the revised claim 'No different to castration in overall survival' bearing in mind the statistical design of Iversen *et al*. The trials were designed to demonstrate equivalence between bicalutimide monotherapy and castration with respect to death, progression and treatment failure by rejecting the hypothesis that bicalutimide was at least 25% worse than castration.

The complainant noted the Panel's ruling that 'AstraZeneca needed to be clear when promoting Casodex 150 first line but such promotion was not necessarily outside the marketing authorization'. The complainant alleged that it was very clearly outside the marketing authorization. Where was the first line licence? There was not a first line licence. From the SPC: 'Casodex 150mg is also indicated for the management of patients with locally advanced, non-metastatic prostate cancer for whom surgical castration or other medical intervention is not considered appropriate or acceptable'. Effectively the above statement relegated Casodex 150 to second line treatment after an LHRH analogue (surgical castration was not widely used).The complainant noted 'In patients with locally advanced prostate cancer Casodex 150 is indicated as immediate therapy either alone or as adjuvant to treatment by radical prostatectomy or radiotherapy' and stated that in this adjuvant trial patients were randomly allocated to Casodex 150 or placebo in addition to receiving standard care (watchful waiting, radical prostatectomy or radiotherapy). Watchful waiting (or active monitoring): many patients with locally advanced disease were elderly, and thus would have a relatively short life expectancy. Watchful waiting might be a valid treatment option in these patients who would often succumb to other co-morbid conditions. This was the group of patients where 'Casodex 150 is indicated as immediate therapy (either) alone or as adjuvant to treatment by radical prostatectomy or radiotherapy'.

The complainant alleged that giving a group of patients active therapy who were considered not to need it categorically did not constitute a first line licence. There was no first line licence.

The complainant noted that this adjuvant trial (also known as the AstraZeneca Early Prostate Cancer (EPC) trial programme) was the subject of the 'Dear Doctor' letters referred to in AstraZeneca's response. In those patients with localised prostate cancer, who would otherwise have been managed only by watchful waiting, there was an increase in the number of deaths for Casodex 150mg patients when compared with patients who received placebo. Presumably if there was some background adverse metabolic effect it could also be in the locally advanced group. It would be purely speculation to consider that this was one possible reason why Casodex 150 was not equivalent to castration. Survival was the ultimate aim of all patients with incurable cancer.

The complainant noted that in Iversen *et al*, at a median follow up of 6.3 years, mortality was 56%. The median survival was 63.5 months in the Casodex 150 group and 69.9 months in the castration group. The complainant alleged that if patients were not informed that Casodex 150 could decrease survival compared with castration their safety was compromised.

As there was no first line licence AstraZeneca should not be allowed to promote it in this fashion. Both Iversen et al trial and the EPC data were considered to have too many faults by the FDA and non-approvable letters were issued. The therapeutic indications were misleading and a corrective statement should be required.

COMMENTS FROM ASTRAZENECA

AstraZeneca noted that the claims at issue related to

the promotion of Casodex 150, in particular the statement 'No different to castration in overall survival' and the positioning of Casodex 150 to include first line use either alone or as adjuvant therapy in patients with locally advanced prostate cancer.

AstraZeneca submitted that the claim, 'No different to castration in overall survival' was supported by Iversen et al. The complainant's view that this study showed that patients did 36% worse than castration in overall survival was an inaccurate interpretation of the 95% confidence intervals associated with the actual result. The hazard ratio for survival was 1.05 (95% CI of 0.81-1.36). The 95% confidence limit indicated the range in which the true value might lie was somewhere between Casodex being up to 19% superior or up to 36% inferior to castration. Overall, no statistically significant difference was found between the two treatments. While this study did not achieve the required threshold for the demonstration of equivalence, it did demonstrate that there was no significant difference between Casodex 150mg and castration. This flowed from the fact that the 95% confidence interval for the difference between Casodex 150mg and castration included unity and hence, by statistical definition and without exception, the difference between the treatments being compared was 'not statistically significant'.

AstraZeneca maintained that this claim was in keeping with the scientific evidence and not in breach of Clause 7.2.

