JOURNALIST, MEMBER OF THE PUBLIC and EX-EMPLOYEE v ASTRAZENECA

Promotion of Seroquel

Three complaints were received about the promotion of Seroquel (quetiapine) by AstraZeneca in the UK.

In Case AUTH/2294/1/10 a journalist alleged that a Seroquel advertisement in the British Journal of Psychiatry, April 2004 featured a claim for 'no weight gain', long after AstraZeneca was aware of precisely such effects.

In Case AUTH/2296/1/10 a member of the public asked the Authority to review an online BBC news item, 'Firm "suppressed" drug test data', published 26 January 2010 in relation to the Code.

The news item stated that a former medical adviser for Seroquel was pressurised to approve promotional material which stated that weight gain was not an issue. The medical adviser stated that clinical data available when Seroquel was launched showed patients gained statistically and clinically significant weight. The medical adviser further stated that he was put under quite significant pressure to sign off claims with regard to lack of weight gain and he was unwilling to sign that off. The news item stated that in the US Seroquel was marketed with claims that it would not cause weight gain. That was not done in the UK except for one advertisement published in the British Journal of Psychiatry, April 2004.

In Case AUTH/2297/1/10 an ex-employee of AstraZeneca referred to a Radio 4 documentary, File on 4, broadcast on Tuesday, 26 January 2010, which criticised promotional claims for Seroquel. In particular the complainant referred to an advertisement which was published in the British Journal of Psychiatry, 2004. The complainant provided a web-link to the File on 4 programme and also to articles in the Washington Post, 18 March 2009, and New York Times, 29 October 2009. The complainant stated that the links were provided to assist in the investigation.

The detailed response from AstraZeneca is given below. The cases were considered under the 2003 Code using the 2008 Constitution and Procedure.

In Case AUTH/2294/1/10 the Panel noted that the Seroquel advertisement at issue featured the claim 'The only atypical with placebo level EPS [extra-pyramidal symptoms] (including akathisia) and placebo level prolactin concentrations and a favourable weight profile across the full dose range'. The Panel thus considered that the claim in full sought to establish Seroquel as an atypical antipsychotic which was distinctly different to the others in the class in that it was the only one to have placebo level EPS, placebo level prolactin concentrations and a favourable weight profile across the full range.

The Panel noted that in the absence of any explanation it was left to the readers' judgement as to what was meant by a 'favourable weight profile'. The Panel noted that Allison *et al* (1999) had estimated and compared the effects of antipsychotics (both conventional and atypical) on bodyweight and concluded that all were associated with weight gain. Among the atypical agents the mean increases in weight were 4.55kg (clozapine), 4.15kg (olanzapine), 2.92kg (sertindole), 2.1kg (risperidone) and 0.04kg (ziprasidone). The mean increase in weight with Seroquel was not calculated due to lack of data.

The Panel considered that if all of the other atypical antipsychotics were known to cause weight gain then it was not unreasonable for readers to assume that if Seroquel was 'The only atypical with … a favourable weight profile across the full dose range' then it might be an atypical with no effect on bodyweight. This was not so. Arvanitis and Rak (1997) reported that the mean increase in weight was 2.2kg (n=1085). (Allison *et al* had reported that the mean increase in weight for risperidone was 2.1kg and 2.92kg for sertindole). Across the dose range for Seroquel, 75/150/300/600/750mg daily, the mean increase in weight was 0.9/2.9/2.0/2.6/2.3kg respectively. Jones and Huizar (2003) reported a mean increase in weight of 1.8kg with Seroquel therapy. Brecher *et al* (2000) reported on the long-term weight changes in 427 patients over 18 months. Weight change differed over time from -1.53kg after weeks 40-52 (n=41) to +1.94kg after weeks 53-78.

The Panel noted that the relevant Seroquel SPC listed weight gain as a common (≥1% - <10%) adverse event which occurred predominantly during the early weeks of therapy.

