CASE AUTH/1910/11/06

SANOFI PASTEUR MSD v GLAXOSMITHKLINE

Cervical cancer disease awareness campaign

Sanofi Pasteur MSD complained about GlaxoSmithKline's field based cervical cancer disease awareness team (CCDAT) alleging that the existence and activities of CCDAT breached, *inter alia*, Clause 2 of the Code.

Sanofi Pasteur MSD and GlaxoSmithKline had each developed prophylactic human papillomavirus (HPV) vaccines. Sanofi Pasteur MSD's vaccine, Gardasil, targeted four HPV types: 6, 11, 16 and 18 and GlaxoSmithKline's candidate vaccine targeted HPV types: 16 and 18. Gardasil was launched in the UK in October 2006. GlaxoSmithKline's candidate vaccine was not licensed.

Sanofi Pasteur MSD was concerned that a Pharmaceutical Field advertisement sought area managers and representatives for the CCDAT to 'shape the future for women in the UK'. The advertisement explained that the successful candidates would, by providing disease awareness education to key primary care health professionals within the territory, develop the understanding of cervical cancer and then at launch of the vaccine be responsible for the sales performance on the territory and account management of customers. A proven track record in sales, with excellent negotiation and influencing skills was required. This implied that the pre-launch disease awareness phase would be an opportunity to develop a network of customers, to be leveraged at launch, in order to achieve sales performance on each territory.

Sanofi Pasteur MSD accepted that provision of information on health and disease by companies could be non-promotional. However, if the information related to a disease area of interest to a particular company, it would be considered promotional and within the scope of the Code, even if no product was mentioned. In addition, the disease awareness and commercial objectives of the team were so closely intertwined that it was unrealistic to expect sales professionals to separate the two.

Sanofi Pasteur MSD provided copies of some of the materials used which included a leavepiece, a brochure and exhibition panels. These followed a common theme with messages about the burden of cervical cancer, the cervical screening programme and the link with HPV infection. All referred to immunity, stating 'Previous infection with HPV may not provide sufficient immunity to prevent another infection'.

The combination of the mention of HPV types 16 and 18, reference to immunity (which would be associated with vaccination) and the fact that GlaxoSmithKline was one of the largest vaccine suppliers in the UK made it highly likely that this material would lead to questions about HPV vaccination and GlaxoSmithKline's candidate vaccine.

The activities of the CCDAT were having the effect of soliciting questions to GlaxoSmithKline about vaccines that it had an interest in, but whose product was currently unlicensed. No amount of training on how to deflect such questions or refer them to the medical department could detract from that. Furthermore, questions being prompted by the concerted activities of the CCDAT could not be considered truly unsolicited and therefore the responses provided, even if under the responsibility of the medical department, could be considered promotional.

Sanofi Pasteur MSD considered it was impossible for the team's activities to be non-promotional.

The Panel noted that the Code permitted certain activities prior to the grant of the marketing authorization. The legitimate exchange of medical and scientific information during the development of a medicine was not prohibited providing that any such information or activity did not constitute promotion prohibited by the Code.

In the Panel's view the closer to the grant of the marketing authorization for a product the more difficult it was to argue that activities were a legitimate exchange of medical and scientific information during the development of a medicine.

The definition of promotion did not include replies made in response to individual enquiries from members of the health professions or appropriate administrative staff or in response to specific communications from them whether of enquiry or comment, including letters published in professional journals, but only if they related solely to the subject matter of the letter or enquiry, were accurate and did not mislead and were not promotional in nature. This exemption applied to unsolicited enquiries only ie whereby companies responded to an enquiry having done nothing to prompt it. In answering an unsolicited enquiry a company could offer to provide further information. If the enquirer subsequently requested additional information this could be provided and would be exempt from the Code provided it met the requirements of the exemption. Information relating to human health or diseases were also exempt from the definition of promotion provided there was no reference either direct or indirect to specific medicines.

In the Panel's view it was not necessarily unacceptable for companies to have employees

focussing on the provision of information prior to the grant of the marketing authorization. The arrangements and activities of such employees had to comply with the Code. Such employees should be comprehensively briefed about the Code. The area was difficult and companies needed to ensure that the arrangements and activities were very carefully controlled and managed.

The Panel noted GlaxoSmithKline's submission that the role of CCDAT was to educate relevant health professionals about the burden of cervical cancer and precancerous lesions, the causal role of oncogenic HPV in cervical cancer and the importance of the screening programme.

A detail aid 'Cervical cancer - a major health issue for women' discussed the incidence and cause of cervical cancer and the success of cervical screening in the UK and stated 'Previous infection with HPV may not provide sufficient immunity to prevent another infection'. The brochure concluded with 'GlaxoSmithKline is committed to supporting you in the prevention of cervical cancer' above 'Cervical cancer prevention for all women' in logo format. Identical statements appeared in a smaller, abridged leavepiece which bore an identical title. Banner headlines on each of the three exhibition panels provided, discussed either the cause, incidence and/or burden of cervical cancer, one stating that '… previous infection with HPV may not provide sufficient immunity to prevent another infection'. Each concluded with the strapline 'Regular cervical screening is vital in the fight against cervical cancer'. A smaller exhibition panel simply read 'Cervical cancer prevention for all women' with the GlaxoSmithKline logo.

The representatives' briefing document, 'Cervical Cancer Disease Awareness Campaign', provided detailed information on the discussion points in the detail aid and leavepiece described above. The need to comply with the Code was highlighted. Representatives were told that '… it is possible that [health professionals] may ask about HPV vaccination and/or GlaxoSmithKline's vaccine in development, which must not be discussed under any circumstances'. A section headed 'To watch out for' gave three model answers. Firstly, to use if health professionals asked about why the representatives were talking about cervical cancer and not selling a product. Secondly, to use after Sanofi Pasteur MSD's product has been launched. If asked specifically about GlaxoSmithKline's candidate HPV vaccine representatives were advised to state that the purpose of the visit was to discuss cervical cancer disease awareness and not specific products and that GlaxoSmithKline's medical information team would be able to assist with any specific product enquiries. The representatives' disease awareness training material did not discuss medicines; it concluded with a section on screening and diagnosis.

The Panel considered that the material would encourage discussion about cervical cancer. This was not necessarily unacceptable so long as the material did not solicit questions about a specific medicine and that any discussion complied with the Code. The references to previous infection not providing sufficient immunity to prevent another infection might solicit general questions about vaccination. Whilst the Panel noted GlaxoSmithKline's explanation that such references emphasised the need for continued regular screening in older woman who remained sexually active the Panel did not consider that this explanation was made clear in any of the materials. Nonetheless, the overall emphasis of each item was on the burden and cause of disease and the need to ensure access to a successful screening programme. The Panel considered that the unqualified statement 'GlaxoSmithKline is committed to supporting you in the prevention of cervical cancer' would encourage doctors to ask about GlaxoSmithKline's role in prevention. The Panel noted that the model answers all indicated that the representative should state that the purpose of their visit was to discuss cervical cancer disease awareness, and not specific products.

