CASE AUTH/1857/6/06

CONSULTANT IN PUBLIC HEALTH MEDICINE v ROCHE

Activities regarding Herceptin

A consultant in public health medicine alleged that Roche, through various activities, had promoted Herceptin (trastuzumab) before the grant of its marketing authorization as an adjuvant treatment of HER2 positive, early breast cancer. For instance Roche's funding of the HER2 test for patients with early breast cancer had led to high expectations that patients with a positive result would be prescribed Herceptin. In that regard the complainant referred to an article which had been published on the website of the International Herald Tribune. When these expectations were unmet they had led to conflict which had undermined trust in the NHS as well as causing some criticism of Roche. The complainant further alleged that there was evidence to suggest that Roche had supported a patient group which pressurised public, political and media opinion in favour of Herceptin before it was licensed.

The complainant stated that Roche also appeared to be directly advertising to patients through its UK accessible HER2 website. On 27 April a headline in the patient section stated that, 'Study results show Herceptin reduces the risk of cancer coming back from women with early-stage HER2 positive breast cancer'. This was before a UK licence had been obtained and illustrated that promotion of the HER2 test was about encouraging patients to expect and demand Herceptin.

The complainant alleged that Roche had supported a patient group which had played a leading role in gaining media attention and pressurizing local and national politicians to fund Herceptin before its marketing authorization. Whilst Roche denied any direct funding, the patient group had reported by personal communication that it had been regularly directed to meeting key people and had supportive links with Roche or the public relation (PR) company that it employed. A Panorama programme, February 2006 reported that the leader of the patient group had visited Roche to give a motivational talk. There was also a summary of important links in a Guardian article, 'The selling of a wonder drug' March 2006, that suggested significant interference in the due processes by promoting Herceptin before marketing authorization.

The complainant stated that from The Guardian article there seemed to have been direct contact of a patient by Roche connected to the possible use of Herceptin. If this was true then it was worrying that Roche had obtained individual details and it was important to know where such information had come from. The complainant was also concerned that many patient groups had donations from pharmaceutical companies and some of those running Herceptin campaigns seemed to have encouraged patient contact when the medicine could not be obtained. One patient group site had a questionnaire on the delays in Herceptin availability, which asked, 'May we pass on your comments to the bodies listed above?' and it included Roche's name in the preamble.

The Panel noted that Herceptin had originally been authorized for the treatment of patients with metastatic breast cancer whose tumours overexpressed HER2. It was thus crucial to know a patient's HER2 status and the Panel noted the submission that establishing this at primary diagnosis was preferable to having to establish it once a patient had developed metastases. The DoH and a national cancer charity had both endorsed such action. Within that context the Panel did not consider that Roche's funding of HER2 testing encouraged patients with early breast cancer to expect that they would be treated with Herceptin. Roche's funding of the service would benefit patients and the NHS; there was no evidence that the service had been linked to the promotion of Herceptin. On the basis of the information before it the Panel considered that high standards had been maintained. No breach of the Code was ruled which was upheld on appeal by the complainant.

The Panel noted that a breast cancer patient, who was known to have received Herceptin therapy and who had set up a patient group, had been invited to talk to Roche staff about her experiences of living with cancer. In that regard the Panel did not consider it unreasonable for a company to invite a patient taking one of its medicines to talk to staff about their experiences. The Panel noted that the patient had only received her expenses and a bouquet of flowers; no monies were paid to the patient group. The Panel considered that any interaction between the group or one of its members and Roche was bound to attract attention. Nonetheless the Panel had no evidence to show that the interaction between the patient group leader and Roche had compromised the position of either. No breach of the Code was ruled which was upheld on appeal by the complainant.

The Panel noted that the patient group had been helped by a PR company, the contact between the two organisations had come about through an ex employee of Roche who worked for the PR company. Roche in the UK did not employ the PR company; it appeared that the only link with Roche and the PR company was through a global team based in Switzerland. The Panel thus considered that Roche had not influenced or supported the patient group through the PR company. No breach of the Code was ruled which was upheld on appeal by the complainant.

The Panel noted the complainant's reference to direct patient contact by Roche as reported in The Guardian. This matter had been considered in Case AUTH/1819/4/06. In that case, as in this case, the Panel noted Roche's submission that its PR agency had contacted a patient to ask her if she was interested in being involved in a breast cancer awareness programme for patients. The patient had already talked publicly about her disease. Roche had submitted that the conversation was short. In Case AUTH/1819/4/06 the Panel did not accept that the information before it was such as to show unequivocally that Roche had attempted to recruit the patient to promote Herceptin, that it had promoted Herceptin to her or had encouraged her such that she would ask her doctor to prescribe it. No breaches of the Code were ruled which were upheld in this case (Case AUTH/1857/6/06) upon appeal by the complainant.

The Panel noted that the article on the International Herald Tribune website had been prompted by an article in The Sun which had stated that Roche had promised money to train laboratory technicians to carry out HER2 testing. In response to a request, Roche had emailed the International Herald Tribune with brief details about its funding of HER2 testing. The Panel did not consider that the relatively short email, which was principally about Roche's funding of HER2 testing, promoted Herceptin. No breach of the Code was ruled which was upheld on appeal by the complainant.

With regard to Roche's HER2 website, the Panel noted that this was a site developed and produced by Roche in Switzerland. Roche in the UK had no input into it and nor did it promote the site in the UK. The Panel thus ruled no breach of the Code. Upon appeal by the complainant the Appeal Board noted from Roche that the website had been aimed at US citizens where promotion of prescription only medicines to the public was permitted. The Appeal Board noted that a Roche UK press release of 13 May 2005 included the website address under further information. The press release had originally been circulated, *inter alia*, to the lay media in the UK and remained available on the archive of the Roche UK website.

Taking all the circumstances into account and in particular noting that the website was aimed at members of the public in the US, the Appeal Board inferred that on the balance of probability at the relevant time, the site promoted prescription only medicines to the public. The Appeal Board thus considered that the reference in the press release of 13 May 2005, aimed at the lay UK media, to a website aimed at a lay US audience, amounted to promotion of a prescription only medicine to the public. The Appeal Board ruled a breach of the Code.

The Panel noted its rulings of no breach of the Code above and consequently ruled no breach of Clause 2 of the Code which was upheld on appeal by the complainant.

A consultant in public health medicine complained that Roche's funding of HER2 testing of patients and its involvement with a patient group had amounted to promotion of Herceptin (trastuzumab) before the grant of its marketing authorization as an adjuvant treatment of HER2 positive, early breast cancer.

COMPLAINT

The complainant alleged that Roche's funding of the HER2 test for patients with early breast cancer prior to Herceptin being granted a market authorization had led to high expectations that those patients with a positive result would benefit from Herceptin and therefore be prescribed it. When these expectations of early prescribing had been unmet they had led to conflict on a wide scale between patients, clinicians and primary care trusts (PCTs). Many PCTs had reasonably sought to await the detail of the licensing criteria in any marketing authorization before agreeing to fund the medicine for this new indication. As such these conflicts had undermined trust in the NHS as well as causing some criticism of the pharmaceutical company involved.

The complainant alleged that there was also evidence to suggest that Roche had sought to promote the role of a patient support group in pressurising public, political and media opinion in favour of the use of Herceptin before it was licensed.

The early promotion of Herceptin and the resultant pressures from patient groups and the media had directly led to political interference in the usual NHS processes for assessing and using a new medicine. This had caused considerable chaos and conflict. The advice on Herceptin use that came from the Department of Health (DoH) to the NHS was interpreted by many PCTs as a directive. This caused confusion in that it appeared to conflict with existing national policies on pharmaceutical licensing and on the role of the National Institute for Health and Clinical Excellence (NICE) in offering guidance on NHS priorities. The perception by many PCTs was that they would be taking unnecessary risks with patient safety by not waiting for the appropriate processes to take place.

The way that this issue arose had also caused some conflict between patients and PCTs with patients considering judicial review when their requests for funding were rejected. The adverse publicity that had been generated had also led to a misunderstanding by the wider community of what PCTs were trying to achieve with a consequent loss of confidence in the local NHS. It was obviously unhelpful to have different parts of the NHS in disagreement and a perception by some patients that the PCTs were acting perversely in not funding Herceptin before market authorization. A dangerous and irresponsible precedent had been set.

