CASE AUTH/2165/9/08

ANONYMOUS EMPLOYEE v ROCHE

Cystic fibrosis patient adherence and incentive programme

The complainant wrote as an anonymous employee of Roche who was very concerned over the lack of action with reference to an adherence programme that the company had run since 2004 and that continued today.

The complainant understood that the programme incentivised children and teenagers suffering from cystic fibrosis (CF) to stay on Pulmozyme treatment. The concept was one that the complainant realised was needed and he/she understood it was not outwith the Code but the complainant did not know whether this was an acceptable means to sell a product.

The complainant was concerned that the incentive was a payment of a £10 voucher or gift card for certain high street stores. Effectively Roche was paying children to continue with a prescription only medicine and the NHS was paying for the medicine which was clearly financially more significant than £10.

The scheme was that a doctor would prescribe Pulmozyme which was presented in an ampoule with a removable cap. The patient would collect the caps and for every 30 returned to Roche's agency the patient would be sent a £10 voucher for the shop of their choice. Every 30 ampoules used meant £10 to the child or parent to spend.

There was no guarantee that the children actually took the medicine as prescribed; they could just take the tops off and get the money. The complainant was particularly concerned that if they had a side effect and either still remained on treatment or just wasted the NHS money by fulfilling the next prescription without taking the medicines, then this raised concerns over patient safety.

The complainant also knew that paying patients to take a medicine was potentially against the law and as such the complainant wished to remain anonymous but had no option but to present the details as set out above.

The detailed response from Roche is given below.

The Panel noted that no new patients had been enrolled since September 2007 and the patient adherence and incentive programme had been finally stopped in September 2008. The letter to patients notifying them of changes and the closure of the programme was dated June 2007. The case was considered under the 2006 Code using the 2008 Constitution and Procedure.

The Panel noted Roche's submission that daily adherence with Pulmozyme was particularly important in CF and that Pulmozyme was the only medicine in its class.

The Panel accepted that there were difficulties with adherence but did not consider the incentive scheme run by Roche was an appropriate means of encouraging patients to take their medicine. There was nothing about the scheme which ensured that patients took Pulmozmye as prescribed. The adherence programme booklet for patients included a section clearly labelled 'The Incentive'. The section labelled 'Your questions answered' mentioned the importance of taking Pulmozyme every day, whether there were symptoms or not. This was in line with the product's summary of product characteristics (SPC).

The Panel noted that Roche representatives were given cycle goals (2004 and 2005) of recruiting patients to the adherence programme. Representatives were, according to Roche, initially financially rewarded on the number of patients enrolled. It was assumed that this would be by means of promoting the scheme to health professionals who would complete the enrolment form. The Panel was concerned that the scheme might have influenced the prescribing of Pulmozyme.

Roche submitted that it had instructed the agency to stop the incentive scheme by the end of September 2007. However this had not happened and vouchers continued to be sent out until the end of May 2008. This showed a serious lack of control by Roche.

The Panel was extremely concerned about the arrangements for many reasons. However it did not consider that the incentive scheme amounted to a gift, benefit in kind or pecuniary advantage given or offered to health professionals or administrative staff as an inducement to prescribe, supply, administer, recommend, buy or sell any medicine. The benefit, in the form of vouchers for high street stores, was to patients not individual health professionals. The Panel thus ruled no breach of the Code.

The Panel did not consider that the vouchers were promotional aids as such. They were clearly linked to the use of the medicine. The vouchers were not promotional aids for health professionals and thus there could be no breach of the Code.

The Panel considered that gifts to patients was a difficult area. There was little guidance in the Code and little case precedent. However the Panel was

very concerned about a pharmaceutical company in effect providing cash as an incentive to patients to use its medicine.

The Panel considered that once enrolled into the programme, and knowing about the £10 vouchers, patients would be likely to ask their doctor to prescribe Pulmozyme and thus a breach of the Code was ruled.