Overall the Panel considered that the material and activities of the representatives did not identify, directly or indirectly, a specific medicine such that GlaxoSmithKline's medicine was being promoted prior to the grant of its marketing authorization. Nor did the material solicit enquiries about GlaxoSmithKline's forthcoming product. The Panel ruled no breach of the Code. This was appealed by Sanofi Pasteur MSD.

The Appeal Board noted that the recruitment advertisement that appeared in the April 2006 issue of Pharmaceutical Field, a journal aimed at sales professionals, stipulated that candidates for the position of representatives should have a proven track record in sales, with excellent negotiation and influencing skills. The advertisement referred to delivering a focussed disease awareness campaign and then implementing the launch of the vaccine in early 2007. The Appeal Board considered that whilst a sales background was not necessarily unacceptable it was, however, consequently important that the company was especially careful about the arrangements and activities given a representative's natural tendency to sell. The Appeal Board also noted the company representatives' submission that approximately 25% of the CCDAT team was recruited from a non-sales position.

The Appeal Board noted GlaxoSmithKline's submission about the CCDAT non promotional role and training but was nonetheless concerned about the scale of the activity; there were 65 members of the CCDAT operating throughout the UK, targeting potential prescribers. It was likely that most of the CCDAT would promote GlaxoSmithKline's vaccine to the same group of prescribers once the product had received its marketing authorization.

The Appeal Board did not accept the GlaxoSmithKline representatives' position that the primary purpose of the CCDAT and materials was to increase screening rates. The company

representatives had explained that the targeted practices were those with large numbers of female patients registered and not those with low uptake of cervical screening.

The Appeal Board noted that HPV types 16 and 18 were responsible for 71.5% of cervical cancers. Fifteen of the 100 HPV types identified could cause cervical cancer. The Appeal Board was concerned about the overall emphasis of the detail aid on HPV types, particularly oncogenic HPV types 16 and 18, given the stated primary objective of the campaign to increase screening levels. The Appeal Board considered that this objective could be achieved without such emphasis. In particular three out of four bullet points on the final page of text (page 13), which the Appeal Board inferred summarized the key take-home message of the detail aid, referred to oncogenic HPV types 16 and 18 and/or HPV infection. There was no mention of screening. Further the references to and undue emphasis on only oncogenic HPV types 16 and 18 could only relate to a specific medicine; GlaxoSmithKline's forthcoming vaccine. (The currently available vaccine Gardasil, was indicated for HPV types 6 and 11 as well as oncogenic HPV types 16 and 18.) The page also stated that 'GlaxoSmithKline is committed to supporting you in the prevention of cervical cancer'. The company explained that the support referred to comprised discussion with health professionals by members of the CCDAT about the importance of screening, sponsorship of educational meetings and the provision of patient leaflets. The Appeal Board did not have copies of the patient leaflets before it.

Overall the Appeal Board considered that the cumulative effect of the arrangements amounted to promotion of a product prior to the grant of its marketing authorization. A breach of the Code was ruled. It thus considered that the arrangements would bring discredit upon and reduce confidence in the pharmaceutical industry; a breach of Clause 2 was ruled.

Sanofi Pasteur MSD Ltd complained about the activities of a field based team of GlaxoSmithKline UK Ltd known as the cervical cancer disease awareness team (CCDAT).

COMPLAINT

Sanofi Pasteur MSD alleged that the existence and activities of CCDAT breached Clauses 2 and 3.1 of the Code.

Sanofi Pasteur MSD explained that it and GlaxoSmithKline had each developed prophylactic human papillomavirus (HPV) vaccines. Sanofi Pasteur MSD had developed Gardasil, which targeted four HPV types: 6, 11, 16 and 18 and GlaxoSmithKline had developed a candidate vaccine which targeted two HPV types: 16 and 18. HPV was the essential cause of cervical cancer, as well as being responsible for various other diseases.

Gardasil was launched in the UK on 17 October 2006. GlaxoSmithKline's candidate vaccine was not licensed.

Recruitment of CCDAT

The advertisement placed by GlaxoSmithKline in the April 2006 issue of Pharmaceutical Field sought area managers and representatives to 'shape the future for women in the UK'. The opening paragraph read:

'As one of the world's leading research-based pharmaceutical and healthcare companies, GlaxoSmithKline develops new products with the objective to enable people to do more, feel better and live longer. We are currently making that vision a reality by preparing to launch a revolutionary new vaccination against human papillomavirus (HPV), the cause of cervical cancer. So by joining us at this crucial time, you'll have the chance to shape the development of this new opportunity and then lead the launch of the brand on your territory. This is a unique career opportunity in a new field of women's health and cancer prevention.'

The advertisement worried Sanofi Pasteur MSD for a number of reasons:

1 The opening paragraph, quoted above, made it clear that the representatives would, in the pre-launch phase, shape the future of vaccination against HPV and then lead the launch of GlaxoSmithKline's candidate vaccine on their territory.

2 The second and third paragraphs stated that the disease awareness campaign would be directed at primary care health professionals, many of whom were prescribers.

3 The third paragraph stated:

'By providing disease awareness education to key Primary Care Health Care Professionals within your territory, you will initially be focussed on developing the understanding of cervical cancer. At launch of the vaccine you will be responsible for the sales performance on your territory and account management of your network of customers. You will need a proven track record in sales, with excellent negotiation and influencing skills.'

This implied that the pre-launch disease awareness phase would be an opportunity to develop a network of customers, to be leveraged at launch, in order to achieve sales performance on each territory. Furthermore, it was a requirement that, although operating as a disease awareness team, all representatives were required to come from a sales background.

It was therefore clear from the advertisement that sales professionals were being recruited to prepare their territories through a disease awareness campaign in readiness for the future launch of GlaxoSmithKline's candidate HPV vaccine. Those same representatives would be responsible for the sales success of the vaccine on those same territories, with the very same

customers. Sanofi Pasteur MSD accepted that provision of information on health and disease by companies could be non-promotional. However, it believed that, if the information related to a disease area of interest to a particular company, it would be considered promotional and within the scope of the Code, even if no product was mentioned. In addition, the disease awareness and commercial objectives of the team were so closely intertwined that it was unrealistic to expect sales professionals to separate the two.

In previous correspondence Sanofi Pasteur MSD had referred GlaxoSmithKline to Cases AUTH/1346/7/02, AUTH/1559/3/04 and AUTH/1560/3/04. In correspondence, GlaxoSmithKline had informed Sanofi Pasteur MSD that 25% of the team were recruited from a non-sales background within GlaxoSmithKline.

Activities of CCDAT and materials used

In correspondence GlaxoSmithKline had stated the objective of the CCDAT was:

> '…to increase awareness and understanding amongst relevant health professionals of the burden associated with Cervical Cancer, the causal role of oncogenic Human Papilloma Virus (HPV) and the importance of regular cervical screening.'

Sanofi Pasteur MSD was aware from feedback from the field that the CCDAT was active in surgeries and at local meetings, interacting on a one-to-one basis with general practitioners and practice nurses. Sanofi Pasteur MSD provided copies of some of the materials used by the team, which included a leavepiece (20959476 CER/LVP/06/27063/1 August 2006), a brochure (CER/DAP/06/26681/1 July 2006) and exhibition panels.