The complainant alleged that this unwarranted promotion of Herceptin had led to a fundamental clash between patients and clinicians on one side and

NHS commissioners on the other. Roche had played a part in this by unreasonably promoting Herceptin for early breast cancer before the medicine received its marketing authorization. The complainant noted from an article 'Roche step is positive signal on Herceptin' 9 December 2005 which appeared on the international Herald Tribune website (www.iht.com) that Roche had helped to fund the HER2 test for women with early breast cancer in the NHS and, with the consequent expectations of treatment for patients from a positive test, this could only be seen as promoting the use of the medicine before it received marketing authorization. Roche also appeared to be directly advertising to patients through its UK accessible HER2 website (www.her2status.com) (accessed on 27 April). It stated as a headline in the patient section that, 'Study results show Herceptin reduces the risk of cancer coming back from women with early-stage HER2 positive breast cancer'. This was before a UK licence had been obtained and again illustrated that promotion of the HER2 test was about encouraging patients to expect and demand Herceptin.

The complainant noted that the evidence that Roche had supported a patient group in its campaign for the funding of Herceptin was more circumstantial but nonetheless potentially serious and there appeared to be a case to answer. The patient group had played a leading role in gaining media attention and pressurizing local and national politicians to fund Herceptin before its marketing authorization. Whilst Roche had denied any direct funding, the patient group had reported by personal communication that it had been regularly directed to meeting key people and had supportive links with Roche or the public relation (PR) company that it employed. A Panorama programme of 5 February 2006 reported that the leader of the group had visited Roche to give a motivational talk. There was also a summary of important links in an article, 'The selling of a wonder drug' 29 March, in The Guardian that suggested significant interference in the due processes by promoting Herceptin before marketing authorization.

The complainant alleged that The Guardian article detailed the support for the patient group from a leading international PR and media company. Whilst the PR company stated that its support was 'pro bono', its UK section also had Roche as a client. It seemed naïve to expect people to believe that it was 'for the public good' when many might firstly disagree with the rationale behind the group's campaign in under cutting the process for drug licensing and secondly might also make a link with Roche through the PR company. Even if Roche had no direct involvement in encouraging the political campaigning of a key patient group so as to promote Herceptin, then it needed to be aware that it could be implicated in the PR chain through a company that it employed. Roche needed to be wary of this and to ensure that it exerted some contractual control over any PR or media support delivered through a third party so that it could not be accused of promoting a medicine before the grant of its marketing authorization.

The complainant further noted from The Guardian article that there seemed to have been direct contact of a patient by Roche connected to the possible use of Herceptin. If this was true then it was worrying that Roche had obtained individual details and it was important to know where such information had come from. The complainant was also concerned that many patient groups had donations from pharmaceutical companies and some of those running Herceptin campaigns seemed to have encouraged patient contact when the medicine could not be obtained. For example, one patient group site had a questionnaire on the delays in Herceptin availability, which asked, 'May we pass on your comments to the bodies listed above?' and it included Roche's name in the preamble. The complainant hoped that the link between the patient groups and the pharmaceutical companies did not extend to the misuse of this sort of information.

The complainant noted that Clauses 1.2, 20.3 and 20.4 should be considered in relation to the above.

When writing to Roche, the Authority asked it to respond, in addition to those clauses cited by the complainant, in relation to Clauses 2, 9.1, 20.1 and 20.4.

RESPONSE

Roche disagreed that its funding of HER2 testing services amounted to promoting Herceptin pre-licence variation.

Herceptin had been on the market in the UK since 2000, 'for the treatment of patients with metastatic breast cancer whose tumours overexpress HER2'. When Herceptin was introduced HER2 testing was not carried out routinely in the UK. Following discussions with leading oncologists and the NHS, Roche funded HER2 testing for the NHS using only three quality-assured reference laboratories for a period for 3 years. Roche submitted that this provision of a medical service was consistent with Clause 18.4.

In addition Roche submitted that it and most leading breast cancer specialists had consistently advised (since the launch of Herceptin for metastatic breast cancer) the early HER2 testing of patients at primary diagnosis. This advice pre-dated the advent of data supporting adjuvant use of Herceptin in 2005.

Roche submitted that the over expression of HER2 in breast cancer was associated with a worse prognosis. HER2 positivity halved patient survival compared with HER2 normal patients (Slamon et al, 1987). This alone justified testing at diagnosis in order to fully inform patients of the nature of their illness. There were also other reasons for HER2 testing at primary diagnosis unrelated to the use of Herceptin in early breast cancer - or indeed in metastatic breast cancer. Early testing (prospective testing) had a number of advantages over late, or retrospective testing.

- The prognostic value of HER2 status might

influence patients and clinicians in their choice of licensed treatments in the adjuvant setting.

- HER2 positive tumours responded better to aromatase inhibitors and anthracyclines in the adjuvant setting than HER2 negative tumours. Clinicians used this information in their decision making on treatments.

- Testing at the time of metastases was often associated with significant delays in establishing the HER2 status. If the test was delayed until advanced stages of breast cancer, which might be several years following initial diagnosis the patient's original tumour block needed to be retrieved from storage - where it might have been held for many years. Blocks could become damaged or lost, or the sample might degrade over time. Moreover, the costs incurred in retrieving the blocks meant that it could be more expensive to test at recurrence.

- Both audits and feedback from clinicians indicated that retrospective testing was often associated with delays, usually of several weeks. When dealing with aggressive metastatic cancer these delays might be clinically significant - with failure, or suboptimal treatment. The knowledge of HER2 status at the time of relapse allowed appropriate treatment to be instigated immediately. If HER2 status was unknown at the time of relapse the window of opportunity for optimal treatment could be missed.

- Early testing was recommended by some guidelines (Bilous *et al* 2003; St Gallen guidelines 2005).

HER2 positivity had clinical relevance beyond the use of Herceptin and early testing allowed better patient management. Similarly it was important that both the treating physician and the patient knew the HER2 status so that the necessary discussions about disease management could be held, and subsequent informed consent granted by the patient.

Roche submitted that despite the consensus that early testing was optimal, by September 2005 only 38% of breast cancer patients were HER2 tested at primary diagnosis. Subsequently, in October 2005 senior government officials issued statements that all early breast cancer patients should be tested for HER2 status at initial diagnosis. This was in part in response to the Herceptin adjuvant trial results but the decision was not influenced by Roche. At the time Roche did not sponsor HER2 testing. Many cancer networks were totally unprepared for the above statements and were unable to implement universal HER2 testing in a timely fashion. Indeed the complainant mentioned this ie 'the advice on Herceptin use that came from the DoH to the NHS was interpreted by many PCTs as a directive'. Moreover this part of the complaint seemed to be more about confusion relating to the NHS interpretation of guidance. There was no evidence that Roche had contributed to this or to the 'conflict between patients and PCTs leading to judicial reviews' which the complainant detailed.

Roche submitted that it was as a result of the statements on HER2 testing detailed above and subsequent discussions with the DoH that Roche agreed to support HER2 testing. Depending upon the network's particular need, Roche offered training for laboratory staff, help with development of local business case development, test kits, funding for laboratory staff for an agreed period or funding for tests to be done via a commercial laboratory. The company consulted and collaborated with the government throughout this process. Roche offered support to all cancer networks - currently 32 networks had an agreement with it. Some networks had not taken up the offer - so Roche's support was not universal.

Based on the above rationale, Roche therefore refuted the allegation that its support and funding for HER2 testing ahead of Herceptin's license extension in early breast cancer had promoted the medicine prior to the grant of its marketing authorization. Given the clinical rationale for determining HER2 status, together with the pre-existing licence of Herceptin in metastatic disease and the recommendation from the DoH that all women should be tested Roche considered its support of HER2 testing complied with Clause 18.4 of the Code, and benefited the NHS.

Roche submitted that it had never set out to promote Herceptin to the public or to encourage the public to request it by name. The publicity surrounding Herceptin in early breast cancer was due to the unprecedented results of the pivotal studies cancer presented at the American Society of Clinical Oncology (ASCO) in the Spring of 2005.