Overall the Panel considered that the advertisement was misleading with regard to the effect on bodyweight that would be expected with Seroquel therapy compared with the other atypical medicines. Although the advertisement did not state 'no weight gain' as alleged it sought to differentiate Seroquel from other medicines in the class in that it was the only one with a 'favourable weight profile across the full dose range'. Given that the other medicines caused weight gain, the

advertisement could be read as implying that Seroquel did not. This was not so. Similarly, the advertisement could be read as implying that Seroquel had a clear advantage regarding its 'favourable weight profile …' and this was not supported by the data submitted by AstraZeneca. The claim 'The only atypical with … a favourable weight profile…' was thus misleading and could not be substantiated. Breaches of the Code were ruled.

In Case AUTH/2296/1/10 the Panel considered that its rulings above in Case AUTH/2294/1/10 applied here also. The Panel further considered that, given the data, high standards had not been maintained. A breach the Code was ruled.

Misleading prescribers about a potential side-effect of therapy could prejudice patient safety and was of an activity likely to be in breach of Clause 2. On balance, however, the Panel considered that the circumstances were not such as to warrant a ruling of a breach of that clause which was reserved as a sign of particular censure. No breach of Clause 2 was ruled.

In Case AUTH/2297/1/10 the Panel only considered allegations regarding material used in the UK. The Panel considered that its rulings above in Cases AUTH/2294/1/10 and AUTH/2296/1/10 applied here also. The complainant in this case unsuccessfully appealed the Panel's ruling of no breach of Clause 2.

Three complaints were received about the promotion of Seroquel (quetiapine) by AstraZeneca in the UK.

Case AUTH/2294/1/10

COMPLAINT

A journalist referred to a Seroquel advertisement (ref 01/03/13526/A), placed by AstraZeneca UK Limited in the British Journal of Psychiatry, April 2004. The complainant alleged that the advertisement featured a claim for 'no weight gain', long after AstraZeneca was aware of precisely such effects.

When writing to AstraZeneca, the Authority asked it to respond in relation to Clauses 7.2, 7.4 and 7.9 of the 2003 Code.

Case AUTH/2296/1/10

COMPLAINT

A member of the public brought to the Authority's attention an online BBC news item, 'Firm "suppressed" drug test data', published 26 January 2010. The complainant asked the Authority to review the item in relation to the Code.

The news item stated that a former medical adviser for Seroquel was pressurised to approve promotional material which stated that weight gain was not an issue. The medical adviser stated that clinical data available when Seroquel was launched showed patients developed significant weight gain, significant both statistically and clinically. The medical adviser further stated that he was put under quite significant pressure to sign off claims with regard to lack of weight gain and he was unwilling to sign that off. The news item stated that in the US Seroquel was marketed with claims that it would not cause weight gain. That was not done in the UK except for one advertisement published in the British Journal of Psychiatry, April 2004.

When writing to AstraZeneca, the Authority asked it to respond in relation to Clauses 2, 7.2, 7.4, 7.9 and 9.1 of the 2003 Code.

Case AUTH/2297/1/10

COMPLAINT

An ex-employee of AstraZeneca referred to a Radio 4 documentary, File on 4, broadcast on Tuesday, 26 January 2010, which criticised promotional claims for Seroquel. In particular the complainant referred to an advertisement published in the British Journal of Psychiatry, 2004. The complainant provided a web-link to the File on 4 programme and also to articles in the Washington Post, 18 March 2009, and New York Times, 29 October 2009. The complainant stated that the links were provided to assist in the investigation.

When writing to AstraZeneca, the Authority asked it to respond in relation to Clauses 2, 7.2, 7.4, 7.9 and 9.1 of the 2003 Code.

* * * * *

The three cases above were considered under the 2008 Constitution and Procedure.

* * * * *

Cases AUTH/2294/1/10 and AUTH/2297/1/10

RESPONSE

AstraZeneca submitted that the Seroquel advertisement was directed to UK health professionals only; the target audience was psychiatrists and claims included in the advertisement should be considered in that context. AstraZeneca could not understand how the complainant in Case AUTH/2294/1/10 could contend that the advertisement claimed 'no weight gain' when it actually stated '… a favourable weight profile across the full dose range' and also listed weight gain as common in the prescribing information.