The materials followed a common theme with messages about the burden of cervical cancer, the cervical screening programme and the link with HPV infection. All three pieces of material also referred to immunity, stating:

> 'Previous infection with HPV may not provide sufficient immunity to prevent another infection.'

The combination of the mention of HPV types 16 and 18, reference to immunity (which many primary care professionals would associate with vaccination) and the fact that GlaxoSmithKline was one of the largest vaccine suppliers in the UK made it highly likely that this material would lead to questions about HPV vaccination and GlaxoSmithKline's candidate vaccine.

Bearing in mind the stated objective of the CCDAT, Sanofi Pasteur MSD noted the messages chosen for the three exhibition panels. The first carried a message about the burden of cancer and precancerous lesions; the second, a message about oncogenic HPV infection; the third, a message about immunity. Cervical screening was referred to only in rather small text at the bottom of each panel.

Sanofi Pasteur MSD submitted photographs of the exhibition stands taken at a cervical screening update meeting attended by approximately 50 practice nurses. The meeting was sponsored by industry and five companies including GlaxoSmithKline had stands. GlaxoSmithKline had confirmed in correspondence that this was being replicated elsewhere in the country.

Requests for information

It was highly likely that a GlaxoSmithKline representative, even if deemed non-promotional, who discussed cervical cancer and HPV would prompt questions about vaccination, and hence GlaxoSmithKline's candidate vaccine. Feedback from the field indicated that this was indeed the case and the possibility was acknowledged by GlaxoSmithKline in its letter dated 19 October 2006, which stated:

'It was acknowledged that HPV vaccination might be raised by some healthcare professionals (HPs) as a result of the disease awareness programme. However, these non promotional representatives have been thoroughly trained and assessed on how to handle potential questions from HPs about this topic specifically in order to prevent any discussion of unlicensed products. If a HP is persistent in their request for information regarding HPV vaccination the disease awareness team has been instructed to refer that HP to our medical information department.'

It was clear therefore that the activities of the CCDAT were having the effect of soliciting questions to GlaxoSmithKline representatives about vaccines that it had an interest in, but whose product was currently unlicensed. No amount of training on how to deflect such questions or refer them to the medical department could detract from that. Furthermore, questions being prompted by the concerted activities of the CCDAT could not be considered truly unsolicited and therefore the responses provided, even if under the responsibility of the medical department, could be considered promotional.

Summary

In the case of the CCDAT, Sanofi Pasteur MSD considered it was impossible for the team's activities to be non-promotional because:

1 Potential prescribers were targeted through one-to-one contact, either in surgeries or at meetings.
2 Awareness of vaccines against cervical cancer was high amongst health professionals.
3 GlaxoSmithKline was one of the largest vaccine suppliers in the UK.
4 The activities of the team were bound to, and had, prompted questions about vaccination, and hence GlaxoSmithKline's candidate HPV vaccine.

In Sanofi Pasteur MSD's view, the existence and activities of the CCDAT breached Clause 3.1 of the Code. The manner in which the team was recruited, the inexorably close ties between disease awareness and future brand success, and the materials and tactics being employed inevitably promoted a product prior to receipt of its marketing authorization. None of the exemptions relating to advance notification of new

products applied to the target audience of primary health professionals.

Furthermore, Sanofi Pasteur MSD was concerned that this represented a new and worrying precedent in the activities of field-based representatives: disease awareness directed one-to-one at future prescribers pre-launch to be followed by traditional promotion post-launch. As well as breaching Clause 3.1 in the pre-launch phase, Sanofi Pasteur MSD believed that the prominence of the CCDAT, the inexorable link between disease awareness and future commercial promotional objectives, and the extent of its activities brought discredit upon, and reduced confidence in, the pharmaceutical industry as a whole and thus breached Clause 2.

RESPONSE

GlaxoSmithKline stated that it had had the spirit and letter of the Code in mind when it had recruited the CCDAT and planned its activities. As such, it was confident that the existence of this non-promotional team and its activities complied with the Code.

The causal role of the oncogenic (cancer causing) HPV in cervical cancer was well documented. However, several recent publications had highlighted that knowledge about oncogenic HPV and its role in this disease was very limited amongst women and that further education for health professionals in this area had been called for. The CCDAT was established to help address this genuine knowledge gap. The CCDAT was launched by GlaxoSmithKline on 4 September 2006 with the clear objective to educate relevant health professionals about the burden of cervical cancer and precancerous lesions, the causal role of oncogenic HPV in cervical cancer and the importance of the screening programme. As such, GlaxoSmithKline strongly refuted a breach of Clause 3.1 and, thus, Clause 2 of the Code.

It was incorrect to assume that it was not possible for non-promotional disease awareness representatives to undertake education in a disease area in which the company had an interest. As Sanofi Pasteur MSD was aware, these activities were permitted under the Code, and as would be noted in correspondence with Sanofi Pasteur MSD, GlaxoSmithKline maintained that the non-promotional representatives of the company (comprising the CCDAT) were permitted to call directly on health professionals.

Sanofi Pasteur MSD referred to Cases AUTH/1346/7/02, AUTH/1559/3/04 and AUTH/1560/3/04 to support its allegations. GlaxoSmithKline was aware of these previous rulings and noted that breaches of Clause 3.1 were demonstrated in each case. However, there were no similarities between those cases and the CCDAT activities. Clear deviation from genuine disease awareness campaigns occurred in each of the cases cited, with representatives either subject to processes or utilising materials that were promotional in nature and therefore inappropriate for a disease awareness team.

The CCDAT representatives' objectives and bonus criteria together with their training, briefing and health professional materials clearly demonstrated the non-promotional nature of this team.

The CCDAT team was primarily measured on activity based criteria with flexible objectives based on other criteria eg budget expenditure and planning which did not relate to promotional activity now or in the future. The bonus for the team from September to December 2006 would be based on an overall company performance (bonus level) and an individual 'multiplier' based on the team's performance against their non-promotional objectives.

The job specifications and advertisement used to recruit the team showed that at the launch of GlaxoSmithKline's candidate HPV vaccine, it was the company's intention that this team would most likely become a promotional team supporting the launch of the product. The objectives for the team would change at this point. GlaxoSmithKline was confident that it had taken great care and consideration to clearly separate these phases of activity in accordance with the spirit and the letter of the Code.

In its complaint, Sanofi Pasteur MSD alleged that 'it is impossible for the CCDAT's activities to be non-promotional for a number of reasons'. These reasons were addressed as follows:

- **'Potential prescribers are targeted through one-to-one contact, either in surgeries or at meetings'**

Primary care professionals who took the lead on, or who were involved in, cervical screening had been targeted in GlaxoSmithKline's disease awareness campaign because the education offered by the CCDAT would be of most relevance to them. The audience would be expected to consist of both prescribers and non-prescribers – not just 'potential prescribers' as stated by Sanofi Pasteur MSD. It was perfectly legitimate for non-promotional representatives to call directly on these health professionals to discuss disease awareness on a one-to-one basis or at educational meetings. Sanofi Pasteur MSD alleged that by engaging with health professionals in this way 'it is impossible for the team's activities to be non-promotional'. Sanofi Pasteur MSD had provided no evidence to substantiate this allegation other than some conjectural 'reasons'. GlaxoSmithKline strongly refuted this allegation and consequently a breach of Clause 3.1.