Four independent studies had been conducted in the use of Herceptin in adjuvant disease. In April 2005 the National Cancer Institute (NCI) announced the first in a series of results for Herceptin use in the adjuvant setting showing a 52% reduction in the risk of breast cancer relapse in HER2 positive patients. Three weeks later a European breast cancer specialist group made an unplanned presentation to the ASCO announcing the HERA data, from a pre-planned interim analysis. Data from these trials received an extremely strong response from ASCO attendees, which included mainly oncologists, but also members of UK patient organisations and media. Post ASCO, it was clear that the data had had a high impact globally, with oncologists around the world changing practice ahead of an official licence. The data were subsequently published as two separate papers and an editorial in the New England Journal of Medicine (NEJM) in October 2005. This issue of the journal included the two pivotal studies, and an editorial which included a comment that some patients might be cured. This was the most prestigious journal in the world, and it was not surprising that the results were highly influential. None of the comments in the NEJM were influenced by Roche.

Given the strength of the data, the strong clinical support for Herceptin, the patient group support for

the medicine and the media environment (eg Kylie Minogue's breast cancer diagnosis) the news was widely covered. The newspapers continued their interest in Herceptin and breast cancer. Over this time, Roche had answered many media queries. On occasion, there had also been the need to send out a press statement to clarify facts and correct mis-reporting. However Roche had also refused interviews with media and participation in television programmes such as Panorama so as to avoid fuelling the media debate around Herceptin - especially at a time when regulatory submissions were being made.

Roche submitted that given its portfolio of products it was not surprising that it had financially supported charities which helped people and their families affected by cancer. This financial support did not compromise the impartiality and integrity of patient groups and activities adhered to the Code.

Roche submitted that a full list of the charities that it supported was available on its website (www.rocheuk.com). Roche had also developed patient group contracts for activities in 2006 to ensure that patient groups retained their impartiality and integrity. This support was within the remit of the ABPI and was not done to influence such groups. Funding was associated with specific projects, such as sponsorship of an event. Roche did not influence the content or programmes of these events. Roche's support featured on any written material associated with these activities.

A number of charities had regularly commented to the media about Herceptin, many of whom had representatives independently present at the HERA data presentation at ASCO. Roche had not sought to influence such charities. In fact one of the most vocal advocates of the strength of the Herceptin data had received no funding from Roche. Another had been vocal in its criticism of Roche for what it perceived as the company's delay in applying for an adjuvant licence.

The complainant highlighted a questionnaire on a patient group website which asked 'May we pass your comments to the bodies listed above [inferring Roche]'. Roche did not know about the questionnaire until informed by the complainant, and it had never received any patient information from the patient group in this regard.

Roche submitted that following presentation of the HERA results at ASCO it had found out about a new patient organisation led by a metastatic breast cancer patient who had originally been treated with Herceptin through an expanded access programme. Roche was asked to fund this group, however given the nature of its campaign the company considered such funding wholly inappropriate for the reasons outlined in the complaint. Thus Roche had not funded this group.

Both The Guardian article and a Panorama programme (cited in the complaint), recognised that there was no evidence of Roche attempting to influence this patient group. As a responsible and ethical pharmaceutical company Roche had provided factual information to the patient organisation on request which was very much in line with requests from the other patient organisations. This included anticipated regulatory and NICE timelines and cost. Roche never encouraged the group to ignite a media campaign.

Roche noted that the complainant had stated that the patient group had been '…regularly directed to meeting key people and had supportive links with Roche'. Roche submitted that it had not directed this group to key people nor had it offered it any support or encouragement to obtain Herceptin prior to licence. The complainant referred to the Panorama programme which suggested that the leader of the group was invited to give a motivational talk at Roche. The patient was invited to speak to Roche international staff who worked in research and development (not sales and marketing) who were involved in the development of cancer medicines but not as a motivational talk; it had nothing to do with motivating sales of Herceptin. The title of her presentation was 'Breast Cancer - a patient's perspective' and as suggested by the title was about her experience of living with the disease; her presentation was not about Herceptin, though she referred to this once when discussing her overall treatment. Roche had not sponsored or in any other way encouraged the patient to speak to any other groups.

In response to a request for further information Roche explained that there were two separate organizations based at its head office site; Roche Pharma Development (PD) which was a global function that dealt with the development of new medicines and regulatory affairs on an international basis and Roche Products Ltd which was the UK marketing affiliate. Staff in PD organised a series of seminars on general interest topics that were not necessarily work-related.

The invitation to talk to the group was offered to the leader of the patient group who was known to the company as a person living with breast cancer and who had been treated with Herceptin. She had subsequently set up the patient group.

The leader of the patient group spoke about her illness and sequence of treatment. No honorarium was paid but she was presented with a bouquet. Her travelling and accommodation expenses were paid (details were provided).

In summary this was not an official company meeting organised by the UK affiliate of Roche for motivational purposes but a meeting organised by a group of employees of PD who arranged occasional seminars for staff on topics of interest.

With regard to the suggested a link between Roche, a PR agency and the patient group referred to in The Guardian, the facts were that an ex-employee of Roche currently working at the PR agency, offered pro-bono media support to the group. This ex-

employee knew of the patient group leader from her employment at Roche. However the offer from the PR agency was not funded or driven by Roche in any way and was a matter for the PR agency. The complainant stated that the PR agency had Roche as a client thus implying Roche must have been involved.

Roche submitted that Roche UK did not employ the PR agency. However a global team, based in Switzerland, employed the PR agency in 2005. Given that Roche UK did not work with the PR agency, and that the PR company's decision to offer unpaid service to the patient group was its decision and outside the control of Roche, it did not agree that 'Roche should be implicated in the PR chain of events', and that it promoted Herceptin to the general public.

In conclusion, Roche noted that patient groups were there to service and support their patients and members that they represented and whilst this would encompass a whole series of important initiatives, access to medicines that had the potential to prolong and save lives had been, and would continue to be an important area for patient groups to engage.

Roche noted that the complainant had referred to The Guardian article in which it was alleged that Roche had approached an individual patient and encouraged her to 'promote Herceptin'. Roche confirmed that the patient was approached by its PR agency shortly after she had appeared in The Observer talking about her HER2 positive breast cancer. The patient was telephoned to see if she would be interested in becoming involved in a general breast cancer awareness project. Roche submitted that in the interests of balance and integrity, the project would have provided information on all diagnostic tests that should be conducted, such as HER2, progesterone receptor and oestrogen receptor and not any individual test or any specific treatment. Due to the brevity of the conversation with the patient when she said that she was not interested in taking part, the PR agency was unable to outline the full scope of this planned activity. No pressure was placed on the patient to participate in the project when she said she wasn't interested. In the end the project was not developed as Roche considered that it had been superseded by the DoH's announcement on HER2 testing discussed above.

Roche submitted that the patient had been invited to participate in this project because of her previous willingness to appear in The Observer talking about her breast cancer and as a guest on television and radio discussion programmes. At no point did Roche or its PR agency offer a financial incentive to become involved, offer to arrange access to the treatment, ask her to promote Herceptin or speak at seminars.

Roche considered that the telephone call had been misrepresented in the newspaper article and it further objected to the untrue allegation that it was 'running a big campaign to promote Herceptin'. Indeed Roche's approach was more accurately represented in this article by the patient who stated that it had provided facts when asked but was quoted as saying Roche 'did not help her campaign at all' and 'they don't' want any involvement with the campaign'.

Roche noted that the allegations made in The Guardian had been reviewed by the Medicines and Healthcare products Regulatory Agency and no breach of Regulation 7 of the Advertising Regulations was found.

In summary Roche submitted that it had acted responsibly, and had not sought to promote Herceptin to the general public or threaten the integrity of the pharmaceutical industry.

Roche submitted that other activity outside of its control had been legal action of patients seeking to gain access to the treatment; the solicitor acting on behalf of these individuals had employed the service of a media relations agency. This again was without Roche's knowledge and there had been no communication between this communications agency, Roche and any other communications agency acting on its behalf. In fact the first that Roche knew about the involvement was when a journalist contacted the communications department at Roche and said they had received a call from its public relations agency.