Health professionals would take from this advertisement that weight gain was associated with

Seroquel and that the profile was favourable given the available data at the time on Seroquel and in the context of the overall class of atypical antipsychotics. The Oxford English dictionary defined favourable as 'satisfactory', and profile as 'an outline of something'. This interpretation was consistent with the prescribing information which listed weight gain as common. This did not imply that there was no weight gain with Seroquel nor did it downplay the weight profile of Seroquel. As such, AstraZeneca strongly refuted any breach of Clause 7.9 of the 2003 Code.

One of the references used to support the claim, 'a favourable weight profile across the full dose range', was a primary registration study for Seroquel in the acute treatment of schizophrenia (Arvanitis and Rak, 1997). In this double-blind, randomised study, efficacy and tolerability (including weight gain) were examined across five fixed doses of Seroquel (75/150/300/600/750mg daily), compared with haloperidol and placebo in patients with acute schizophrenia. The mean increases in weight observed with Seroquel, from low to high dose, were 0.9/2.9/2.0/2.6/2.3kg, respectively. This was clearly consistent with the claim 'a favourable weight profile across the full dose range'. This was also consistent in the context of the wider data at the time: a meta-analysis conducted a few years previously found an estimated mean weight gain change with the new antipsychotics of 4.45kg (clozapine), 4.15kg (olanzapine), 2.92kg (sertindole), 2.1kg (risperidone) and 0.04kg (ziprasidone) after 10 weeks (Allison *et al*, 1999). While Seroquel was not included in that meta-analysis because insufficient data were available at the time, the weight changes observed with other atypical antipsychotics were predominantly greater than those observed for Seroquel by Arvanitis and Rak. AstraZeneca therefore considered that the claim about a favourable weight profile was a fair and balanced reflection of the overall evidence relating to weight change associated with atypical usage at the time. As such, the company denied any breach of Clauses 7.2, 7.4 and 7.9.

Jones and Huizar (2003) cited in the advertisement, also supported the claim. In this pooled analysis of two 12-week randomised, double-blind studies of Seroquel, in bipolar mania, the mean weight change from baseline in the Seroquel arm was 1.8kg, compared with –0.2kg in the placebo arm (n=604). While 9.1% of patients reported weight gain as an adverse event in the quetiapine arm, compared with 1.5% in the placebo arm, none withdrew from the study due to weight gain. The mean weight gain observed in this 12-week study relative to that observed in Allison *et al* at 10 weeks, again supported the claim of a favourable weight profile for Seroquel.

Such a weight profile was an important consideration for health professionals, as the clinical significance of weight gain must also be considered against long-term treatment data (Brecher *et al*, 2000).

Brecher *et al*, which was cited in the advertisement at issue, also substantiated the weight profile claim. This study assessed the long-term weight changes (from 6 weeks to beyond 18 months) observed in a cohort of 427 patients with schizophrenia in a review of controlled and uncontrolled clinical trials of Seroquel and respective open-label extensions (patients received a mean dose of 475mg/day after one year of open-label treatment). The mean weight change from baseline was +1.58kg after 9-13 weeks (n=170), +0.26kg after 14-26 weeks (n=165), +1.66kg after 27-39 weeks (n=134), -1.53kg after 40-52 weeks (n=41) and +1.94kg after 53-78 weeks (n=146).

In the same study, weight changes in relation to baseline body mass index (BMI) were analysed in 178 patients from patients who had received Seroquel therapy long-term for at least 6 months (mean duration 18.6 months). BMI was widely accepted as a measure of weight change and classification, since it described relative weight for height (WHO, 1998). Brecher *et al* reported a tendency towards weight gain in those with low pre-treatment BMI, and towards weight loss in those with high pre-treatment BMI. Additionally, the 95% confidence intervals for the mean change in weight overlapped zero in the group as a whole and in all subgroups except the severely obese (BMI≥35kg/m², n=14) in whom slight weight loss was observed. AstraZeneca thus regarded the above data supported the favourable weight profile claim used in the advertisement.