- **'Awareness of vaccines against cervical cancer is high amongst health professionals'**

GlaxoSmithKline was not aware of the data used to support this claim, although it was aware that knowledge amongst health professionals about the role of oncogenic HPV in cervical cancer was limited as previously referenced. The CCDAT was strictly non-promotional and disease focussed. It was acknowledged that there was some awareness of HPV vaccination among health professionals and, as such, this topic might be raised. As part of GlaxoSmithKline's risk management strategy to avoid

precisely the allegation that had been made, its non-promotional representatives had been thoroughly trained and assessed on how to handle potential situations from health professionals about HPV vaccination, specifically in order to prevent any discussion about unlicensed products. GlaxoSmithKline had gone to great lengths to ensure that the CCDAT responded to any such situation in a consistent and professional manner; thus the following statement was clearly outlined in the representatives' briefing document:

'GSK has a research and development interest in the area of cervical cancer. It is very common for manufacturers to provide medical education on relevant disease areas and the purpose of my visit today is to discuss CCa disease awareness, and not specific products.'

If a health professional was persistent in a request for information regarding HPV vaccination the CCDAT had been instructed to refer that health professional to the company's medical information department. The following statement had been included in the representatives' briefing document, which was only to be used reactively in response to persistent requests for information regarding specific products:

'The purpose of my visit today is to discuss CCa disease awareness, and not specific products. GSK's Medical Information Team will be able to assist you with any specific product enquiries.'

This was the process for enquiries relating to any unlicensed GlaxoSmithKline medicine or indication and was reiterated in Clause 2.2 of GlaxoSmithKline's own European Code of Practice which was in line with the ABPI Code. Contrary to Sanofi Pasteur MSD's assertion, the company's acknowledgement and proactive training on this topic was one of probity, not promotion, and took into account previous rulings. GlaxoSmithKline therefore strongly disagreed that this constituted a breach of Clause 3.1.

- **'GlaxoSmithKline is one of the largest vaccine suppliers in the UK'**

GlaxoSmithKline was the largest UK-based pharmaceutical company and manufactured medicines for a wide variety of therapy areas that might be known to primary care professionals. It disagreed with Sanofi Pasteur MSD's implication, by association rather than evidence, that GlaxoSmithKline's vaccine heritage meant that it was 'impossible for the team's activities to be non-promotional'.

- **'The activities of the team are bound to, and have, prompted questions about vaccination, and hence GlaxoSmithKline's candidate HPV vaccine'**

GlaxoSmithKline again stressed the safeguards that it had put in place to specifically prevent discussion about unlicensed products. All of its non-promotional representatives had a background in the pharmaceutical industry and a good working knowledge of the Code. They were fully aware of the important ethical regulations surrounding disease awareness activities. In addition, as already mentioned, they had been thoroughly trained and assessed on how to handle potential questions from health professionals about HPV vaccination, and were supported by their non-promotional area managers and the wider organisation to operate in accordance with the Code and the company's own high ethical standards. GlaxoSmithKline did not consider that the provision of genuine disease awareness education in this area amounted to soliciting questions on its HPV vaccination. The company denied a breach of Clause 3.1.

Sanofi Pasteur MSD then went on to state that the same representatives would be leading the launch of GlaxoSmithKline's candidate vaccine on their territory. This assertion had come directly from the recruitment advertisement, but Sanofi Pasteur MSD was confusing the fact that promotional activities had not and would not happen until such time as GlaxoSmithKline's candidate vaccine was approved and launched. Any subsequent promotion would be consistent with the marketing authorization for the vaccine. A decision upon the precise role of the staff in the CCDAT would be made based upon the best use of resources. Although Sanofi Pasteur MSD alleged a breach of Clause 3.1 because of the nature of the advertisement, it had incorrectly assumed that the CCDAT's activities were currently promotional. This was not the case. All current activities were strictly educational. No promotional activity was ongoing.

GlaxoSmithKline had stringent safeguards for the separation of non-promotional and promotional roles and although some of these CCDAT individuals might become promotional once the vaccine was approved, they were not conducting any promotional activity either directly or indirectly in their activities within the CCDAT. To allege a breach of Clause 3.1 based on a strategic plan when no promotion had taken place suggested that Sanofi Pasteur MSD had misunderstood the 'modus operandi' of the CCDAT.

Educational materials used by the CCDAT – leavepiece (CER/LVP/06/27063/1) and brochures (CER/DAP/06/26681/1)

Sanofi Pasteur MSD had cited examples of materials used by the CCDAT. It correctly stated that the materials followed a common theme (the objectives of the CCDAT were to raise awareness about the burden of cervical cancer, the causal role of oncogenic HPV in cervical cancer and the importance of regular screening). However, Sanofi Pasteur MSD raised concerns about some of the wording contained within these materials. It alleged that the combination of the mention of HPV types 16 and 18, reference to immunity and the fact that GlaxoSmithKline was one of the largest vaccine manufacturers in the UK made it highly likely that these materials would lead to questions about HPV vaccination and GlaxoSmithKline's candidate vaccine.

GlaxoSmithKline did not agree that the use of the word 'immunity' in the context of HPV types 16 and 18 would inevitably lead to questions about its candidate

vaccine. These specific types had been mentioned because they were the types responsible for around 70% of cervical cancer cases. An educational document about oncogenic HPV and its relationship to cervical cancer would not be complete without this information.

The immune system played a role in very many disease states, so the suggestion that the discussion of immunity would inevitably lead to questions about HPV vaccination was speculative and unfounded. The statement *'Previous infection with HPV may not provide sufficient immunity to prevent another infection'* was highly relevant in an educational document on the importance of regular cervical screening – it emphasised the need for continued regular screening in older women who remained sexually active, even if they had been treated for cervical lesions in the past, as they could never be considered 'immune' to oncogenic HPV infections.

All of the information contained within the materials was factual, balanced and fully referenced. It reflected key epidemiological and clinical data on cervical cancer and HPV. GlaxoSmithKline believed it essential to include all of this information in order to communicate a complete picture of the disease. All of this material had been through GlaxoSmithKline's approval process and had been certified as non-promotional.

Materials employed by the CCDAT – exhibition panels (CER/EXP/06/27062/1)

GlaxoSmithKline submitted that all of the information contained on the exhibition panels was factual, balanced and fully referenced. The panels always appeared together and, as such, highlighted the burden of disease, the causal role of oncogenic HPV and the importance of regular screening. At the bottom of each exhibition panel was the clear statement 'Regular cervical screening is vital in the fight against cervical cancer'. As above, these panels had also been approved as non-promotional material.