In summary Roche submitted that the unprecedented interest in Herceptin was due to:

- The strength of the data presented at ASCO and published in the NEJM which showed that this class of medicines was dramatically changing the course of breast cancer.
- The strong clinical support for Herceptin from breast cancer specialists, which was almost universal.
- The media environment (eg Kylie Minogue's breast cancer diagnosis).
- The patient group support for the medicine (as deemed by their medical advisory committees).
- Patient legal action and solicitor-driven publicity.
- Individual patient campaigners.

Roche submitted that the significant interest in Herceptin was not due to a campaign organised by Roche and it had not sought to promote Herceptin to the general public. Conversely Roche had tried to maintain a degree of fairness, balance and accuracy in the reporting of Herceptin and to manage expectations about the treatment. Due to a series of events not in the control of Roche, its communications department had answered a lot of media enquires relating to Herceptin.

Roche hoped the above helped explain how its activities were developed and implemented. Roche considered its activities to be responsible, and within the letter and the spirit of the Code, and had not

compromised the impartiality and integrity of patient groups. Roche did not consider it had promoted Herceptin (Clause 1.2) or that its actions had discredited the industry (Clause 2), and that it maintained high standards (Clause 9.1). Roche had not advertised a prescription medicine to the public (Clause 20.1). Roche had never sought to encourage members of the public to ask their doctors for a specific medicine (Clause 20.2). Roche had supported patient groups, in line with the Code, to ensure impartiality and integrity (Clause 20.3). Roche had made factual information about Herceptin registration, NICE guidelines and cost, available to patient groups who had requested such. Finally, Roche had never advised members of the public on personal medical matters (Clause 20.4).

In response to a further request for more information Roche noted that the complainant had referred to an article that had appeared on the International Herald Tribune's website detailing Roche's provision of £1.5million HER2 testing funding support to the NHS. The International Herald Tribune had asked Roche for details of this financial support following the publication of an article in The Sun newspaper which gave brief details of an agreement between Roche and the DoH for Roche to provide financial support to help the NHS cope with an expected surge in the demand for HER2 testing. Roche had had no involvement with the article in The Sun.

The International Herald Tribune asked Roche why, as this was potentially a 'good news' story, had Roche not released details of it to the media. Roche replied that it had decided not to release these details to the general media, due to concern it would ignite media interest in Herceptin, prior to a decision on licence. As the information had already appeared in The Sun and the International Herald Tribune had specifically requested them, the details were sent in a non-promotional email that reiterated the company's original decision not to release details of this funding commitment. The article which was balanced in tone appeared the following week.

Roche also noted that the complainant had referred to a website which discussed the importance of HER2 testing. This website was developed and produced by Roche group headquarters in Switzerland. Roche UK has had no input into the website is nor did it promote it in the UK. Clause 21.2 stated 'Information or promotional material about medicines … which is placed on the internet outside of the UK will be regarded as coming within the scope of the Code if it was placed there by a UK company or an affiliate of a UK company or at the instigation or with the authority of such a company'. Given that Roche was a Swiss company and that Roche UK had had no involvement in the development or content of the site, nor did it use the web address in promotional materials or promote it within the UK, the company considered the complainant's reference to this site was outside the scope of the Code and the responsibility of Roche UK. In the section of the website that detailed patient support groups Roche noted that a range of such organisations were listed from a range of countries. The inclusion of hyperlinks to UK-based patient support information appeared to be in the context of providing the most appropriate support and information to patients, some of which happened to originate from UK charity sites and certainly did not indicate that Roche in the UK intended UK patients to visit this site.

PANEL RULING

The Panel noted that Herceptin had originally been authorized for the treatment of patients with metastatic breast cancer whose tumours overexpressed HER2. It was thus crucial that a patient's HER2 status was known and the Panel noted the submission that establishing this at primary diagnosis was preferable to having to establish it once a patient had developed metastases. The DoH and a national cancer charity had both endorsed such action. Within that context the Panel did not consider that Roche's funding of HER2 testing encouraged patients with early breast cancer to expect that they would be treated with Herceptin. Roche's funding of the service would benefit patients and the NHS; there was no evidence that the service had been linked to the promotion of Herceptin. On the basis of the information before it the Panel considered that high standards had been maintained. No breach of Clause 9.1 was ruled.

The Panel noted that a breast cancer patient who had set up a patient support group had been invited to talk to Roche staff about her experiences of living with cancer, she was known to have received Herceptin therapy. In that regard the Panel did not consider it unreasonable for a company to invite a patient taking one of its medicines to talk to staff about their experiences. The Panel noted that the patient group leader had not received any payment as such - only her expenses and a bouquet of flowers; no monies had been paid to the patient group. The Panel considered that any interaction between the group or one of its members and Roche was bound to attract attention. Nonetheless the Panel had no evidence to show that the interaction between the patient group leader and Roche had compromised the position of either. No breach of Clause 9.1 was ruled.

The Panel noted that the patient group had received some help from a PR company, the contact between the two organisations had come about through an ex employee of Roche who worked for the PR agency. Roche in the UK did not employ the PR agency; it appeared that the only link with Roche and the PR agency was through a global team based in Switzerland. The Panel thus considered that Roche had not influenced or supported the patient group through the PR agency. No breach of Clause 9.1 was ruled.

The Panel noted the complainant's reference to direct patient contact by Roche as reported in The Guardian. This matter had been considered in Case AUTH/1819/4/06. In that case, as in this case, the Panel noted Roche's submission that its public

relations agency had contacted a professor to ask her if she was interested in being involved in a disease awareness programme for breast cancer patients. The professor had already talked publicly about her disease. Roche had submitted that the conversation was short. In Case AUTH/1819/4/06 the Panel did not accept that the information before it was such as to show unequivocally that Roche had attempted to recruit the professor to promote Herceptin, that it had promoted Herceptin to her or that it had encouraged her such that she would ask her doctor to prescribe Herceptin. No breaches of Clauses 20.1 and 20.2 were ruled.

The Panel noted that Roche had not known about the patient questionnaire on the patient group website until it had received this complaint. Given the company's lack of involvement the Director determined that there was no *prima facie* case to answer.

The Panel noted that the article which had appeared on the International Herald Tribune website had been prompted, in the first instance, by an article in The Sun which had stated that Roche had promised more than £1million to train laboratory technicians to carry out HER2 testing. In response to a request from a correspondent on the International Herald Tribune, Roche had provided brief details about its funding of HER2 testing. The Panel did not consider that the relatively short email from Roche to the correspondent promoted Herceptin. The email was principally about Roche's funding of HER2 testing not about Herceptin. No breach of Clause 20.1 was ruled.

With regard to the website HER2status.com, the Panel noted that this was a site developed and produced by Roche in Switzerland. Roche in the UK had no input into the site and nor did it promote the site in the UK. The Panel thus ruled no breach of Clause 20.1.

The Panel noted its rulings of no breach of the Code above and consequently ruled no breach of Clause 2.

APPEAL BY THE COMPLAINANT

The complainant noted that he had complained about the promotion of Herceptin for its use in early breast cancer, before it had been given the appropriate marketing authorization to try and make pharmaceutical companies aware that it was unacceptable to create a climate where commissioners of healthcare were put under severe pressure to act against major policies. This pressure with Herceptin came from the public, patients, press and clinicians, and was focussed through the politicians such that a number of commissioners felt obliged to undermine the law regarding market authorization and circumvent the national policy on using NICE to advise on NHS funding. The complainant wanted to ensure that NHS commissioners had the appropriate time to consider the clinical evidence, safety and cost effectiveness of a new treatment without taking undue risks with patients' safety or NHS funds. The complaint was not about the use of Herceptin for metastatic breast cancer.

The complainant alleged that Roche's timing of financial support for HER2 testing through the NHS in 2005 belied the arguments about the value of the test as a prognostic indicator. Whilst the HER2 test might have value as a prognostic indicator for a clinician this was not the business of Roche. Press releases from Roche clearly related the HER2 test to the use of Herceptin for patients . The press release from Roche dated 13 May 2005, which quoted a leading clinician endorsed the obvious link between the HER2 test and Herceptin: 'This is a very important advance for patients with so-called HER2 positive breast cancer, which is generally more aggressive. We now need to make plans quickly for measuring the HER2 status of all breast cancer patients at diagnosis, to determine everyone who could benefit from such treatment.'