In summary the claim that Casodex 150 was 'No different to castration in overall survival' was accurate and not misleading and therefore not in breach of Clause 7.2. The licensed indication included use in the first line setting and promotion in this context was within the licensed indication and not in breach of Clause 7.2.

FURTHER COMMENTS FROM THE COMPLAINANT

The complainant referred to the Casodex 150 Sales Campaign June 2005 (Date of prep: May 2005 Ref: 16127) for use with Casodex 150/Zoladex Sales Aid (ref 15790):

> 'Key Message
>
> Casodex 150mg has equivalent efficacy to castration.
>
> Make the page live
>
> Use this page to demonstrate that Casodex 150 has equivalent efficacy to castration (138 medical (i.e. Zoladex), 22 surgical).
>
> Whilst survival is the ultimate aim for incurable cancer, such as locally advanced prostate cancer, ensure the customer knows that randomised controlled trial data is regarded as the most valuable type of evidence for demonstrating the efficacy of therapies.
>
> Ensure that the customer knows that this is a robust study (a randomised controlled trial) in 480 patients. After a median follow up of 6.3 years when 56% of patients had died and the trial was mature, Casodex 150 and castration therapy were shown to be equivalent in terms of time to disease progression and overall survival. Can the customer think of any data that contradict this result?
>
> Consider the benefit of equivalent efficacy to both the customer and the patient; now there is a real and alternative choice of treatments that provide equivalent efficacy in treating locally advanced disease. How will this make the clinician and customer feel? Again, can the customer think of any data that contradict this result?
>
> Ask the customer how confident and comfortable they feel about the efficacy of Casodex 150 for patients with locally advanced disease - ask whether they would be willing to use Casodex 150 in place of Zoladex with these new active patients with locally advanced disease.'

The complainant alleged that this did not fit with the licensed indication from the SPC: 'Casodex 150mg is also indicated for the management of patients with locally advanced, non-metastatic prostate cancer for whom surgical castration or other medical intervention is not considered appropriate or acceptable'. Effectively the above statement relegated Casodex 150 to second line treatment after an LHRH analogue (surgical castration was not widely used).

The complainant noted that according to the Casodex 150mg SPC 'In patients with locally advanced prostate cancer Casodex 150 is indicated as immediate therapy either alone or as adjuvant to treatment by radical prostatectomy or radiotherapy'. In this adjuvant trial patients were randomly allocated to Casodex 150 or placebo in addition to receiving standard care (watchful waiting, radical prostatectomy or radiotherapy). Watchful waiting (or active monitoring). Many patients with locally advanced disease were elderly, and thus would have a relatively short life expectancy. Watchful waiting might be a valid treatment option in these patients who would often succumb to other co-morbid conditions. This was the group of patients where 'Casodex 150 is indicated as immediate therapy (either) alone or as adjuvant to treatment by radical prostatectomy or radiotherapy'.

The complainant alleged that giving a group of patients active therapy who were considered not to need it categorically did not constitute a first line licence. There was no first line licence.

The complainant alleged that the misleading and unlawful campaign ran for over two years and a corrective statement should be published. If patients were not informed that Casodex 150 could decrease survival compared with castration their safety was compromised.

APPEAL BOARD RULING

The Appeal Board noted that according to its SPC Casodex 150 was indicated first line either alone or as adjuvant therapy in patients with locally advanced prostate cancer. In patients with locally advanced, non-metastatic prostate cancer it could be used in those for whom surgical castration or other medical intervention was not considered appropriate or acceptable.

The Appeal Board considered that AstraZeneca needed to be clear when promoting Casodex first line but such promotion was not necessarily outside the marketing authorization.

The Appeal Board noted that data from IversEn *et al* was reflected in Section 5.1 of the Casodex 150mg SPC which stated 'At 56% mortality and a median follow-up of 6.3 years, there was no significant difference between Casodex and castration in survival (hazard ratio = 1.05 [CI 0.81 to 1.36]); however equivalence of the two treatments could not be concluded statistically'. The Appeal Board noted AstraZeneca's explanation that the 95% confidence interval indicated that the range in which the true value might lie was somewhere between Casodex being up to 19% superior or up to 36% inferior to castration. Whilst the study did not achieve the required threshold to demonstrate equivalence, as the 95% confidence interval included unity, it did demonstrate that there was no statistically significant difference between Casodex 150 and castration. The Appeal Board considered that the target audience would understand the claim in question to mean that, overall, no meaningful or clinically significant difference in survival had been reported between Casodex 150 and castration which was not an unfair reflection of the data and SPC on this point. The Appeal Board upheld the Panel's ruling of no breach of Clause 7.2 in relation to the revised claim 'No different to castration'. The appeal on this point was unsuccessful.