In conclusion, GlaxoSmithKline strongly refuted Sanofi Pasteur MSD's allegations and reiterated that it had taken the spirit and letter of the Code to heart in the recruitment of the CCDAT and in the planning and implementation of its activities. In summary:

- The highly trained non-promotional representatives' 'raison d'etre' was to increase awareness and understanding amongst relevant health professionals of the burden associated with cervical cancer, the causal role of oncogenic HPV and the importance of regular cervical screening.
- All of these non-promotional representatives (25% of whom came from a non-sales' background in GlaxoSmithKline) had been fully trained, assessed and were supported by their non-promotional area managers and the wider organisation to operate in accordance with the Code and the company's own ethical standards.
- GlaxoSmithKline's non-promotional representatives had not been trained on its HPV candidate vaccine as their discussions with health professionals were strictly disease focussed. The non-promotional nature of the CCDAT was also supported by objectives and bonus criteria for the team, briefing documents and training materials.
- All educational materials used by the CCDAT were educational and non-promotional in nature. The material was factual, balanced and fully referenced and reflected key epidemiological and clinical data on cervical cancer and HPV. It had not been designed to solicit questions on GlaxoSmithKline's candidate HPV vaccine.

GlaxoSmithKline considered that the ethos and activities of its CCDAT complied with the Code and denied that Clauses 3.1 and 2 had been breached.

PANEL RULING

The Panel noted that the Code permitted certain activities prior to the grant of the marketing authorization. The supplementary information to Clause 3 stated that the legitimate exchange of medical and scientific information during the development of a medicine was not prohibited providing that any such information or activity did not constitute promotion prohibited by Clause 3 or any other clause.

In the Panel's view the closer to the grant of the marketing authorization for a product the more difficult it was to argue that activities were a legitimate exchange of medical and scientific information during the development of a medicine.

The definition of promotion in Clause 1.2 did not include replies made in response to individual enquiries from members of the health professions or appropriate administrative staff or in response to specific communications from them whether of enquiry or comment, including letters published in professional journals, but only if they related solely to the subject matter of the letter or enquiry, were accurate and did not mislead and were not promotional in nature. The relevant supplementary information explained that this exemption applied to unsolicited enquiries only ie whereby companies responded to an enquiry having done nothing to prompt it. In answering an unsolicited enquiry a company could offer to provide further information. If the enquirer subsequently requested additional information this could be provided and would be exempt from the Code provided it met the requirements of the exemption. Information relating to human health or diseases was also exempt from the definition of promotion provided there was no reference either direct or indirect to specific medicines.

In the Panel's view it was not necessarily unacceptable for companies to have employees focussing on the provision of information prior to the grant of the marketing authorization. The arrangements and activities of such employees had to comply with the Code. Such employees should be comprehensively briefed about the Code. The area was difficult and companies needed to ensure that the arrangements and

activities were very carefully controlled and managed. The importance of documentation and instruction could not be overestimated.

The Panel noted GlaxoSmithKline's submission that the role of CCDAT was to educate relevant health professionals about the burden of cervical cancer and precancerous lesions, the causal role of oncogenic HPV in cervical cancer and the importance of the screening programme.

A detail aid (CER/DAP/06/26681/1) 'Cervical cancer - a major health issue for women' discussed the incidence and cause of cervical cancer and the success of cervical screening in the UK. A bullet point read 'Previous infection with HPV may not provide sufficient immunity to prevent another infection'. The brochure concluded with 'GlaxoSmithKline is committed to supporting you in the prevention of cervical cancer' above 'Cervical cancer prevention for all women' in logo format. Identical statements appeared in a smaller, abridged leavepiece (20959476 CER/LVP/06/27063/1) which bore an identical title. Banner headlines on each of the three exhibition panels provided, discussed either the cause, incidence and/or burden of cervical cancer, one stating that '… previous infection with HPV may not provide sufficient immunity to prevent another infection'. Each concluded with the strapline 'Regular cervical screening is vital in the fight against cervical cancer'. A smaller exhibition panel (20959475 CER/EXP/06/27062/1) simply read 'Cervical cancer prevention for all women'. The GlaxoSmithKline logo appeared in the top left hand corner.

The representatives' briefing document, 'Cervical Cancer Disease Awareness Campaign', provided detailed information on the discussion points in the detail aid and leavepiece described above. The need to comply with the Code was highlighted. Representatives were told that '… it is possible that [health professionals] may ask about HPV vaccination and/or GlaxoSmithKline's vaccine in development, which **must not** be discussed under any circumstances'. A section headed 'To watch out for' gave three model answers. Firstly, to use if health professionals asked about why the representatives were talking about cervical cancer and not selling a product. Secondly, to use after Sanofi Pasteur MSD's product has been launched. If asked specifically about GlaxoSmithKline's candidate HPV vaccine representatives were advised to state that the purpose of the visit was to discuss cervical cancer disease awareness and not specific products and that GlaxoSmithKline's medical information team would be able to assist with any specific product enquiries. The representatives' disease awareness training material did not discuss medicines; it concluded with a section on screening and diagnosis.

The Panel considered that the material would encourage discussion about cervical cancer. This was not necessarily unacceptable so long as the material did not solicit questions about a specific medicine and that any discussion complied with the Code. The references to previous infection not providing sufficient immunity to prevent another infection might solicit general questions about vaccination. Whilst the Panel noted GlaxoSmithKline's explanation that such references emphasised the need for continued regular screening in older woman who remained sexually active the Panel did not consider that this explanation was made clear in any of the materials. Nonetheless, the overall emphasis of each item was on the burden and cause of disease and the need to ensure access to a successful screening programme. The Panel considered that the unqualified statement 'GlaxoSmithKline is committed to supporting you in the prevention of cervical cancer' would encourage doctors to ask about GlaxoSmithKline's role in prevention. The Panel noted that the model answers provided in the representatives' briefing document all indicated that the representative should state that the purpose of their visit was to discuss cervical cancer disease awareness, and not specific products.

Overall the Panel considered that the material and activities of the representatives did not identify, directly or indirectly, a specific medicine such that GlaxoSmithKline's medicine was being promoted prior to the grant of its marketing authorization. Nor did the material solicit enquiries about GlaxoSmithKline's forthcoming product. No breach of Clause 3.1 was ruled. The Panel consequently ruled no breach of Clause 2.

APPEAL BY SANOFI PASTEUR MSD

Sanofi Pasteur MSD noted that GlaxoSmithKline had recruited a team of representatives and area managers whose current role was to promote disease awareness of cervical cancer - the CCDAT. The advertisement placed to recruit these individuals stated that, following the launch of GlaxoSmithKline's candidate HPV vaccine, the team would switch from promoting disease awareness to promoting the vaccine. Sanofi Pasteur MSD alleged that the existence and activities of the CCDAT were in breach of Clause 3.1 of the Code. The manner in which the team was recruited, the inexorably close ties between disease awareness and future brand success, and the materials and tactics employed inevitably promoted a product prior to receipt of its marketing authorization. Furthermore, this represented a new and worrying precedent in the activities of field-based representatives: disease awareness directed one to one at future prescribers pre-launch to be followed by traditional promotion post-launch. As well as breaching Clause 3.1 in the pre-launch phase, the prominence of the CCDAT, the inexorable link between disease awareness and future commercial promotional objectives, and the extent of its activities brought discredit upon, and reduced confidence in, the pharmaceutical industry as a whole and thus was in breach of Clause 2 of the Code.