The complainant alleged that the press release continued to emphasise the link between the diagnostic test and treatment through to the notes section. Whilst early testing might be useful, the context at this time was that the research was not published in a peer-reviewed journal and Herceptin was a year away from authorization in the UK. As such the encouragement to use the test prejudged the marketing authorization and was highly likely to lead patients, who might have had the test following early breast cancer, to expect that they should receive the medicine. This in turn undermined the independence of the licensing authority, the EMEA, as well as the role of NICE.

The DoH endorsed the funding of early HER2 testing following the support of senior government officials. This action was seen as misguided by many as it caused a conflict between national policies (the Medicines Act and NICE authorization) and subsequent chaos amongst NHS funding authorities (PCTs in England and local health boards in Wales). One senior government official, whilst encouraging the funding of Herceptin, acknowledged this legal conflict in a speech on 25 October 2005 without clarifying how this could be resolved by PCTs. This political action could be seen as promoting the use of a medicine before its market authorization although where that sat with individuals in terms of the Medicines Act was not clear. The DoH letter of 17 October 2005 linked HER2 testing with the assumption that Herceptin was to be licensed and to be given NICE approval. However, this unprecented political action could not be interpreted as an invitation for Roche to participate and become part of the unwarranted promotion of Herceptin at this early stage.

The complainant provided copies of letters and emails relating to funding by Roche of the HER2 test to a local cancer network. A letter from Roche was very specific in its expectations and from comments in the emails its representative was seen as pushing the commissioning clinician into an arrangement she was unhappy with.

Part of this was an unease with the fact that Roche wanted to be given the data from the HER2 test results. Why Roche needed this data if it was only supporting a DoH initiative was unclear and could only lead to the inference that it was for commercial reasons related to the marketing of the Herceptin.

As regards Clause 18.4 of the Code the complainant presumed that the provision of patient services to the NHS was only intended to relate to general support and not to the funding of services such as the HER2 test that promoted a specific product particularly when the product was not licensed. As stated before, the timing and nature of this sponsorship suggested that it was largely intended to raise the pressure for Herceptin to be funded in advance of marketing authorization and also to make that authorization appear inevitable.

The complainant noted the points raised by Roche about the ASCO conference and the HERA trial. Many healthcare commissioners saw this conference as an important place for the early promotion and marketing of pharmaceuticals that had yet to be fully assessed and given marketing authorization.

The complainant noted that the ASCO conference in late spring appeared to be well orchestrated in the way that it promoted new treatments in a commercial way. Immediately preceding the 2005 conference Roche issued an investor update, dated 28 April 2005, on its worldwide website in which it announced the interim analysis of the HERA trial. In this case the reference by Roche in its response to 'an unplanned presentation' was misleading. The ASCO conference had specific sessions for 'late-breaking results' and a publicity machine that would make the most of any announcements on interim results. There were well-recognised problems with presentations at conferences that announced incomplete analyses (neither peer-reviewed in a journal nor validated for presentation for marketing authorization). These problems, often of undue optimism based on incomplete results (Montori *et al* 2005), were likely to be compounded by the attendance at conferences, such as ASCO, of the media, UK patient organisations and the public. Clearly it was not just a conference for the exchange of information between clinicians and researchers.

The complainant alleged that the group that had made the 'unplanned announcement' had collaborated with Roche in the HERA trial (Roche UK press release 13 May 2005). From the complainant's knowledge of research trials this usually meant that the sponsoring pharmaceutical company would have a well-specified contract with the trial participants and therefore some control over how, when and where the results were presented. Roche also had some sponsorship of ASCO and it was important to know if this included direct sponsorship of the conference where its trial results were presented.

The complainant alleged that there was no disputing the widespread interest and media environment around Herceptin at this time. The reasons for this were not as straightforward as Roche suggested. The expectations from new research could be given a large boost by the one-sided publicity and marketing that could be engineered by careful targeting at an ASCO conference. The wider view that emerged from the evidence and the media impact was that an astute pharmaceutical company such as Roche could set its marketing campaign alight at ASCO.

Searching Roche UK's media release archive for Herceptin brought up one news item. This was the press release dated 13 May 2005 referred to above which acknowledged the role of the influential ASCO conference. There were also a number of press releases on Roche's international website that were listed as media or investor updates at around the same time. Whilst these could be seen to be general marketing for a large multinational company, issuing such a specific press release in the UK was marketing that was inappropriate under the Code.

The complainant alleged that there was also an issue around the Herceptin research data, and the interpretation of the data by the public and breast cancer patients, that in its marketing was misleading and inappropriate. This point emphasised again the context, which led to the political pressure and the consequent pressure on PCTs. There were a number of examples where patients and even an MP thought that being given Herceptin allowed patients to survive and being denied it meant death. It was not surprising that patients and a lot of the public viewed PCTs as perverse in not funding Herceptin at an early stage. In reality the prognosis for early breast cancer was relatively good and was one of the reasons that Herceptin had a number needed to treat (NNT) of the order of 16 to allow one extra patient to survive at four years. Much of the data was presented as relative risk information rather than as the more meaningful absolute risk information and often the figure of a 50% decrease in disease recurrence was used without a clear explanation of the survival data. Given this issue it would be useful to have more of the press statements that Roche referred to in its response to the complaint as being helpful to clarify facts and correct misreporting.

The complainant alleged that Roche had acknowledged the role that the ASCO conference played but completely understated its part in helping to set up this role and allowing the subsequent patient, media and political campaigns to gather force so as to pressurise healthcare funders.

The complainant noted that the patient group, founded by the breast cancer patient who had subsequently given a talk to Roche personnel, had played an unprecedented role in raising the profile of Herceptin in the UK. For this reason and those given in more detail below it was important to see more evidence from Roche regarding the link between Roche in Switzerland and the PR agency which had helped the patient group.

The complainant alleged that the patient group had gained widespread local and national publicity and as

a consequence had directly influenced local and national politicians who in turn were unhappy about the adverse newspaper comment that it generated for the Government. This sequence of events was fundamental to the national polarisation of views around Herceptin and the conflict that occurred between PCTs and the DoH, as well as seeing conflict between PCTs and their patients on a scale that had not occurred before. This explanation was important not just to understand the importance of this patient group but also to try and understand how it happened.

The patient group was founded by a breast cancer patient, who had also set up a registered eponymous breast cancer charity with local aims and an income of around £8,000 in 2004. The complainant submitted that it did not seem rational to outside observers that such a small group should be courted by one of the top ten international public relations company, which was linked with the sixth largest pharmaceutical company in the world, without there being some longer term aim. Given that Roche UK had refused to fund this group, it seemed dangerous territory for a subsidiary company in the same building to invite the patient group leader to give a talk when that patient group was not a charity but had specific aims to widen the use of Herceptin. The patient group was not set up after the leader of it talked to Roche staff in December 2005; it was already well established by the middle of 2005.

The complainant suspected that Roche was right in stating that there was no evidence of it attempting to influence this patient group. However, given the uncertainties that were raised about possible links it was important to see evidence relating to the links between the Roche global team and the PR agency. The importance of this was that the PR agency had a reputation for fostering conflicts of interest. A disconcerting example was that a president from the PR agency had lead a conference session on guerrilla media tactics – generating buzz on media radar without news. This was a remarkably apt description of how the PR agency affected the campaign of the patient group. Many would not see this as pro-bono activity when it actually cut across the public interest by undermining the Medicines Act. It was important to have the details of the Roche/PR agency relationship clarified.

The complainant noted that Roche stated that Roche UK had no involvement in the development or content of the HER2 testing website. At the time it was accessed and before UK market authorization had occurred this website carried a news update box on the patients' home page stating: 'Interim analyses of three major Herceptin studies show that Herceptin has the potential to significantly increase the length of time after treatment during which no disease is found (disease-free survival) for women with early-stage HER2 positive breast cancer'. The complainant submitted that it was disingenuous to claim that as a subsidiary company there was no responsibility at Roche in Switzerland or in the UK for the role that this website could play. Other parts of Roche should know well that their activities might impact on the legal position of a company such as Roche UK and should be cautious in their role where they might be seen to be promoting a medicine ahead of its market authorization.