The Panel considered that the incentive scheme was totally unacceptable. It did not consider that Roche had maintained high standards. A breach of the Code was ruled. The Panel considered that the arrangements brought discredit upon, and reduced confidence in, the pharmaceutical industry. A breach of Clause 2 was ruled.

The Panel also considered that the incentive scheme for patients warranted consideration by the Appeal Board in relation to the possibility of additional sanctions. In addition the Panel was concerned that Roche's procedures had allowed vouchers to be distributed for over 6 months after the scheme had closed. The company was currently suspended from membership of the ABPI in relation to another matter. The Panel decided to report Roche to the Appeal Board in accordance with Paragraph 8.2 of the 2008 Constitution and Procedure.

Roche accepted all the Panel's rulings of breaches of the Code.

The Appeal Board accepted that daily treatment with Pulmozyme was particularly important in CF. Irrespective of whether or not the scheme complied with the Code, the Appeal Board was concerned that a patient adherence scheme was introduced with no means of measuring its effectiveness. The scheme was aimed at patients aged between eight and sixteen. The choice of the high street stores seemed odd given this age group.

The Appeal Board was extremely concerned that vouchers were still being distributed following Roche's decision to withdraw the programme in September 2007 and instructions to its agency at this time. This showed a serious lack of control by the company.

The Appeal Board noted that Roche was currently suspended from membership of the ABPI and undergoing a series of audits (Cases AUTH/2099/2/08 and AUTH/2100/2/08 and AUTH1819/4/06). The Appeal Board was very concerned about Case AUTH/2165/9/08 but decided that in the circumstances no further action was required in relation to possible further sanctions.

An anonymous employee complained about Roche Products Limited's cystic fibrosis (CF) patient adherence and incentive programme. Roche marketed Pulmozyme (dornase alpha) for the management of CF.

COMPLAINT

The complainant stated that having recently received a large amount of ABPI training, awareness of what was right and wrong had been raised and as such the complainant wrote as a member of Roche who was very concerned over the lack of action with reference to an adherence programme that the company had run since 2004 and that continued today.

The complainant understood that the programme incentivised children and teenagers suffering from CF to stay on Pulmozyme treatment. The concept was one that the complainant realised was needed and he/she understood it was not outwith the Code but the complainant did not know whether this was an acceptable means to sell a product.

However, the complainant's concern was that the incentive was a payment of a £10 voucher or gift card for Boots, Tesco and Toys R Us. Effectively Roche was paying children to continue with a prescription only medicine and the NHS was paying for the medicine which was clearly financially more significant than £10.

The system was that a doctor would prescribe Pulmozyme and the patient got the medicine. Pulmozyme was presented in an ampoule with a removable cap. The patient would collect the caps and for every 30 returned to the agency acting on Roche's behalf the patient would be sent a £10 voucher for the shop of their choice. Every 30 ampoules used meant £10 to the child or parent to spend.

There was no guarantee that the children actually took the medicine as prescribed by their doctor and they could just take the tops off and get the money. The complainant was particularly concerned that if they had a side effect and either still remained on treatment or just wasted the NHS money by fulfilling the next prescription without taking the medicines, then this raised concerns over patient safety.

The complainant knew that this was potentially a very serious matter but with the company being suspended and the fact that senior management had known about this for over three months but not closed it down, as the complainant felt they should have, they were now acting irresponsibly and did not take action because of profit over safety.

The complainant also knew that paying patients to take a medicine was potentially against the law and as such the complainant wished to remain anonymous but had no option but to present the details as set out above so the authorities could investigate further and make their own judgement.

When writing to Roche, the Authority asked it to respond in relation to Clauses 2, 9.1, 18.1 and 22.2 of the Code and to consider the supplementary information to Clause 18.2 about items given to or

for use by patients. Except for the numbering of Clause 22.2 (formerly Clause 20.2) these were all the same in the 2006 Code as in the 2008 Code.