Sanofi Pasteur MSD stated that GlaxoSmithKline had misunderstood, or chosen to misrepresent, its understanding of the recruitment advertisement for the CCDAT. Before the launch of its candidate vaccine representatives would be asked to raise awareness of cervical cancer; after the launch they would be asked to

promote the vaccine itself. This was evident from the advertisement. However, in its response, GlaxoSmithKline had stated that a decision upon the precise role of the CCDAT would be made based upon the best use of resources. This deviated from the advertisement where the two elements were inexorably linked.

Sanofi Pasteur MSD alleged that GlaxoSmithKline had argued that the CCDAT's objectives and bonus criteria indicated its non-promotional nature. Yet, in the longer term this team, primarily composed of sales professionals, hoped to be involved in the launch of its candidate vaccine. One therefore could not only consider the influence of short term objectives, but also needed to consider the longer term influence of future 'sales performance on your territory' (quoted from the advertisement).

Sanofi Pasteur MSD noted that GlaxoSmithKline had stated that the target audience of the CCDAT was primary care professionals who took the lead on, or who were involved in, cervical screening. It also stated that the objective of the CCDAT was to educate relevant health professionals about the burden of cervical cancer and precancerous lesions, the causal role of oncogenic HPV in cervical cancer and the importance of the screening programme. Sanofi Pasteur MSD alleged that these were somewhat at odds. Those involved in cervical screening, which had existed as an organised programme since 1988, were likely to be the best informed about the subject matter of the CCDAT, so why would they be the target audience for an educational programme?

Sanofi Pasteur MSD alleged that GlaxoSmithKline had acknowledged not only that its representatives might be asked why they were talking about cervical cancer and not selling a product, but also that they might be asked about HPV vaccination itself. The model answers attempted to deflect these questions but the answers would stimulate further enquiry. For example, the answer that GlaxoSmithKline had a research and development interest in cervical cancer was bound to result in further questioning about the nature of that interest. The final answer in the chain of escalation referred the health professional to GlaxoSmithKline's medical information team for 'specific product enquiries'. Since such questions could not be considered truly unsolicited, the responses provided, even if under the responsibility of the medical department, should be considered promotional. Sanofi Pasteur MSD queried if the Panel had requested information from GlaxoSmithKline about the number of enquiries its medical information team had answered that were stimulated by the CCDAT, and whether their content had been scrutinised.

Sanofi Pasteur MSD alleged that the level of enquiry from health professionals would be influenced by the level of public relations activity surrounding GlaxoSmithKline's candidate vaccine. For example, the following were recent press releases from GlaxoSmithKline's website (accessed 29 January 2007) that related to its candidate vaccine:

January 18 2007:	GlaxoSmithKline initiated head-to-head study of cervical cancer vaccines
September 29 2006:	Mathematical model predicted that Cervarix might prevent nearly 80% of cervical cancers
July 12 2006:	Latest data show GlaxoSmithKline's proprietary adjuvant system for Cervarix induced a stronger and more sustained immune response than a conventional adjuvant formulation

Sanofi Pasteur MSD noted that GlaxoSmithKline had refuted that its status as one of the largest vaccine suppliers in the UK had any bearing, referring to the fact that it manufactured medicines for a wide variety of therapeutic areas. GlaxoSmithKline had eighty eight prescription only brands listed in the Electronic Medicines Compendium. Sixteen of these were vaccines; six were in the field of oncology. The Panel had acknowledged that the materials employed by the CCDAT (a) would encourage doctors to ask about GlaxoSmithKline's role in cervical cancer prevention; and (b) might solicit general questions about vaccination. In this context, GlaxoSmithKline's prominence in the field of vaccines and relative lack of prominence in the field of oncology was important.

Sanofi Pasteur MSD alleged that finally, the focus on the oncogenic HPV types 16 and 18 (the two types targeted by GlaxoSmithKline's candidate vaccine) in the CCDAT materials, combined with the points described above, made it inevitable that the materials and activities of the CCDAT would solicit enquiries about GlaxoSmithKline's candidate vaccine. Indeed, this was acknowledged by GlaxoSmithKline itself in the questions and answers provided to its representatives.

Sanofi Pasteur MSD alleged that the material and the activities of the CCDAT had (a) indirectly identified GlaxoSmithKline's candidate HPV vaccine; and (b) solicited enquiries about it. Therefore Sanofi Pasteur MSD appealed the Panel's ruling of no breach of Clauses 3.1 and 2 of the Code.

With regard to GlaxoSmithKline's documents headed 'Performance and Development Plan' and 'Welcome to the Performance and Development planning process' Sanofi Pasteur MSD submitted that it had a number of concerns regarding the true motives for the CCDAT. GlaxoSmithKline had stated in its response that the CCDAT team was primarily measured on activity based criteria with flexible objectives based on other criteria eg budget expenditure and planning which did not relate to promotional activity now or in the future. Furthermore, GlaxoSmithKline also stated that it had stringent safeguards for the separation of non-promotional and promotional roles and that members of the CCDAT were not conducting any promotional activity either directly or indirectly.

Sanofi Pasteur MSD alleged that these two claims were at odds with some of the elements of the Performance and Development Plan for the area manager. The area

manager's department was referred to as 'CBU'; this stood for Cervarix business unit. That in itself spoke volumes. The fact that the area managers were an integral part of a business unit whose remit must be to deliver commercial success for Cervarix showed flagrant disregard for the spirit and the letter of the Code.

Additionally, Sanofi Pasteur MSD noted the following objectives were of specific concern.

The final performance measure listed was '2-way communication with brand team'. If non-promotional and promotional roles were so stringently separated, why would the CCDAT area managers need to communicate with the brand team?

Although the section on specific alignments was not completed, it was totally inappropriate to even refer to 'achieving expectations for brand champions' in the performance and development plan for an allegedly non-promotional role.

The endorsement section appeared to refer to endorsement from 'customers' at regional and national level. A number of issues caused concern:

(a) The reference to 'customers', a term that was traditionally used in a commercial context.
(b) 'Role clarity in terms of ownership and responsibilities agreed with [named manager]'. This presumably referred to who would be responsible for each 'customer'. That manager was the Senior Brand Manager, Vaccines, for GlaxoSmithKline. This was further evidence of the intertwined relationship between the allegedly non-promotional CCDAT and the brand team.
(c) 'KOL [key opinion leader] mobilisation plan in place'. Typically key opinion leader referred to respected, knowledgeable and influential health professionals. It would be instructive to know what they were being mobilised to do and why the plan was only to be put in place, rather than executed. Perhaps the execution was for a later time.

Sanofi Pasteur MSD alleged in summary that the content of the area manager's performance and development plan reinforced its concerns about the existence and activities of the CCDAT.