With regard to the claim at issue, Brecher *et al* reported the mean change in weight for each of three dosage groups (≤300mg, >300-≤500mg and >500mg/day). Using the modal dose value for the last recorded weight value, these longitudinal data and associated confidence intervals showed no effect of Seroquel on weight at any dose, and there was no correlation between increasing dose and mean long-term weight changes. AstraZeneca considered this data strongly supported the claim, 'favourable weight profile across the full dose range'. Indeed, the authors stated: 'Quetiapine appeared to have a weight neutral or 'normalizing' effect, with a tendency towards favourable shifts in bodyweight in underweight patients (BMI <18.5 kg/m²) and severely obese patients (BMI> 35 kg/m²)'.

AstraZeneca noted that the articles in the Washington Post and New York Times, referred to by the complainant in Case AUTH/2297/1/10, were published by lay journalists in US newspapers for a US audience and did not represent a scientific analysis of the Seroquel trial data.

In summary, AstraZeneca considered that the advertisement was a fair and balanced reflection of the overall evidence at the time relating to Seroquel and more broadly, relating to weight change associated with atypical usage.

AstraZeneca submitted that weight gain was listed as common, with the corresponding footnote: 'Occurs predominantly during the early weeks of

treatment', in the October 2003 SPC which was current when the advertisement at issue was published in 2004. Indeed, the SPC had referred to weight gain since the product was first marketed. At launch, the UK label listed weight gain as an adverse event, occurring in 2% of patients on Seroquel, compared with 0% of patients on placebo. 'Increased appetite' was first listed (as a common undesirable effect) on the SPC dated 9 September 2009.

In summary, AstraZeneca strongly refuted the allegation in Case AUTH/2294/1/10 that the advertisement claimed no weight gain with Seroquel long after the company was aware of precisely such effects. As such, AstraZeneca did not consider that the advertisement had breached Clauses 7.2, 7.4 and 7.9 of the 2003 Code. Similarly in Case AUTH/2297/1/10, AstraZeneca denied breaches of Clauses 7.2, 7.4 and 7.9 of the 2003 Code. Further, taking into account the points outlined above and that the advertisement was published in a journal directed at a specialist audience, AstraZeneca disagreed that it had not maintained high standards or could be considered to have brought discredit upon or reduced confidence in the pharmaceutical industry. The company denied breaches of Clauses 9.1 and 2 of the Code.

Case AUTH/2296/1/10

RESPONSE

AstraZeneca noted that the complainant asked the Authority to review the BBC news item in relation to the Code. No complaint was alleged.

AstraZeneca noted that the news item, which was an online summary of a Radio 4 news programme and the File on 4 programme, that was first broadcast on 26 January 2010, only referred to one claim from a single UK promotional item: an advertisement for Seroquel in the April 2004 edition of the British Journal of Psychiatry. This advertisement included a claim 'favourable weight profile across the full dose range'.

AstraZeneca further noted that the Authority had referred to a quotation from its former medical adviser for the Radio 4 programme referring to the certification of 'claims with regard to the lack of weight gain'. However, in the programme the medical adviser further stated that he was 'unwilling to sign that off'. Therefore, AstraZeneca did not understand why the Authority had asked it to respond in relation to all relevant Seroquel material used with UK health professionals in addition to the British Journal of Psychiatry advertisement mentioned above.

AstraZeneca submitted that it did not currently use any marketing materials which stated a 'lack of weight gain' for Seroquel. However, for a product that had been marketed for more than 12 years in the UK, the company did not believe that it could reasonably investigate and respond to such a broad request in relation to specific clauses of the Code.

AstraZeneca restated that weight gain was listed as common in the October 2003 SPC which was current when the 2004 advertisement was published. Indeed, the SPC had referenced weight gain since the product was first marketed. As regards increased appetite, this was first listed (as a common undesirable effect) on the SPC of 9 September 2009. The relevant SPCs were provided and reflected all such listings and modifications according to relevant regulatory guidance and processes.