RESPONSE

Roche stated that it had considered very carefully whether its historical actions in relation to the CF patient adherence and incentive programme could fairly be said to constitute breaches of Clauses 2, 9.1, 18.1 and 22.2 of the 2008 Code.

Background summary

In 2004, in discussions with clinicians who treated CF, Roche was made aware of the particular problem of patient compliance. Roche then devised health educational materials concerning CF intended to encourage children and teenagers to take Pulmozyme every day as prescribed. Pulmozyme was supplied in ampoules for use with a nebuliser.

In 2007, it was decided to replace the voucher system for the adherence and incentive programme with an on-line educational programme as a way of encouraging more effective adherence. All patients who were enrolled in the programme at that time were sent letters informing them that the voucher scheme was to close in September 2007. Since then, no new patients had been enrolled in the voucher programme.

Although the agency running the programme on Roche's behalf was instructed by Roche to send letters out to patients in order to end the programme, in June 2008 Roche discovered that applications for vouchers were still being processed.

Chronological order of events

- June 2004 — Adherence programme developed
- August 2004 — Adherence programme certified
- September 2004 — CF adherence programme live
- By September 2007 — Voucher scheme closed and moved to on-line education. Roche told agency to advise patients and health professionals of closure by letter
- June 2008 — Discovery of vouchers still being reimbursed
- June – August 2008 — Investigation period
- July 2008 — All health professionals contacted with written declaration of closure
- August 2008 — Patient letters produced to reinforce closure
- September 2008 — Letters sent to patients who had claimed since 2007

Cystic fibrosis

CF was the UK's most common, life-threatening, inherited disease with over 8,000 people affected. One of the symptoms of CF was thick mucus production resulting in frequent lung infections. Often, symptoms of CF appeared in infancy and childhood.

One of the treatments for CF was Pulmozyme, a recombinant human deoxyribonuclease, which broke down DNA in the sputum, thus decreasing its viscosity. Pulmozyme was the only medicine in its class and there was no therapeutic alternative to it that worked in the same way. Pulmozyme, combined with other treatments, helped prevent chronic inflammation and infection and consequent damage to the lungs.

Regular use of Pulmozyme prevented the decline in lung function that ultimately resulted in the need for lung transplantation or contributed to patient death. Compliance was particularly important because every day of treatment missed was another day that a child's lungs were exposed to the damaging effects of mucus. Furthermore, clinical trials had shown that the beneficial effects of Pulmozyme were lost if a patient only used Pulmozyme intermittently and were not regained if the patient later restarted regular therapy. This made daily adherence a vital feature of Pulmozyme therapy (Pulmozyme summary of product characteristics (SPC) Section 4.2).

With the advent of modern treatments, the proportion of CF patients becoming adults had increased as had the median life expectancy and many patients now lived into their 40s compared to 1990 for example, when girls had a median survival age of 25, 30 years for males (US CF registry data).

Adherence programme detail

In 2004, Roche UK began an adherence and incentive programme. The programme was developed following discussions with clinicians and a child psychologist regarding the problems of patient compliance with CF, and was intended to encourage children and teenagers to take their medicine as prescribed (once daily). Patients were advised of the programme by their doctor, who would complete an enrolment form and send it to an external agency which managed the programme on behalf of Roche. The agency provided the patients with an introduction booklet that contained educational material on CF including background information on CF, tips to help increase compliance, including daily adherence record sheets, and questions and answers concerning CF generally. The last page of this booklet contained a voucher request form which could be completed and returned to the agency. In exchange for 30 Pulmozyme ampoule tops, the agency would provide a voucher or gift card for £10 together with a new claim form and free post envelope for the next set of ampoule tops. Roche was informed of

the names of doctors enrolling patients, the number of patients enrolled, and how many vouchers had been requested. Doctors received no payment or other benefit for enrolling patients. The agency informed clinicians which of their patients had taken up the programme.

The programme went through Roche's internal approval procedure but the company had not retained all documents surrounding the process. The programme was explained by sales representatives to treating clinicians. Representatives were initially financially rewarded on the number of patients enrolled.