During its consideration of this case the Appeal Board queried AstraZeneca's submission that it took 'swift and positive action' with regards to the claim 'equivalent efficacy to castration'. The company had been notified of concerns about the claim at the end of November 2005 and accepted that it was not in accordance with the SPC in January and the brand manager advised sales teams of the change on 17 February 2006. At the appeal hearing the representatives accepted that the way the matter had been dealt with was convoluted particularly given the statement in the SPC. The company had not acted swiftly to withdraw the claim in question.

2 Call rates

COMPLAINT

The complainant stated that if the carrot in the form of the AZpiration scheme failed to induce representatives into breaching the Code (Case AUTH/1899/10/06) then a stick in the form of short-term performance measures was threatened.

This was viewed as the first step in a disciplinary process and was a threat which was used, formally and informally, to bully and harass representatives into achieving the frequency of 12 face to face calls. This amounted to harassment to breach the Code.

During 2004 and 2005 over 70% of the oncology team left AstraZeneca as they thought they were no longer working for an ethical company and bringing the industry into disrepute. In 2004/05 37 people left. In 2004 only 2 exit interviews were conducted.

Many customers complained. Oncologists specialising in breast and prostate cancer would be targeted 36 times a year by the company (12 x Faslodex, 12 x Arimidex, 12 x Casodex/Zoladex).

The complainant noted that the findings in Case AUTH/1899/10/06 regarding frequency of calling referred to this campaign in terms of incentivisation to break the Code. The complainant requested a response concerning the fact that representatives could be put on short-term performance procedures for failing to be incentivised to break the Code in terms of frequency of visits. In the complainant's area, 2 out of 6 representatives were on these procedures (33%) which were viewed as the first step in a disciplinary process.

When writing to AstraZeneca the Authority asked it to respond in relation to Clause 9.1.

RESPONSE

AstraZeneca stated that the complainant referred to both call rate and to call frequency which were defined as follows:

- The call rate was the number of calls made by a representative against specified customers in a given period of time. A call rate of 4 per day meant that a representative had seen 4 of their customers in a day
- The call frequency was the number of times a specified customer was seen by an individual representative over a given period of time

This complaint concerned matters closely similar to ones which had been the subject of previous adjudications. Case AUTH/1737/7/05 was based on statements made at two divisional meetings held by AstraZeneca in September 2002. Case AUTH/1714/5/05 related to materials used and activities of AstraZeneca during 2004.

The specific area AstraZeneca was asked to consider was the allegation of placing representatives on short-term performance procedures for 'failing to be incentivised to break the Code' in relation to call frequency.

The allegation of incentivising representatives to break the Code had already been addressed by AstraZeneca in Case AUTH/1737/7/05. Prior to Case AUTH/1714/05/05, representative incentive (which represented on average less than 20% of their base salary) was based on Cash Creator and AZpiration.

Cash Creator accounted for 80% of the incentive and was based on sales and market share performance. The AZpiration scheme that accounted for the other 20% and which was historically based on call frequency and call rates, was revised following Case AUTH/1714/05/05 to ensure that call frequency was no longer incentivised.

In the response to Case AUTH/1737/7/05 AstraZeneca clearly described its processes for managing poor performance. It was also pointed out that during the first half of 2005 (the latter part of the period in question) only 2 representatives out of an oncology sales force of 80-85 were placed on short-term objectives with specific action plans to improve performance.