Case AUTH/2294/1/10

PANEL RULING

The Panel noted that the Seroquel advertisement at issue featured the claim 'The only atypical with placebo level EPS [extra-pyramidal symptoms] (including akathisia) and placebo level prolactin concentrations and a favourable weight profile across the full dose range'. The Panel thus considered that the claim in full sought to establish Seroquel as an atypical antipsychotic which was distinctly different to the others in the class in that it was the only one to have placebo level EPS, placebo level prolactin concentrations *and* a favourable weight profile across the full range.

The Panel noted that in the absence of any explanation it was left to the readers' judgement as to what was meant by a 'favourable weight profile'. The Panel noted that Allison *et al* had estimated and compared the effects of antipsychotics (both conventional and atypical) on bodyweight. The authors concluded that all of the antipsychotics examined were associated with weight gain. Among the atypical agents the mean increases in weight were 4.55kg (clozapine), 4.15kg (olanzapine), 2.92kg (sertindole), 2.1kg (risperidone) and 0.04kg (ziprasidone). The mean increase in weight with Seroquel was not calculated due to lack of data.

The Panel considered that if all of the other atypical antipsychotics were known to cause weight gain then it was not unreasonable for readers to assume that if Seroquel was 'The only atypical with … a favourable weight profile across the full dose range' then it might be an atypical with no effect on bodyweight. This was not so. Arvanitis and Rak reported that the mean increase in weight was 2.2kg (n=1085). (Allison *et al* had reported that the mean increase in weight for risperidone was 2.1kg and 2.92kg for sertindole). Across the dose range for Seroquel, 75/150/300/600/750mg daily, the mean increase in weight was 0.9/2.9/2.0/2.6/2.3kg respectively. Jones and Huizar reported a mean increase in weight of 1.8kg with Seroquel therapy. Brecher *et al* reported on the long-term weight changes in 427 patients over 18 months. Weight change

differed over time from -1.53kg after weeks 40-52 (n=41) to +1.94kg after weeks 53-78.

The Panel noted that the relevant Seroquel SPC listed weight gain as a common (≥1% - <10%) adverse event which occurred predominantly during the early weeks of therapy.

Overall the Panel considered that the advertisement was misleading with regard to the effect on bodyweight that would be expected to be observed with Seroquel therapy compared with the other atypical medicines. Although the advertisement did not state 'no weight gain' as alleged it sought to differentiate Seroquel from other medicines in the class in that it was the only one with a 'favourable weight profile across the full dose range'. Given that the other medicines caused weight gain, the advertisement could be read as implying that Seroquel did not. This was not so. Similarly, the advertisement could be read as implying that Seroquel had a clear advantage regarding its 'favourable weight profile …' and this was not supported by the data submitted by AstraZeneca. The claim 'The only atypical with … a favourable weight profile…' was thus misleading and could not be substantiated. A breach of Clauses 7.2 and 7.4 was ruled. The Panel considered that the claim did not reflect the evidence regarding the side-effect of weight gain. A breach of Clause 7.9 of the Code was ruled.

Case AUTH/2296/1/10

PANEL RULING

The Panel considered that its rulings above in Case AUTH/2294/1/10 of breaches of Clauses 7.2, 7.4 and 7.9 applied here also. The Panel further considered that, given the data, high standards had not been maintained. A breach of Clause 9.1 was ruled.

Misleading prescribers about a potential side-effect of therapy could prejudice patient safety and this was referred to in the supplementary information to Clause 2 as an example of an activity likely to be in breach of that clause. On balance, however, the Panel considered that the circumstances were not such as to warrant a ruling of a breach of Clause 2 of the Code which was a sign of particular censure and reserved for such use. No breach of Clause 2 was ruled.

Case AUTH/2297/1/10

PANEL RULING

The Panel only considered allegations regarding material used in the UK.

The Panel considered that its rulings above in Cases AUTH/2294/1/10 and AUTH/2296/1/10 applied here also.

The complainant in this case appealed the Panel's ruling of no breach of Clause 2.

* * * * *

The Panel had considered the matter based on an email sent to complaints@pmcpa.org.uk and the links that appeared in that email. The Panel in error did not consider an almost identical email with additional attachments (including Spielmans and Parry, 2010) that was sent to the Director. Both emails and the attachments were provided to AstraZeneca together with the complainant's appeal.