By October 2005 at an advisory board meeting, UK key doctors were informed that the programme included: 302 registered patients, 185 patients had returned tops, 34 CF centres had registered, average of 8.8 patients per centre, average adherence rate – 44% and average adherence rate of responders – 64%.

In April 2006, Roche changed the external agency involved with the programme. At that time there were 367 patients enrolled and 69 consultants participating.

Closure of the CF adherence programme

By July 2007, numbers in the programme had increased to 501 patients and 71 consultants. At that time, it was decided to replace the programme with a web based educational tool. The agency wrote to the patients then in the programme to let them know of this change and to explain that any outstanding claims for vouchers should be submitted by 20 September 2007. It seemed that this did not have the effect of ending the original programme entirely and the agency continued to receive tops and send out vouchers until the end of May 2008. All of these claims were submitted by patients enrolled before September 2007 as no new patients had been enrolled since that date. Since the end of September 2007, 160 patient claims had been received and 254 vouchers had been sent. As of 15 September 2008 there were claims from 10 patients seeking a total of 31 vouchers.

The fact that the programme had not ended from September 2007 came to light when a brand manager left Roche and files were examined. It then became apparent that vouchers were still being sent out by the agency despite it being thought that the programme had been closed.

Roche action

Roche had investigated the facts surrounding the programme. All health professionals involved in treating CF patients were telephoned to ensure that it was clear that the programme had ended. Roche contacted the 70 CF clinicians at the end of July 2008 to confirm that the programme was closed and to provide a declaration that they had no registration forms in their possession. In addition, all those patients who had claimed since September 2007 received a certified letter, sent by recorded delivery by the agency, to again reinforce the closure of the programme.

Breach of Code – Clauses 2, 9.1, 18.1, 22.2

The Authority asked Roche to consider the complaint in the light of the 2008 Code. The one significant difference which the Authority might consider relevant to the investigation of this complaint was that, whilst the 2008 and 2006 Codes required express certification of non-promotional activities, the 2003 Code did not, In fact, the CF adherence programme was vetted for compliance with the Code in 2004 when it was introduced but Roche drew this point to the Authority's attention should it later become relevant to its determination. In that event, Roche would rely on the provisions of the 2003 and 2006 Codes in judging actions taken during the currency of those Codes.

Roche did not consider that it was possible to claim that the CF adherence programme amounted to a breach of Clause 18.1 of the 2008 (or 2003 or 2006) Code. Clause 18.1 was written in the same terms in each of the Codes and reflected the provisions of Directive 2001/83/EC and the transposing Medicines (Advertising) Regulations 1994. The aim, as set out in Recital 50 to the Directive and as clearly drafted in the Directive, Regulations and Code was that:

'Persons qualified to prescribe medicinal products must be able to carry out those functions objectively without being influenced by direct or indirect financial inducements.'

Clause 18.1 of the Code provided that:

'No gift, benefit in kind or pecuniary advantage shall be offered or given to members of the health professions or to administrative staff as an inducement to prescribe, supply, administer, recommend, buy or sell any medicine, subject to the provisions of Clause 18.2.'

At no time during the operation of the CF adherence programme was any gift, benefit in kind or pecuniary advantage offered or given to any health professional or to any administrative staff, whether as an inducement to prescribe, administer, recommend, buy or sell any medicine or otherwise. The CF adherence programme did not amount to the distribution of a promotional aid, consequently, the final proviso relating to Clause 18.2 was not relevant.

With regard to the supplementary information to Clause 18.2 'Gifts To or for Use by Patients', Roche submitted that since the CF adherence programme was not a promotional programme and did not involve the distribution of promotional aids, Clause 18.2 was not relevant. The concept of an adherence programme that would be attractive to children with CF when set against the discomfort and disruption of daily nebulisers was clearly highly relevant to

their treatment and as Roche had explained, arose originally out of advice it had received from CF consultants. Roche acknowledged the intention behind the clear words of the supplementary information to Clause 18.2 preventing the offer of gifts or promotional aids to patients for the purpose of encouraging patients to request a particular medicine. Roche did not believe that, on the particular facts of this case, patients were encouraged to request a particular medicine from their consultant in breach of Clause 22 of the 2008 Code. Roche had, however, made sure that this principle was observed in all educational material now supplied to CF patients.