Disciplinary action was only used if the individuals were not meeting their objectives and performance was at an unacceptable standard; it was a last resort in this situation. All managers received extensive training in the use of various coaching techniques and performance action planning. There was no evidence to support the allegation that disciplinary action was used as a threat either formally or informally, however all employees were fully aware of their targets and objectives as set out in their performance plans. The complainant's assertion was contradicted by the fact that in 2004 only 2 members of the entire oncology sales force were placed on short-term objectives yet continued to work for AstraZeneca.

In response to the allegation that 2 out of 6 representatives in the complainant's team were on short-term performance measures, AstraZeneca submitted that only 1 representative was placed on short-term objectives.

AstraZeneca noted that the complainant had asserted that 37 representatives left the company during 2004/05 but only 2 exit interviews were performed in 2004. The complainant had been given full details of the number of leavers and the number of exit interviews for the oncology sales force as part of his grievance procedure and so it was disappointing that he now selectively used that information. It was true that 2 exit interviews out of 14 leavers were performed in 2004. However, in 2005, 19 of 23 leavers had an exit interview. As leavers were not obligated to attend or take part in an exit interview, a response rate of over 50% was very reasonable.

AstraZeneca submitted that the allegation that during 2004/05 over 70% of the oncology team left the company as they thought they were no longer working for an ethical company and bringing the industry into disrepute had already been addressed in Case AUTH/1899/10/06. In 2004 attrition rates were similar across the business while in 2005 the rate of attrition was higher but far less than 70% and followed on from a significant reorganisation of the team. Only 4 of the 21 leavers who had an exit interview cited 'unhappy with the environment' as their reason for leaving; none of them cited 'no longer working for an ethical company and bringing the industry into disrepute' as a reason for leaving.

AstraZeneca noted that the complainant had not provided any evidence to support his claim that many customers complained. Similarly AstraZeneca did not have any record of customers complaining.

On the basis of the above, AstraZeneca firmly denied a breach of Clause 9.1.

PANEL RULING

The Panel noted that in the previous case, Case AUTH/1899/10/06, it had been ruled that representatives' call rates and incentivisation were in breach of the Code as alleged. In the present case, Case AUTH/1950/1/07, the complainant had asked the Panel to consider the specific allegation that placing representatives on short-term objectives for failing 'to be incentivised to break the Code' in terms of frequency targets was in breach of the Code. This had not been addressed as a discrete issue previously.

The Panel noted the points raised by the complainant and AstraZeneca's comments about the number of representatives on short-term objectives and reasons given by those leavers who attended exit interviews. In 2004 two members of the entire oncology sales force of 80-85 were on short-term objectives. AstraZeneca's submission that less than 70% of the oncology team had left during 2004/05 was also noted.

Taking all the evidence into account the Panel decided that on the balance of probabilities there was insufficient evidence to show a breach of the Code as alleged. The Panel therefore ruled no breach of Clause 9.1. This ruling was not appealed.

3 Advice on staying within the Code

COMPLAINT

The complainant stated that during 2004 and the first 6 months of 2005 the oncology team were under extreme pressure to achieve metrics which included (in 2004) 12 face to face calls a year on the main group of target customers. The complainant and others tried to raise their concerns about achieving these metrics and staying within the Code via the union representative.

Concern was raised at all levels of management including hospital area sales manager, national sales manager, human resources, UK director level, the whistleblowing line and the chief executive. Most of this was documented via the union representative; no advice was received.

The complainant noted a hospital area sales manager witness report which stated 'It was mentioned at a management group, [a named individual] kept saying that we were breaching the ABPI'. The concerns were not escalated as a management team because 'we were all in fear of losing our jobs'.

The complainant provided farewell emails and two witness reports from hospital area managers which might give insight into this fear culture which prevented concerns being raised. ABPI complaints forced a change of culture and the medical director had to acknowledge this with an email in November 2005 entitled 'Embracing our People'. The complainant alleged that AstraZeneca ignored the concerns about the Code effectively demeaning the Code and this brought discredit to the pharmaceutical industry in breach of Clause 2.

When writing to AstraZeneca the Authority asked it to respond in relation to Clause 15.9 and in addition, to Clause 2 in relation to the cumulative effect of points 1, 2 and 3.

RESPONSE

AstraZeneca stated that this specific complaint was not raised under Case AUTH/1899/10/06. However, this part of the complaint concerned matters closely similar to those that were the subject of previous adjudications and related solely to past activities within the company.