* * * * *

APPEAL BY THE COMPLAINANT

The complainant noted that AstraZeneca had been unable to produce the certificate approving the advertisement from its archive. What proof, if any, did AstraZeneca have that it was ever approved?

The complainant noted that the Panel had failed to consider Spielmans and Parry (2010) due to an error for which it had apologized. Whilst the complainant encouraged the Appeal Board to read the whole paper, he referred particularly to pages 11 and 12 and the associated references.

The complainant noted that in an article in the online Pharmaceutical Journal, AstraZeneca had stated that 'In response to these complaints, AstraZeneca UK asserted to the PMCPA that it believed the content of the advertisement to be a fair and balanced reflection of the overall evidence relating to weight change associated with atypical usage at the time concerned. Given the historical nature of the complaint, AstraZeneca UK will not appeal the decision'.

The complainant questioned if AstraZeneca had accepted the Panel's decision and alleged a breach of Clause 2.

COMMENTS FROM ASTRAZENECA

AstraZeneca submitted that before it responded to the appeal, it had to first clarify the specific complaint that was the subject of the appeal. This clarification was important as significant additional information had been submitted by the complainant on appeal that was not relevant to the underlying complaint at issue.

AstraZeneca submitted that there was no clear articulation of a specific complaint. The complainant complained about promotional claims made for Seroquel as referenced in a recent File on 4 documentary first broadcast on BBC Radio 4 on 26 January 2010, but did not specify the particular claim that was the subject of his complaint. AstraZeneca noted that the only UK claim for

Seroquel referred to in this radio programme was one in an advertisement published in the British Journal of Psychiatry in April 2004, '…a favourable weight profile across the full dose range'. Therefore, the initial complaint now being appealed related only to that claim. The target audience of the advertisement in question was UK psychiatrists.

AstraZeneca did not agree with the complainant's contention that there was a breach of Clause 2. Clause 2 of the Code was reserved for cases in which activities or materials associated with promotion brought discredit upon, or reduced confidence in, the pharmaceutical industry; the supplementary information noted that a ruling of a breach of this clause was reserved as a sign of particular censure. This clause was not applicable in this case.

AstraZeneca did not agree that the complainant's reasons for appeal were valid and the rationale for this conclusion was set out below.

AstraZeneca noted that based on the subject of the underlying complaint (ie the challenged 2004 UK advertisement regarding '…a favourable weight profile across the full dose range' for Seroquel) the multiple enclosures and attachments submitted by the complainant as part of the appeal were not relevant. These irrelevant materials included:

- Spielmans and Parry and associated references
- Links to articles from the Washington Post and New York Times
- Internal AstraZeneca emails produced and used as exhibits in connection with the US litigation process

AstraZeneca noted that the complainant stated that the Panel had failed to consider Spielmans and Parry in its ruling due to an administrative error by the Authority. The complainant had requested that the Appeal Board consider Spielmans and Parry in relation to his appeal. To be clear, Spielmans and Parry provided a US context, and although the paper referenced Seroquel (among other medicines), the Seroquel references had no relationship to the advertisement at issue or to any alleged AstraZeneca practices. Therefore, AstraZeneca submitted that this paper was irrelevant and therefore not a valid reason for overturning the Panel's ruling of no breach of Clause 2. The content of the attached US news articles and internal emails likewise bore no relationship to the challenged 2004 UK advertisement and provided no basis for overturning the Panel's ruling.

The complainant also noted that AstraZeneca had been unable to produce the certificate approving the advertisement from its archive. As previously stated the certificate approving the advertisement was not available from the archive. Clause 14.6 stated 'Companies shall preserve certificates and the relevant accompanying information for not less than three years after the final use of the promotional material …'. The advertisement was last published over 5 years ago and the fact that the actual certificate was not available in the archive was not a substantive reason for overturning the Panel's ruling of no breach of Clause 2.