The material provided to patients was balanced and put the treatment in the context of the effects of the disease. As Roche had described, consultants initiated the enrolment of patients into the programme by contacting the agency after deciding to prescribe Pulmozyme. The programme only operated at the level of secondary care and, as would be expected at each clinic visit, usually six monthly, children would be subjected to careful and objective assessment of lung function. Appropriate treatment advice would then be given by the consultant or on his or her behalf and there would have been simply no opportunity for the fact that a patient was or was not enrolled in the programme to affect the prescriber's judgment. Neither would enrolment in the programme have caused patients to ask for a particular medicine because there was no alternative to Pulmozyme. It was the only medicine in its class, and it was indicated in nearly all CF patients, except a very small number who proved to be intolerant. The purpose of the programme was to encourage patients, mainly children, to take their medicine on a daily basis, once it had been prescribed. It was not intended, and did not, interfere in the decision to prescribe by influencing either the prescriber or patient in their choices. Roche believed that these specialists saw the programme as a positive contribution from Roche towards encouraging strict compliance in patients for whom compliance was critical.

Conclusion

In all of its actions concerning this programme Roche had taken its duty to act professionally and ethically and to uphold the high standards of the pharmaceutical industry very seriously. Roche believed it had discharged this duty and did not consider that the operation of the CF patient adherence and incentive programme had brought discredit to the pharmaceutical industry.

PANEL RULING

The Panel noted Roche's comments regarding the relevant Code and the timing of various activities. No new patients had been enrolled since September 2007 and the patient adherence and incentive programme had been finally stopped in September 2008. Arrangements which spanned many years needed to be rechecked when changes to the Code were made. The letter to patients notifying them of changes and the closure of the programme was dated June 2007. Taking all the circumstances into account the Panel considered that the case would be considered under the 2006 Code using the 2008 Constitution and Procedure.

The Panel noted Roche's submission that daily adherence with Pulmozyme was particularly important in CF and that Pulmozyme was the only medicine in its class.

The Panel accepted that there were difficulties with adherence but did not consider the incentive scheme run by Roche was an appropriate means of encouraging patients to take their medicine. There was nothing about the scheme which ensured that patients took Pulmozmye as prescribed. The adherence programme booklet for patients included a section clearly labelled 'The Incentive'. The section labelled 'Your questions answered' mentioned the importance of taking Pulmozyme every day, whether there were symptoms or not. This was in line with the product's SPC.

The Panel noted that Roche representatives were given cycle goals (2004 and 2005) of recruiting patients to the adherence programme. Representatives were, according to Roche, initially financially rewarded on the number of patients enrolled. It was assumed that this would be by means of promoting the scheme to health professionals who would complete the enrolment form. The Panel was concerned that the scheme might have influenced the prescribing of Pulmozyme.

Roche submitted that it had instructed the agency to stop the incentive scheme by the end of September 2007. However this had not happened and vouchers continued to be sent out until the end of May 2008. This showed a serious lack of control by Roche.

The Panel was extremely concerned about the arrangements for many reasons. However it did not consider that the incentive scheme amounted to a gift, benefit in kind or pecuniary advantage given or offered to health professionals or administrative staff as an inducement to prescribe, supply, administer, recommend, buy or sell any medicine. The benefit, in the form of vouchers for high street stores, was to patients not individual health professionals. The Panel thus ruled no breach of Clause 18.1.