COMMENTS FROM GLAXOSMITHKLINE

GlaxoSmithKline assured the Appeal Board that it had taken the spirit and letter of the Code to heart in the recruitment of the CCDAT and in the planning and implementation of its activities. As such, GlaxoSmithKline was confident that the existence of this non-promotional team and its activities complied with the Code. GlaxoSmithKline supported the Panel in its interpretation and ruling on the comprehensive response submitted to the original complaint.

GlaxoSmithKline submitted that it appeared that Sanofi Pasteur MSD's appeal was anchored to the content of the initial recruitment advertisement. The content and intent of the advertisement alluded to the team changing its objectives once a marketing authorization was granted for the company's candidate HPV vaccine. However, the CCDAT was an entirely non-promotional team which was engaged in a genuine disease awareness campaign. The non-promotional nature of the team was evidenced by the CCDAT briefing document, training, health professional materials and objectives and bonus criteria together with the comprehensive material and guidance on handling possible questions from health professionals.

GlaxoSmithKline submitted that in future, individuals from the CCDAT might become part of a promotional team which would support the product when it was licensed. The training, materials, objectives and bonus criteria for any such new team would reflect its promotional nature and as such, would be completely different from those of the non-promotional CCDAT. The existence and activities of the CCDAT could only be judged by what was happening now, not what activities might or might not be undertaken by a promotional team in the future. The CCDAT did not discuss HPV vaccination under any circumstances and had been thoroughly trained and assessed on how to handle potential situations where health professionals might ask about HPV vaccination. Contrary to Sanofi Pasteur MSD's assertion, the company's proactive approach and training on this topic was one of probity, not promotion, and took into account previous rulings.

GlaxoSmithKline addressed Sanofi Pasteur MSD's assertion that those involved in cervical screening, which had existed as an organised programme since 1988, were likely to be the best informed about the subject matter of the CCDAT. This statement was addressed by the publications cited previously which highlighted the need for further education of health professionals in this area, a conclusion which was also supported by market research commissioned by GlaxoSmithKline. GPs and most practice nurses were involved in cervical screening as they provided the backbone of the national cervical screening programme. GlaxoSmithKline decided to target those health professionals who had shown an active interest in cervical cancer as the information was likely to be of more interest and relevance to them. They were also more likely to be concerned about the dramatic decline in uptake of screening in younger women and be keen to motivate all of their eligible female patients to attend. Raising health professionals awareness in this area in a way that might subsequently improve patient care could only be a positive outcome.

In response to Sanofi Pasteur MSD's allegation regarding the public relations activity undertaken by GlaxoSmithKline, all three press releases clearly related to important events in the vaccine development programme and did not constitute a concerted public relations campaign to drive enquiries from health professionals as inferred.

GlaxoSmithKline noted that Sanofi Pasteur MSD had alleged that its prominence in the field of vaccines and relative lack of prominence in oncology was important.

GlaxoSmithKline was the largest UK-based pharmaceutical company and manufactured medicines for a wide variety of therapy areas that might be known to primary care health professionals. Health professionals did not make an inevitable assumption that it was developing a vaccine for cervical cancer as no specific medicine was referred to, either directly or indirectly, in any of the CCDAT materials or activities.

GlaxoSmithKline noted that Sanofi Pasteur MSD re-iterated its claim that there was a focus on oncogenic HPV types 16 and 18 and that this invited enquiries about GlaxoSmithKline's candidate vaccine, as these two HPV types were targeted by its vaccine. As previously outlined, the material made it clear that there were around 100 types of HPV, of which 15 could cause cervical cancer but types 16 and 18 were responsible for the majority, representing over 70% of cases.

In summary, GlaxoSmithKline submitted that the CCDAT was non-promotional; educated doctors and nurses on the epidemiology, burden and prevention of cervical cancer through screening. None of the materials or activities either directly or indirectly referred to specific medicines or encouraged enquiries about unlicensed products. The team had been thoroughly briefed on the Code and how to work within it. It had not been trained on any products in this therapeutic area, and had been instructed to refer any queries about medicines to medical information. GlaxoSmithKline had taken a responsible approach to training the representatives to ensure they operated within the Code and were aware of potential pitfalls.

GlaxoSmithKline noted Sanofi Pasteur MSD's additional comments on its 'Performance and Development Plan' and 'Performance and Development Plan Planning Process' documents.

GlaxoSmithKline re-iterated that the CCDAT was not measured or incentivised on criteria that would encourage the representatives to promote its candidate HPV vaccine, Cervarix, prior to it receiving its marketing authorization and this was quite clear from the 'Performance and Development Plan'. Sanofi Pasteur MSD's latest concerns appeared to centre around its assumptions based on terminology and nomenclature.

GlaxoSmithKline submitted that the department within the company responsible for the CCDAT was correctly identified as the Cervarix business unit (CBU). This title was strictly not referred to in interactions with health professionals. As such, it did not appear on business cards and was not referenced in any verbal or written correspondence with health professionals. GlaxoSmithKline was comprised of a number of business units which were each responsible for all activities related to its major brands and the associated disease areas. The CCDAT activities, materials, training, objectives and bonus criteria clearly established the CCDAT as a non-promotional team and the fact that they were part of the Cervarix business unit **did not** influence the nature of their role. Both product and non-product related activities fell within the remit of the Ceravix business unit and all members of the UK company who worked on GlaxoSmithKline's candidate HPV vaccine formed part of the Cervarix business unit.

GlaxoSmithKline submitted that all CCDAT activities, materials, guidance and training were certified to ensure compliance with both the spirit and letter of the Code. The CCDAT undertook no promotional activity as evidenced by the information provided to and ruled on by the Panel. GlaxoSmithKline strongly refuted Sanofi Pasteur MSD's allegation of 'flagrant disregard' for the Code.

GlaxoSmithKline submitted that as evidenced by previous correspondence on this case, disease awareness activities were permitted under the Code and in the Medicines and Healthcare products Regulatory Agency's (MHRA) Blue Guide S5.11 as quoted below.

'Campaigns relating to human health directed at the general public with a view to providing information, promoting awareness or educating the public about a particular condition or disease are encouraged. Care must be taken to ensure that the information provided does not make product claims for the material to remain outside the definition of an "advertisement" under the Regulations. In particular, use of brand names, restricting the range of treatments described in the campaign or drawing attention to the campaign by advertising which is likely to lead to the use of a specific prescription only medicine or medicines can all lead to a potential breach of the Regulations.'

GlaxoSmithKline submitted that neither the Code nor the MHRA required disease awareness teams to have a specific reporting line. It was clear in all documentation that the requirements and the spirit of the Code and the MHRA Blue Guide had been strongly upheld by GlaxoSmithKline. It was customary practice in GlaxoSmithKline for non-promotional roles to be aligned with brand teams, and it was a source of pride that GlaxoSmithKline was able to achieve a clear distinction of promotional and non-promotional activities through its significant internal investment in its ongoing ethics programme.

GlaxoSmithKline submitted that with regard to the '2 way communication' with the brand team it was worth clarifying the constitution of a brand team. Within GlaxoSmithKline, the 'brand team' were not exclusively marketeers or sales people - medical advisors, researchers and scientific advisors also formed part of the team. The 'brand' referred to in the performance and development plan was cervical cancer disease awareness. As highlighted previously, the CCDAT team was exclusively focussed on cervical cancer disease awareness. As mentioned above, there was no restriction on the reporting line of disease awareness teams as long as the required separation occurred between product and non-product related activities. The CCDAT activities were purely non-promotional and non-product related.