The complainant submitted that Roche UK was well aware of this website. The news article on Roche UK's website under the media release archive section (dated 13 May 2005) listed the website address at the end of a section headed, 'About breast cancer and Herceptin'. This contradicted Roche UK's statement that it did not use the web address so as to promote it within the UK and negated the disclaimer on the website. It also suggested that Roche UK was well informed about the website and was in close communication with its Swiss headquarters. Some of the information contained in an investor update from Roche International's website (dated 28 April 2005) was identical to some of that in the Roche UK press release. This update also included the website address, www.HER2status.com. By its very nature a press release was about publicity. A complaint with some parallels although obviously differing in the details was upheld as a breach of the Code at appeal (Case AUTH/1801/2/06).

In summary, the complainant submitted that the unprecented interest in Herceptin that Roche itself highlighted was initiated at the ASCO conference and supported in a number of ways by both Roche International and Roche UK.

The complainant alleged that it was difficult to separate the worldwide campaign from the initiatives in the UK as the evidence linked both. To deny that there were close links between the headquarters and its subsidiary and that their responsibilities were interrelated would undermine the Medicines Act. The promotion of the HER2 test and, more importantly, the way that the test was funded in advance of market authorization so as to raise the expectations of patients that they would receive Herceptin were both evidence that Roche UK sought to prematurely promote the funding and use of the medicine.

The complainant alleged that there was much other evidence as discussed above that gave a context to the unprecedented interest in Herceptin. The number of factors that Roche described in its response were set in train at the ASCO conference and fostered by Roche. Healthcare commissioners in the UK needed to work well with the pharmaceutical industry in the interests of the patients and the wider public. If the Herceptin scenario was not to be repeated then the Appeal Board must consider seriously the documented breaches of the Code.

COMMENTS FROM ROCHE

Roche reiterated that HER2 status was a key prognostic indicator, and that it initially supported HER2 testing prior to the adjuvant data becoming available. In addition to the details previously provided, a group of experts had recently published

new guidance on risk assessment in early breast cancer which demonstrated the importance of HER2 status in defining risk and in deciding whether treatment with chemotherapy was appropriate. The guidelines considered that no patient with a HER2 positive tumour could be classified as 'low risk' (Goldhirsch *et al* 2006).

Roche submitted that patients should know the nature and prognosis of their disease and that clinicians should take informed decisions regarding their management, particularly as approximately 77% of patients were HER2 negative and did not require HER2 targeted therapy such as Herceptin. These patients had less aggressive tumours and a better prognosis.

Similarly, whilst Roche acknowledged the complainant was concerned about Herceptin in early breast cancer, it was important to note that Herceptin had been licensed for 6 years in metastatic disease. As previously stated, 5 years after Herceptin was licensed in metastatic disease, only 38% of breast cancer patients were HER2 tested at primary diagnosis. This meant that in September 2005, 62% of patients did not know their HER2 status on diagnosis, clearly not optimal for their disease management. Therefore the rationale for HER2 testing was just as important for metastatic patients as it was for adjuvant patients.

Roche submitted that its financial support of HER2 testing services was in response to Government statements that all breast cancer patients should be HER2 tested on initial diagnosis. The complainant himself had noted that the DoH had endorsed the funding of HER2 testing and cancer networks had been encouraged to liaise with Roche regarding HER2 testing. Given Roche's support and extensive knowledge about HER2 testing services from its experiences in metastatic disease it would have been surprising if it had not been involved in an initiative aimed at ensuring that all breast cancer patients were HER2 tested on diagnosis.

Roche considered that funding HER2 testing that had prognostic importance, in response to ministerial and NHS statements, was not promotion of Herceptin as made clear previously and did not undermine the independence of the licensing authority, the EMEA or NICE and complied with Clause 18.4 of the Code.

Roche noted that the complainant referred to a quote from a leading clinician in its press release of 13 May 2005. This media release was issued by Roche UK in relation to the publication of the HERA trial at ASCO; the principal UK investigator stated 'This is an important advance for patients with so-called HER2 positive breast cancer, which is generally more aggressive. We now need to make plans quickly for measuring the HER2 status of all breast cancer patients at diagnosis, to determine everyone who could benefit from such treatment'. The main body of the press release also highlighted that 'the infrastructure needs to be in place to cope with an increased demand for HER2 testing when Herceptin becomes more widely used for early stage breast cancer'.

Roche submitted that the interest in Herceptin highlighted the low level of HER2 testing in the UK, in September 2005 only 38% of patients were being tested. Roche submitted that it had not breached the Code in highlighting that HER2 testing services needed to be improved and did not agree that these statements constituted promotion of its medicine prior to marketing authorization. Also the decision to encourage HER2 testing at initial diagnosis was taken by the DoH as noted above.

Roche had reviewed the correspondence provided by the complainant relating to funding by Roche of the HER2 test for a local cancer network. With regard to the company's expectations Roche submitted that it was not good practice to simply award grants without a specific agreement in place, and to ensure that funding was being used in accordance with the Code. Roche was willing to fund the specific needs of each network in setting up an efficient HER2 testing service; it thus specified very clearly exactly what the funding was in order to avoid any subsequent issues.

With regard to wanting data from the HER2 test results, Roche explained that before embarking upon this project it undertook to tell the Cancer Action Team at the DoH how many tests were being conducted and the numbers that were HER2 positive in each cancer network. These data contained no individual patient information and were not related to commercial activity. Roche had discussed with the National External Quality Assessment Service issues about handing over this information to help it with quality assessments. Confidentiality was clearly laid out in the initial agreement.

Roche understood that the Cancer Action Team nominated a HER2 lead in networks following the initial DoH announcement, and this person would be the Roche contact for service development. The majority of networks met with Roche fairly early in the process (before the end of 2005) and it was able to develop a tailored contract in collaboration with their HER2 lead. Roche put together a draft contract as a basis for discussion, and mailed it via its healthcare management team, to the HER2 lead as a starting point in discussion. The enclosure provided by the complainant suggested this approach was made on 28 February 2006, with a follow-up email three months later (25 May 2006). The clinician involved had every opportunity to comment on the agreement, and any follow-up from Roche would have been in terms of obtaining a response to the offer.

Roche submitted that given the clinical rationale for determining HER2 status, together with the pre-existing licence of Herceptin in metastatic disease, the fact that only 38% of breast cancer patients were HER2 tested on diagnosis in September 2005 and the recommendation from the DoH that all women should be tested, it considered that its support of HER2 testing complied with Clause 18.4 of the Code, and benefited the NHS. This service did not constitute promotion of a specific product, nor pre-marketing of

that product. Roche disagreed that its support of HER2 testing raised the pressure for Herceptin to be funded in advance of licence.

Roche submitted that ASCO was a large, clinical oncology society which by its very definition was integral to the treatment of cancer. An independent scientific committee evaluated and agreed the scientific content and the format of the annual conference. Pharmaceutical companies provided money to support logistics and for exhibition space at the conference, however this was not related to scientific content. The scientific committee of ASCO selected data for presentation (either oral or poster) and information that was publicised from the conference; the industry did not influence the scientific content or ASCO-generated publicity although companies might choose to issue their own press releases on data relevant to their medicines. If the complainant was concerned about the way ASCO was organised then he should contact the conference organisers directly.

Roche submitted that the group that had made the unplanned announcement about the HERA trial at ASCO was a multinational group of independent researchers who conducted clinical trials on new investigational medicines, not exclusive to Roche. Roche Switzerland led the contact with the group and funded it to run the HERA trial. The steering committee of the group also decided on progress and procedure of its trials, including when data was published. This was overseen by an independent data review committee.

Roche understood that the clinical results from two other studies of Herceptin in adjuvant breast cancer run by the US National Cancer Institute became available after the deadline for 'latebreaker' abstracts. The ASCO scientific committee realising the importance of this newly available data decided to organise a special 'unplanned' session reviewing advances in breast cancer. This session included the two US studies, HERA, and a study involving another unlicensed treatment, bevacizumab. This type of special session had never been instituted before which underscored Roche's contention that the results of these studies had driven the worldwide interest in Herceptin treatment.