The Panel did not consider that the vouchers were promotional aids as such. They were clearly linked to the use of the medicine. The supplementary information to Clause 18.2 stated that gifts to patients should be inexpensive and related to the condition under treatment or general health. Any such activity had to meet the requirements of the Code, in particular Clause 20. The Panel did not consider that vouchers for high street stores met this supplementary information. The Panel noted

that Clause 18.2 set out the requirements for promotional aids to health professionals. The vouchers were not promotional aids for health professionals and thus there could be no breach of Clause 18.2.

The Panel considered that gifts to patients was a difficult area. There was little guidance in the Code and little case precedent. However the Panel was very concerned about a pharmaceutical company in effect providing cash as an incentive to patients to use its medicine.

The Panel noted that Clause 20.2 required that statements should not be made for the purpose of encouraging members of the public to ask their health professional to prescribe a specific prescription only medicine. Clause 20.2 applied regardless of whether a patient was about to receive the first prescription of a particular medicine or was already regularly prescribed a particular medicine. The Panel considered that once enrolled into the programme, and knowing about the £10 vouchers, patients would be likely to ask their doctor to prescribe Pulmozyme and thus a breach of Clause 20.2 was ruled.

The Panel considered that the incentive scheme was totally unacceptable. It did not consider that Roche had maintained high standards. A breach of Clause 9.1 was ruled. The Panel considered that the arrangements brought discredit upon, and reduced confidence in, the pharmaceutical industry. A breach of Clause 2 was ruled.

The Panel also considered that the incentive scheme for patients warranted consideration by the Code of Practice Appeal Board in relation to the possibility of additional sanctions. In addition the Panel was concerned that Roche's procedures had allowed vouchers to be distributed for over 6 months after the scheme had closed. The company was currently suspended from membership of the ABPI in relation to another matter. The Panel decided to report Roche to the Appeal Board in accordance with Paragraph 8.2 of the Constitution and Procedure.

COMMENTS FROM ROCHE ON THE REPORT

Roche confirmed that the patient adherence programme was last fully operational in September 2007. No vouchers had been redeemed since June 2008 and a final letter reinforcing the closure of the scheme was sent in September 2008.

Roche was grateful for the guidance provided in the Panel's ruling in relation to items that might be provided to patients by way of incentives to compliance. As noted there had hitherto been little guidance or case precedent in this area.

Whilst Roche did not appeal the Panel's rulings of breaches of the Code, it wanted to present to the Appeal Board in relation to the case and, in particular, to deal with any wider concerns that the Appeal Board might have about the scheme. The application of Clause 20.2 involved a judgement based upon the particular facts and, whilst Roche respected and understood the basis for the Panel's rulings, it was very clear that this particular scheme was very unlikely to have had adverse consequences for public health that outweighed its obvious benefits in terms of promoting compliance.

At the consideration of the report Roche provided correspondence from a consultant clinical psychologist with expertise in cystic fibrosis and a clinical director of a CF unit in support of its submission that no further sanctions be applied.

APPEAL BOARD CONSIDERATION

The Appeal Board noted the Panel's rulings in the case which were not appealed by Roche.

The Appeal Board accepted that daily treatment with Pulmozyme was particularly important in CF. Irrespective of whether or not the scheme complied with the Code, the Appeal Board was concerned that a patient adherence scheme was introduced with no means of measuring its effectiveness. The scheme was aimed at patients aged between eight and sixteen. The choice of voucher seemed odd given this age group.

The Appeal Board was extremely concerned that vouchers were still being distributed following Roche's decision to withdraw the programme in September 2007 and instructions to its agency at this time. This showed a serious lack of control by the company.

The Appeal Board noted that Roche was currently suspended from membership of the ABPI and undergoing a series of audits (Cases AUTH/2099/2/08 and AUTH/2100/2/08 and AUTH1819/4/06). The Appeal Board was very concerned about Case AUTH/2165/9/08 but decided that in the circumstances no further action was required in relation to possible further sanctions.

Complaint received	**3 September 2008**
Undertaking received	**17 October 2008**
Appeal Board consideration	**13 November 2008**