Whilst AstraZeneca sought to promote a culture of open communication, it acknowledged that at the time in question there was a failure to provide clarity and guidance on staying within the Code and promptly address certain concerns, in relation to call frequency. On this basis, AstraZeneca accepted a retrospective breach of Clause 15.9 but noted that significant measures had been put in place to address past shortcomings.

In response to the ruling in Case AUTH/1714/05/05 AstraZeneca put in place strengthened measures to ensure that all employees understood the requirements of the Code. Full details were provided in AstraZeneca's response to Case AUTH/1737/7/05. The measures previously taken were relevant to the current complaint and included the following:

1 Sales force briefing regarding call frequency and Code requirements
2 Establishment of field force discussion group
3 Company-wide email communication of coverage and frequency requirements
4 Senior managers conference
5 Company-wide cascades of information
6 Availability of call frequency Q&A document on corporate website

In addition, all internal meetings involving representatives included five mandatory slides summarising key aspects of the requirements of the Code. The requirement that no more than 3 unsolicited calls per representative per customer per year were allowed was explicitly highlighted.

In the response to Case AUTH/1737/7/05 AstraZeneca outlined the mechanisms and structures that enabled employees to raise concerns and ensured that this was done fairly. In addition to these general fora, AstraZeneca had established a corporate reputation team that reported into the legal function. Within this team, a compliance officer had the primary responsibility of ensuring business compliance as well as being responsible for running the compliance hotline

that enabled the confidential reporting of compliance issues.

In addition to the above three complaints, the complainant alleged a breach of Clause 2 of the Code. In relation to all of these complaints there was no dispute that they related to historical materials and activities at AstraZeneca. There was even recognition in the complaint that it was solely concerned with issues arising in 2004 and the first half of 2005.

The aim of the Code was to ensure that the promotion of medicines was carried out within a robust framework to support high quality patient care. In each case where a breach of the Code was ruled, the company concerned must give an undertaking that the practice in question had ceased forthwith and that all possible steps had been taken to avoid a similar breach in the future. There was no complaint that AstraZeneca had not complied with the undertaking given in the previous cases and details of the company's comprehensive action plan had already been provided. Additionally, there was no suggestion that there was an ongoing cultural issue within AstraZeneca, indeed it was recognized in some of the papers submitted by the complainant that significant steps had been taken.

The only element to consider here that could lead to a potential ruling of a breach of Clause 2 was that there were multiple/cumulative breaches of a similar and serious nature in the same therapeutic area within a short period of time.

AstraZeneca noted that the three previous cases essentially dealt with 7 breaches (3 breaches of Clause 9.1 (failure to maintain high standards); 2 breaches of Clause 15.4 (call activity out of line with the supplementary information) and 2 breaches of Clause 15.9 (failure to provide suitable briefing material for representatives)) in neurology and oncology over more than three years. In Cases AUTH/1714/5/05 and Case AUTH/1899/10/06, AstraZeneca was found in breach of Clauses 15.4 and 9.1. In Case AUTH/1737/7/05, AstraZeneca was found in breach of Clauses 15.9 and 9.1. In addition, in each of these cases AstraZeneca was asked to respond in relation to Clause 2 and in each case no breach of Clause 2 was ruled.

There was nothing therefore in the current case that justified a ruling of a breach of Clause 2. In light of this complaint, AstraZeneca requested that the broader policy issue of whether the Code was best served by being used in this way to allow previous rulings to be re-opened as part of employment disputes, should be considered.

In addition, AstraZeneca believed it was not appropriate for the complainant to use witness statements, that were provided under strict terms of

confidentiality, for these purposes. However, in the interests of transparency AstraZeneca dealt with the inaccuracies contained within those reports.

Furthermore, AstraZeneca asked the Authority to consider whether it was appropriate and in accordance with the spirit of the Code, to allow different complaints based on the same facts to proceed, particularly when the company had taken very significant corrective action in response to a previous ruling.