Roche submitted that the investor update the complainant referred to related to an announcement made from its headquarters in Switzerland (Basel 28 April 2005) which did not include the actual data itself from HERA, but confirmed that interim data met its primary endpoint and showed improved disease free survival in women. Companies of the Roche Group, had a financial obligation, to some extent even a legal obligation, to inform investors of new information that might impact share price.

Roche submitted that the widespread public interest in Herceptin was multifactorial. The strength of the data, the strong clinical support for Herceptin, the patient group interest and the media environment (eg Kylie Minogue's breast cancer diagnosis during the ASCO congress) contributed to the news being widely covered. Roche had distributed the press release mentioned by the complainant dated 13 May in the UK from ASCO, which was in line with Clause 20.2 of the Code. Supplementary information to Clause 20.2 stated 'This clause allows for provision of non-promotional information about prescription only medicines to the public either in response to a direct enquiry from an individual, including enquiries by journalists, or by dissemination of such information via press conferences, press announcements, television and radio reports, public relations activities and the like'. Roche therefore disagreed that distribution of a press release based on the HERA results presented at ASCO was inappropriate under the Code.

Roche submitted that the press release from ASCO stated the data presented and made it clear that Herceptin reduced the risk of breast cancer returning by 46%. Roche agreed that some of the media reporting misrepresented the data, which was why it distributed a fact sheet in February 2006 and thereafter to counteract the misinformation circulating. Roche also disagreed with the complainant's statement that 'in reality the prognosis for early breast cancer is relatively good…'. Whilst that might be so for HER2 negative patients, it was not the case for HER2 positive patients (Goldhirsch *et al* and Slamon *et al*).

Turning to the issue of the patient group, Roche submitted that the PR agency was appointed by a team in Basel to organise one internal meeting. This had nothing to do with breast cancer, Herceptin, or Roche UK, and it did not have any more information on this other than what had been provided.

Roche noted that the leader of the patient group was invited in a personal capacity to talk to staff at Roche Pharma Development about her experiences of living with breast cancer. Roche noted that what the statement in its response that the lady 'had subsequently set up' the patient group meant was that she was known to the company as a person living with breast cancer and who, after being treated with Herceptin, subsequently set up the patient group not that she had set up the organisation subsequent to her presentation to Roche in December 2005.

Roche submitted that it had no involvement in the development or content of the HER2 testing website. Roche UK did not use this website to 'promote' Herceptin prior to licence. The Roche UK website allowed access to information on products. In the product section, if Herceptin was selected the viewer would only be shown the summary of product characteristics and the patient information leaflet which was in line with Clause 21. In addition a separate section of this website was intended for members of the media and contained archived media releases which could be searched using key words. The media release identified by the complainant concerned the HERA study and had been discussed in detail above. The HER2status website was referred to at the bottom of the release under the heading further information.

Roche had not promoted this website in any promotional materials. The investor relations update referred to by the complainant was from Roche Basel on the corporate site in Switzerland.

Roche did not reject the assumption that there were links between Roche UK and its headquarters in Switzerland however the Code covered activities conducted in the UK itself; Switzerland and other Roche affiliates adhered to their own country codes of conduct. The interest from the media, oncologists, and the public in Herceptin was unprecedented and was due to this being an exceptional treatment heralding a new era of treatment in breast cancer. This opinion was substantiated by statements from oncologists, leading scientific journals and government agencies such as NICE which noted that 'survival of this magnitude due to therapeutic intervention have rarely been recorded in women with metastatic breast cancer'. This was an important statement which reflected the opinion of experts in oncology as well. It was not surprising therefore that this changed the management of metastatic breast cancer but because of the need for HER2 testing and cardiac monitoring it was a complex situation to manage in the NHS.

Roche submitted that the results of the adjuvant trials presented at ASCO resulted in more interest. When these results were finally published in full in the NEJM, October 2005 an editorial included the statements 'The results are simply stunning. With very brief follow-up (one to two and a half years), all three trials show highly significant reductions in the risk of recurrence of a magnitude seldom observed in oncology trials. In fact only tamoxifen administered for five years …in primary breast cancer produces a 50% reduction in the risk of recurrence. Many recent phase 3 trials of adjuvant systemic therapy highlighted absolute benefits of 2 to 6 percent after four to six years of follow up. In contrast, an absolute difference of 6 percent is evident in the HERA trial at two years, with a benefit of 8 percent in the joint analysis …By four years these two trials project an absolute benefit of 18 percent, exceeding all previously reported therapeutic benefits in breast cancer'. The editorial went on to state, 'This observation suggests a dramatic and perhaps permanent perturbation of the natural history of the disease, maybe even a cure'. Moreover it also stated 'On the basis of these results, our care of patients with HER2 positive breast cancer must change today'. The NEJM did not make such statements lightly nor frequently. The immediate and long-term interest generated in the UK by these results had been a challenge for Roche and many other relevant institutions to manage but it firmly believed that it had not exacerbated or encouraged unwarranted expectations. Roche had always tried to work with the regulatory bodies, NICE and the NHS to reach a satisfactory outcome. Roche understood the difficulties that PCTs and commissioners faced but considered that it had acted appropriately and within the Code, as concluded by the Panel and hoped that the additional information outlined above clarified the further points raised.

FURTHER COMMENTS FROM THE COMPLAINANT

The complainant noted that the overarching point of the complaint and appeal was that there was a general background of promotional activity by Roche global and Roche UK that had substantially contributed to untoward actions by senior policy makers. This background activity had been reinforced by the identifiable activities of Roche in the UK that occurred before the grant of the marketing authorization and were promotional in nature. The activity relating to the ASCO conference was a key starting point in this background activity and whilst presumably supported by Roche global helped to promote Herceptin for early breast cancer around the world. The media release by Roche UK, the issue of early HER2 testing, and the HER2 testing website were specific examples of the reinforcement of the results of the earlier and more general promotional activity.

The complainant noted that whilst there might be evidence for the use of HER2 testing in other ways away from direct treatment, Roche's approach did not appear to be about a concern for achieving the best prognostic advice for the patients. If only 38% of patients were being HER2 tested 5 years after Herceptin's licence for metastatic disease why had the company not addressed this issue earlier? Goldhirsch *et al* was a recent paper that had no bearing on the approach that the company appeared to display 18 months ago.

Statements by Government officials were about HER2 testing in anticipation of the use of Herceptin for early breast cancer, not about establishing a prognosis for patients. The statements were seen by many to conflict with pre-existing national policy and possibly undermine the independence of the EMEA licensing process and NICE appraisal. Given that this NHS activity could be seen as promotion before the grant of the marketing authorization for Herceptin it was unwise of Roche to be directly involved in this initiative particularly when it had not sought in the past to support its extensive knowledge of HER2 testing with direct financial support. It appeared that Roche assumed that ministerial support would protect it from any accusation of undue promotional activity at this time. It was not part of Roche's business, at this early stage of seeking a licence, to encourage HER2 testing so that patients who tested positive would expect to have Herceptin and to see its licensing as inevitable.

The complainant alleged that Roche's press release of 13 May 2005 was both part of the general background promotional activity that contributed to pressure from patients and clinicians and also specifically encouraged HER2 testing as a necessary way in to establishing a need for Herceptin. The pressure was such that the perceived need for Herceptin would be established before obtaining marketing authorization and a favourable view of cost effectiveness. As such, the parts of this press release highlighted in relation to HER2 testing were further demonstrations of Roche's approach to stimulating public opinion in support of the wider use of Herceptin.

The complainant alleged that correspondence between Roche and a local cancer network was an example of the action that Roche took to implement its support for HER2 testing. Whilst it was obviously sensible to have a contractual relationship, Roche was promoting the need for Herceptin at an early stage when it should not have been. This correspondence was passed on by a colleague and it reflected their comments and concerns.