Finally, the complainant had also referred to a reactive statement provided by AstraZeneca to the Pharmaceutical Journal online. AstraZeneca submitted that this was made in response to public disclosure by a third party of a provisional Panel ruling in relation to one of three complaints above following on from the File on 4 programme. The complainant implied that such a statement indicated that AstraZeneca had not accepted the Panel's decision which was not the case. AstraZeneca had accepted the Panel's ruling. AstraZeneca did not understand how this reactive statement, which simply characterized AstraZeneca's initial position, was a reason for overturning the Panel's ruling of no breach of Clause 2.

AstraZeneca submitted that this case did not constitute a breach of Clause 2 as alleged. As previously stated, the 2003 Code stated a ruling of a breach of Clause 2 was a sign of particular censure and was reserved for such circumstances, which, as explained above, was not applicable in this case. Further, AstraZeneca contended that the complainant had failed to provide sufficient evidence to justify any reasonable grounds for appeal.

FINAL COMMENTS BY THE COMPLAINANT

The complainant stated that he was happy for the Appeal Board to review his comments, Spielmans and Parry and a transcript of the BBC File on 4 radio progamme (provided) and decide whether AstraZeneca had brought the industry into disrepute.

The complainant stated that from 1992 to 2001 he was employed by AstraZeneca Pharma UK and from 1995 to 2000 he was responsible for the medical aspects of the UK launch and subsequent marketing of Seroquel. The complainant alleged that when promotional materials were being prepared for the launch of Seroquel (September 1997) he was informed by a colleague that:

- certain members of the Seroquel headquarters team were attempting to coordinate the burying and manipulation of data to paint the product in a better light than the totality of the data suggested.
- That other members of the Seroquel headquarters team were being pressured and manipulated into aiding them.

A member of the Seroquel headquarters team had confirmed these allegations and provided more information. The complainant reported these allegations to his manager. They resolved to be

vigilant regarding the approval of marketing claims for Seroquel in the UK. This was done up until February 2000 when the complainant in effect left the company.

In the spring of 2009 the complainant became aware of a number of documents released onto the internet as part of class action lawsuits brought against AstraZeneca in the US regarding the promotion of Seroquel. These documents were usefully summarised in Spielmans and Parry.

APPEAL BOARD RULING

The Appeal Board noted that between 1997 and 2004 there was increasing evidence that weight gain was an issue with Seroquel. Spielmans and Parry reported that in July 2008 an internal analysis of quetiapine studies in schizophrenia conducted from 1993-1999, concluded that 'the incidence rate in adult patients with weight gain ≥7% in all trials was 18.2%'. In the 2004 SPC weight gain was listed as a common (≥1% - <10%) adverse event; in the 2009 SPC it was listed as a very common (>10%) event. There was also data to show that in terms of the amount of weight gained, Seroquel was no different to some other atypical antipsychotics. The Appeal Board was concerned that the claim 'The only atypical with placebo level EPS [extra-pyramidal symptoms] (including akathisia) and placebo level prolactin concentrations and a favourable weight profile across the full dose range' had favoured Seroquel in terms of its weight gain profile vs other atypical antipsychotics yet the evidence had not supported this.

The Appeal Board noted from the AstraZeneca representatives at the appeal that although the job bag for the advertisement at issue still existed, it did not contain the relevant certificate. The representatives stated that the company had not investigated how many times the advertisement at issue had been used or in which publications. The Appeal Board considered that generally it would be unusual for an advertisement to only be used once.

The Appeal Board was concerned about the lack of information provided by AstraZeneca about the generation of the advertisement at issue. It was also extremely concerned about email trails which implied that the company was keen not to disclose certain data. However, the Appeal Board noted that it was limited to making its decision based on activity in the UK and in that regard the advertisement at issue was the only one that had been specifically identified. The Appeal Board noted the Panel's ruling of breaches of the Code which had been accepted by AstraZeneca. The Appeal Board did not consider that the circumstances warranted a ruling of a breach of Clause 2 and so it upheld the Panel's ruling of no breach of that clause. The appeal was thus unsuccessful.

	Complaint received	**Case completed**
Case AUTH/2294/1/10	**26 January 2010**	**12 March 2010**
Case AUTH/2296/1/10	**26 January 2010**	**12 March 2010**
Case AUTH/2297/1/10	**27 January 2010**	**19 May 2010**