In summary, AstraZeneca had responded comprehensively through internal procedures to the concerns raised by the complainant and was disappointed that, subsequently, the same issues had formed the basis of complaints to the MHRA and the Authority. Nevertheless, AstraZeneca had responded fully to these latter complaints. AstraZeneca accepted historical breaches of Clauses 7.2 and 15.9 and did not accept a breach of Clause 2 for the reasons stated.

PANEL RULING

The Panel noted AstraZeneca's response to this allegation and its general points about the complaint.

The Panel noted that in the previous cases breaches of Clauses 15.4 and 15.9 had been ruled. The Panel noted that the allegation now to be considered was wider than that in Case AUTH/1714/5/05 which related specifically to references to the Code in the campaign notes. The Panel considered that the briefing material had been inadequate in relation to the general allegation now before it. The Panel therefore ruled a breach of Clause 15.9 as acknowledged by AstraZeneca.

The Panel was concerned that AstraZeneca's promotional material was inconsistent with information in the Casodex SPC (point 1 above). It noted that the complaint about call rates and call frequency had been dealt with in previous cases but the complainant had now alleged that those rulings together with points 1, 2 and 3 above amounted to a breach of Clause 2.

Taking all the circumstances into account and bearing in mind its rulings in the previous case, Case AUTH/1899/10/06, the Panel did not accept that the cumulative effect of the Panel's rulings at points 1, 2 and 3 above and the previous case were, on balance, sufficient to warrant a ruling of a breach of Clause 2 which was a sign of particular censure and reserved for such use.

APPEAL BY COMPLAINANT

The complainant was surprised that Clause 2 was not ruled. The complainant was interested in the Appeal Board's opinion of the House of Commons Health Committee report on The Influence of the Pharmaceutical Industry which stated:

'373. The PMCPA and MHRA do not effectively co-ordinate their work in the assessment and approval of medicines advertising and promotional material. The defences in place against the inappropriate or misleading promotion of medicines are weak. The MHRA, which has admitted it cannot vet all such material, seems reluctant to punish companies that commit offences in the promotion of medicines in a swift and effective manner. Publishing upheld complaints on the MHRA website is an inadequate response; so is forcing companies to make minor changes to their advertising catchphrases. We recommend that the MHRA and the PMCPA better co-ordinate their work relating to the promotion of medicines to avoid duplication. Complaints should be investigated swiftly, particularly when claims for new drugs are involved. When the PMCPA has evidence that a company has breached the regulations it should inform the MHRA of their findings. When companies are found to be in breach of advertising or marketing regulations by the MHRA, we recommend that corrective statements always be required and that such statements are given as much prominence as the original promotional piece. The publication of misleading promotional material is a criminal offence and the punishment should befit such a status.'

The complainant noted AstraZeneca's response to the original complaint enclosed a leavepiece (ref 05/15791). The complainant noted that he had quoted this merely as an example, and alleged that all the items associated with this campaign were misleading. The campaign ran for over two years and was refreshed every quarter. A further detail aid (ref 05/15790, 04/15075) and a representative briefing document dated May 2005 (ref 16127) being further examples. If the Authority had asked for all the materials associated with this misleading campaign a hefty postbag would result. Lots of law breaking. Surely this was much more serious than wining and dining wives and girlfriends in a sporting environment? So if this law breaking did not justify a breach of Clause 2 what would?

COMMENTS FROM ASTRAZENECA

AstraZeneca noted in response to the complaint that Casodex 150 was promoted in a first line indication for prostate cancer, that this was consistent with the SPC. Casodex 150 was indicated for immediate use alone or as adjuvant to surgery or radiotherapy for the treatment of locally advanced prostate cancer, in addition to being indicated for the management of patients with locally advanced, non-metastatic prostate cancer for whom surgical castration or other medical intervention was not considered appropriate or acceptable.

AstraZeneca noted the complainant had cited the Health Select Committee Report on the Influence of the Pharmaceutical Industry as a cause for ruling a breach of Clause 2 in this matter. The current Code followed the publication of this report and the more measured Government response to it (provided) and took into account the subsequent views of the MHRA. A ruling solely in accordance with the current Code was

therefore up-to-date and appropriate.

AstraZeneca submitted the above claims were not misleading, were not in breach of any clause of the Code and certainly not Clause 2.