GlaxoSmithKline submitted that none of the documentation referred to vaccination or any product

related to cervical cancer. GlaxoSmithKline reiterated the entirely non-promotional nature of the CCDAT and noted that Sanofi Pasteur MSD had not provided any evidence of any promotional activities being conducted by the CCDAT. This was because none existed.

GlaxoSmithKline submitted that in addition to the 'brand team' reference, Sanofi Pasteur MSD also highlighted additional areas of concern, particularly around the use of 'customers' and 'KOL [key opinion leader] mobilisation'. 'Customers' was an umbrella term used to identify the recipient of goods or a service. However, its use was not restricted to a commercial context within GlaxoSmithKline, where, for example, medical information teams also referred to health professionals as their 'customers'. In the context of the CCDAT, 'customer' referred to the recipient of the cervical cancer disease awareness educational programme. 'Endorsement' from customers at a regional and national level referred to health professional agreement with and support of the need for education in the area of cervical cancer. The level of their endorsement might vary from simply agreeing with the need for further education in this area, to being prepared to speak locally or nationally about cervical cancer, and one of the aims of the CCDAT was to mobilise key opinion leaders to educate other health professionals about this disease area. As with all CCDAT activities, the content of such educational sessions was entirely disease focussed.

With regard to Sanofi Pasteur MSD's allegation about one of its managers, GlaxoSmithKline explained that he was a senior brand manager within the Cervarix business unit. His role was focussed on external health professionals relationships and meeting arrangements and he oversaw the planning and logistics of external meetings within the Cervarix business unit. As such, it was entirely appropriate that he and the CCDAT would communicate with each other regarding the educational meetings outlined above, and this was entirely in line with their non-promotional role. The bullet point in the performance and development plan referred to CCDAT clarity in terms of key opinion leader contact. The CCDAT consisted of 65 educational representatives. Therefore, in order to limit the frequency and volume of requests made of each key opinion leader, each key opinion leader had one point of contact within GlaxoSmithKline. The management of this process fell within the manager's remit.

GlaxoSmithKline submitted that in summary, none of the area managers' performance and development plans referred directly or indirectly to either increasing health professional's knowledge, or sales, of GlaxoSmithKline's candidate HPV vaccine. Furthermore, none of the CCDAT's materials or activities referred to specific medicines either directly or indirectly, nor did they encourage enquiries about unlicensed products. The CCDAT had not been trained on HPV vaccination and did not discuss HPV vaccination with health professionals under any circumstances. In addition, they had been rigorously trained on how to deal with situations in which the health professionals raised the subject of HPV vaccination.

GlaxoSmithKline submitted that it had clearly not promoted any medicine in advance of its marketing authorization. As such it urged the Appeal Board to uphold the Panel's ruling of no breach of Clause 3.1 and thus Clause 2.

FURTHER COMMENTS FROM SANOFI PASTEUR MSD

Sanofi Pasteur MSD noted that GlaxoSmithKline had stated that no evidence existed of any promotional activities having been conducted by the CCDAT. However, Sanofi Pasteur MSD alleged that it had feedback from its own representatives both of CCDAT representatives actively mentioning vaccination and also of customers asking CCDAT representatives about vaccination. These were not isolated incidents and no doubt reflected (a) the inherent difficulties in constructing a disease awareness team that would have future promotional responsibilities; and (b) the difficulty in a pharmaceutical company field-based team conducting disease awareness with no product mention and the inevitable questions that would be raised by health professionals.

APPEAL BOARD RULING

In the Appeal Board's view it was not necessarily unacceptable for companies to conduct a disease awareness campaign and to use materials with health professionals that generated discussion prior to the grant of a relevant marketing authorization. The arrangements had to comply with the Code. Employees involved in delivering such a campaign should be comprehensively briefed about the Code. The area was difficult and companies needed to ensure that the arrangements and activities were very carefully controlled and managed. The importance of documentation and instruction could not be overestimated. All of the circumstances had to be taken into account when deciding whether such arrangements complied with the Code.

The Appeal Board noted that the recruitment advertisement that appeared in the April 2006 issue of Pharmaceutical Field, a journal aimed at sales professionals, stipulated that candidates for the position of representatives should have a proven track record in sales, with excellent negotiation and influencing skills. The advertisement referred to delivering a focussed disease awareness campaign and then implementing the launch of the vaccine in early 2007. The Appeal Board considered that whilst a sales background was not necessarily unacceptable it was however, consequently important that the company was especially careful about the arrangements and activities given a representative's natural tendency to sell. The Appeal Board also noted the company representatives' submission that approximately 25% of the CCDAT team was recruited from a non-sales position.

The Appeal Board noted GlaxoSmithKline's submission about the CCDAT non promotional role

and training but was nonetheless concerned about the scale of the activity; there were 65 members of the CCDAT operating throughout the UK, targeting potential prescribers. It was likely that most of the CCDAT would promote GlaxoSmithKline's vaccine to the same group of prescribers once the product had received its marketing authorization.

The Appeal Board did not accept the GlaxoSmithKline representatives' position that the primary purpose of the CCDAT and materials was to increase screening rates. The company representatives had explained that the targeted practices were those with large numbers of female patients registered and not those with low uptake of cervical screening.

The Appeal Board noted that HPV types 16 and 18 were responsible for 71.5% of cervical cancers. Fifteen of the 100 HPV types identified could cause cervical cancer. The Appeal Board was concerned about the overall emphasis of the detail aid (CER/DAP/06/26681/1) on HPV types, particularly oncogenic HPV types 16 and 18, given the stated primary objective of the campaign to increase screening levels. The Appeal Board considered that this objective could be achieved without such emphasis. In particular three out of four bullet points on the final page of text (page 13), which the Appeal Board inferred summarized the key take-home message of the detail aid, referred to oncogenic HPV types 16 and 18 and/ or HPV infection. There was no mention of screening. Further the references to and undue emphasis on only oncogenic HPV types 16 and 18 could only relate to a specific medicine; GlaxoSmithKline's forthcoming vaccine. (The currently available vaccine Gardasil, was indicated for HPV types 6 and 11 as well as oncogenic HPV types 16 and 18.) The page also stated that 'GlaxoSmithKline is committed to supporting you in the prevention of cervical cancer'. The company representatives explained that the support referred to comprised discussion with health professionals by members of the CCDAT about the importance of screening, sponsorship of educational meetings and the provision of patient leaflets. The Appeal Board did not have copies of the patient leaflets before it.

Overall the Appeal Board considered that the cumulative effect of the arrangements amounted to promotion of a product prior to the grant of its marketing authorization. A breach of Clause 3.1 of the Code was ruled. It thus considered that the arrangements would bring discredit upon and reduce confidence in the pharmaceutical industry; a breach of Clause 2 was ruled. The appeal was successful.

Complaint received **3 November 2006**

Case completed **2 May 2007**