The complainant noted that there was a fine line between sponsorship that supported the reasonable dissemination of clinical information and that which contributed towards an opportunity to promote a new treatment so that unbalanced optimism was created at an early stage. Roche did not take sufficient control of ensuring that the dissemination of the information was reasonable and balanced at a stage when Herceptin was not licensed for early breast cancer anywhere in the world. Roche failed to acknowledge the role that it played at events such as the ASCO conference. There was also research to support the view that conference presentations were misleading and over optimistic when compared to the later publication of full trial results in peer-reviewed journals (Dundar *et al* 2006). The media reporting of scientific meetings was also seen as misleading (Schwartz *et al* 2002).

The complainant alleged that 'unplanned' in relation to the ASCO conference presentation was clearly a relative term in this context. The Roche UK media release relating to the research was dated 13 May 2005. The annual ASCO conference was from 14-16 May 2005 with the HERA trial results presented on the last day. As breast cancer was common a number of celebrities had had publicity when they had been diagnosed with the condition. As the ASCO conference was about impressing clinicians the complainant doubted that Kylie Minogue's diagnosis and the related news coverage played much part in promoting Herceptin. The sort of approach that was taken to the annual ASCO conference could be illustrated by a section on the Forbes website. Whilst this web page was about another company preparing for the ASCO conference in May 2006 it illustrated the nature of the conference.

The complainant did not understand the point that Roche was making in relation to the press release dated 13 May 2006. This press release, which was originally submitted in the appeal, appeared to promote Herceptin before it was licensed for early stage breast cancer, anticipated the presentation of the HERA results and was inappropriate in the UK according to the Code. In this sense Herceptin was not then a prescription only medicine as the quote of Clause 20.2 appeared to claim.

The complainant noted that he had asked to see further examples of the press releases that Roche claimed to have issued to counter the misinformation that was common amongst patients and the media. However, Roche's media statement of 6, February 2006 provided no further evidence to substantiate this. As a media statement it did not appear to be an exact copy from an original press release and there were errors in it such as in the incomplete reference. Its primary purpose and content would not suggest that it was about correcting mis-reporting and a prevalent view that Herceptin was a 'cure'. The statement only seemed to repeat the limited information given in other releases and did not present a balanced view of the information then available.

The complainant stated that it was unfortunate that Roche could not provide reassurance about the details of the use of the PR agency as suspicions had been raised in the national media as referenced in The Guardian (29 March 2006) (Case AUTH/1819/4/06). Also, Roche made no mention of the fact that the advertising agency that it had used for Herceptin, and the PR company were both owned by the same group. Presumably Roche either did not know about this link or did not wish to draw attention to a potential conflict of interest.

The complainant alleged that Roche did not adequately address the issue about its press release 13 May 2005 which clearly referenced a website that linked HER2 testing to Herceptin treatment for early breast cancer. Roche seemed to suggest that a media release accessed through the Roche UK website was not promotional because Roche did not see this as promotional material. Websites and press releases such as these were about the promotion of a product or an idea. Given that the promotion was to an unknown public either directly through the internet or indirectly through the media it was impossible to know to what degree the promotion had occurred. Nonetheless the intention was clear.

The complainant considered that an appropriate investor update through a press release might be a part of commercial life but the point of including the Roche global press release of April 2005 was to demonstrate how Roche UK's actions were tied in to their headquarters' actions and accountability could not be avoided.

The complainant alleged that the train of events that led to the widespread interest in Herceptin was initiated by the release of information at ASCO's conference in 2005. Roche must have had some control over this even if it could not predict how far the publicity would go. Roche UK supported this promotion of the early information and did itself little service by quoting the editorial in the NEJM, October 2005. The use of the words, 'simply stunning' and, 'maybe even a cure', supported the view that Roche wished to spread an over optimistic view of a medicine recognised as having some reasonable effects but certainly not seen as being a cure. This was also not helped by the recognition that the editorial's author was a paid consultant of Roche's commercial partner, a fact that it was not necessary to declare in the editorial.

The complainant alleged that he had added some additional information to substantiate the nature of the early promotional activity around Herceptin. The

early publicity at the ASCO conference initiated a complex chain of events. It achieved an unprecedented degree of promotion and caused considerable problems in the UK and for this Roche needed to be accountable.

APPEAL BOARD RULING

The Appeal Board noted that Herceptin had originally been authorized for the treatment of patients with metastatic breast cancer whose tumours overexpressed HER2. It was thus crucial that a patient's HER2 status was known and the Appeal Board noted the submission that establishing this at primary diagnosis was preferable to having to establish it once a patient had developed metastases. The DoH and a national cancer charity had both endorsed such action. Roche's funding of the service would benefit patients and the NHS; there was no evidence before the Appeal Board that the service had been linked to the promotion of Herceptin as alleged. The Appeal Board upheld the Panel's ruling of no breach of Clause 9.1. The appeal on this point was unsuccessful.

The Appeal Board considered that any interaction between the patient group or one of its members and Roche was bound to attract attention. Nonetheless the Appeal Board had no evidence to show that the interaction between the breast cancer patient and Roche had compromised the position of either. Neither the patient nor the patient group had received any payment. Whilst the managing director of Roche had met the patient group there was no evidence to show that Herceptin had been discussed or that this meeting was otherwise inappropriate. The Appeal Board upheld the Panel's ruling of no breach of Clause 9.1. The appeal on this point was unsuccessful.

The Appeal Board noted that the patient group had received help from a PR agency via an ex employee of Roche who worked for it. Roche in the UK did not employ the PR agency; it appeared that the only link between Roche and the PR agency was through a Roche global team based in Switzerland, which had worked with the agency on one meeting. The Appeal Board found no evidence that Roche had influenced or supported the patient group through the PR agency as alleged and so it upheld the Panel's ruling of no breach of Clause 9.1. The appeal on this point was unsuccessful.

The Appeal Board noted the complainant's reference to direct patient contact by Roche as reported in The Guardian; this had been considered in Case AUTH/1819/4/06 wherein no breach of Clauses 20.1 and 20.2 was ruled. In the present case the Appeal Board did not consider that the evidence before it showed, on the balance of probabilities, that Roche had attempted to recruit a patient to promote Herceptin, that it had promoted Herceptin to her or that it had encouraged her such that she would ask her doctor to prescribe Herceptin. The Appeal Board thus upheld the Panel's rulings of no breaches of Clauses 20.1 and 20.2. The appeal on this point was unsuccessful.

The Appeal Board did not consider that the email from Roche to the correspondent at the International Herald Tribune promoted Herceptin. The email was principally about Roche's funding of HER2 testing not about Herceptin. The Appeal Board upheld the Panel's ruling of no breach of Clause 20.1. The appeal on this point was unsuccessful.

The Appeal Board noted that the website HER2status.com was developed and produced by Roche in Switzerland. Roche UK had submitted in its response to the Panel that it had not promoted the site in the UK. The Appeal Board noted from the Roche representative that the website had been aimed at members of the public/patients in the US where promotion of prescription only medicines to the public was permitted.

The Appeal Board noted that a Roche UK press release dated 13 May 2005 had included the HER2status.com web address under further information. The Appeal Board noted from the Roche representative that the press release had been circulated, *inter alia*, to the lay media in the UK. The Appeal Board noted that it had not been provided with a copy of the website contemporary to the 13 May 2005 press release. The relevant Code at that time was the 2003 edition. The HER2status.com website as at 28 April 2006 stated that 'Herceptin Shows Positive Interim results in Early-Stage HER2-Positive Breast Cancer'. The relevant Code at that time was the 2006 edition. The website was currently under revision. The Appeal Board noted that the 13 May 2005 press release remained available on the archive of the Roche UK website.

Taking all the circumstances into account and in particular noting that the website was aimed at members of the public in the US, the Appeal Board inferred that on the balance of probability at the relevant time, the site promoted prescription only medicines to the public. The Appeal Board thus considered that the reference in the press release dated 13 May 2005 and aimed at the lay UK media to a website aimed at a lay US audience, amounted to promotion of a prescription only medicine to the public. The Appeal Board ruled a breach of Clause 20.1 of the Code. The appeal on this point was successful.

The Appeal Board noted its rulings of no breach of the Code above and consequently upheld the Panel's ruling of no breach of Clause 2. The appeal on this point was unsuccessful.

Complaint received	**30 June 2006**
Case completed	**12 January 2007**