AstraZeneca submitted the earlier claim of 'equivalent efficacy to castration' was accepted as misleading and had been promptly withdrawn in February 2006 after it was brought to its attention, as described in the response to this complaint. It was subsequently the subject of a complaint to the MHRA brought by the complainant and was accepted by AstraZeneca as a breach of Clause 7.2 in this case, ahead of the Panel ruling. AstraZeneca was committed to the Code and had acted promptly and appropriately in regard to this claim from the point at which the issue was raised. The materials were withdrawn promptly before any external complaint and the MHRA upheld the subsequent complaint made to it but determined that 'no further action will be taken' against AstraZeneca. This prompt action and assessment by the MHRA of no further action required suggested that there were no grounds for any complaint under Clause 2. AstraZeneca restated that it had introduced a number of measures to ensure that employees understood the requirements of the Code. These measures included the following:

1 Sales force briefing regarding call frequency and ABPI Code requirements.
2 Establishment of field force discussion group.
3 Company-wide email communication of coverage and frequency requirements.
4 Senior managers conference.
5 Company-wide cascades of information.
6 Availability of call frequency Q&A document on corporate website.

In addition, all internal meetings involving representatives included five mandatory slides summarising key aspects of the requirements of the Code (provided). The requirement that no more than 3 unsolicited calls per representative, per customer per year were allowed was explicitly highlighted.

AstraZeneca now had clear mechanisms and structures in place to enable employees to raise concerns and to ensure that this was done fairly. In addition, AstraZeneca had established a corporate reputation team that reported into the legal function. Within this team, a compliance officer had the primary responsibility of ensuring business compliance; the compliance officer was also responsible for running the compliance hotline that enabled the confidential reporting of any compliance issues. AstraZeneca's action in response to this issue was prompt, comprehensive and robust.

AstraZeneca noted that in this case, the Panel had considered the failure to refer to the Code in the campaign notes. This of itself could not be considered a breach of Clause 2 and the subsequent action suggested an approach that was consistent with upholding the reputation of the industry.

AstraZeneca noted that as described in its response to this complaint, the only reason a breach of Clause 2 might be considered was in regard to similar and cumulative serious breaches of the Code in the same therapy area within a short period of time. There had been two previous breaches ruled of Clause 15.9, in different therapy areas over a period of some three years. Similarly, with regard to call rates and breaches of Clause 15.4, there were two such rulings, similarly distributed over time and therapy area. None of the individual cases were considered to be serious enough to warrant a breach of Clause 2.

AstraZeneca noted that in the case of both call rates and advice on staying within the Code in campaign roll-outs it could not be claimed that there were multiple/cumulative breaches of a similar and serious nature in the same therapeutic area within a short period of time.

FURTHER COMMENTS FROM THE COMPLAINANT

Further comments as set out in point 1 above.

APPEAL BOARD RULING

The Appeal Board noted the supplementary information to Clause 2 listed activities likely to be in breach of Clause 2 and referred, inter alia, to multiple and cumulative breaches of a similar and serious nature in the same therapeutic area within a short period of time.

The Appeal Board noted the previous cases referred to by the complainant; Cases AUTH/1714/5/05, AUTH/1737/7/05 and AUTH/1899/10/06. Two therapeutic areas were involved: psychiatry and oncology. Case AUTH/1899/10/06 was closely similar to the present case but concluded at Panel level. Rulings of breaches of the Code had been made in relation to call rates and incentivisation (Cases AUTH/1714/5/05 and AUTH/1899/10/06) and also in relation to comments made by a senior executive at a national sales conference (Case AUTH/1737/7/05). Rulings of no breaches of the Code were also made. The Appeal Board also noted the rulings in the present case.

Taking all the circumstances into account the Appeal Board did not consider that the cumulative effect of previous cases and the Panel and Appeal Board rulings in the present case were, on balance, sufficient to warrant a breach of Clause 2 of the Code which was a sign of particular censure and reserved for such use. The Appeal Board upheld the Panel's ruling of no breach of Clause 2 of the Code. The appeal on this point was unsuccessful.

Complaint received **22 January 2007**

Case Completed **14 June 2007**