CASE AUTH/2582/2/13

VOLUNTARY ADMISSION BY ROCHE

Promotion before the grant of a marketing authorization

Roche voluntarily admitted that an uncertified, promotional mailing for Perjeta (pertuzumab) had been sent to UK health professionals in February 2013, before it had received the relevant marketing authorization.

The detailed response from Roche is given below.

The Panel noted that the Perjeta mailing at issue had been distributed before Roche had received the marketing authorization which permitted the medicine's sale or supply. Copies of the mailing had been sent to the mailing house before it had been certified. The mailing house should have waited for confirmation from Roche that the material had been certified before distribution. The Panel noted, however, that in an email to the mailing house a Roche employee had asked 'In order to hit the target list on 19th Feb – when do you need the material?' There was no indication in the email that the date of 19 February was subject to confirmation.

The Panel noted Roche's submission that there was a contract between Roche and the mailing house and a standard agreed production process in place at the mailing house. The contract required the parties to establish a project confirmation and Roche to place a project brief with the agency. There was, however, no project confirmation between the company and its agency for the mailing at issue and no formal project brief.

The Panel noted that a Perjeta mailing had been sent to health professionals before the product had been granted a marketing authorization. A breach of the Code was ruled. The mailing was sent before it had been certified. A further breach of the Code was ruled.

The Panel noted that the mailing appeared to have been sent in error due to a combination of poor communication, contractual errors and human error; high standards had not be maintained. A breach of the Code was ruled.

In the Panel's view, companies must be extremely careful to ensure that material for new medicines were not distributed before the relevant marketing authorization had been received. Given the seriousness with which promotion before the grant of a marketing authorization was viewed, Roche's failure to follow set procedures and its reference to a mailing date without making it abundantly clear that the date was subject to confirmation, the Panel considered that the company, by promoting an unlicensed medicine had brought discredit upon, and reduced confidence in, the pharmaceutical industry. A breach of Clause 2 was ruled.

Roche Products Limited voluntarily admitted that it had promoted Perjeta (pertuzumab) before the medicine had been granted a marketing authorization to permit its sale or supply.

As Paragraph 5.6 of the Constitution and Procedure required the Director to treat a voluntary admission as a complaint, the matter was taken up with Roche.

COMPLAINT

Roche stated that on Thursday, 21 February 2013, an uncertified promotional mailing for Perjeta was sent in error by a third party mailing house to 2,260 UK health professionals.

Roche stated that it was committed to the appropriate use of medicines and protecting patient safety and strove to maintain high standards in the ethical promotion of its medicines. As such, the company and its employees understood the strict requirements of UK medicines regulations and the Code not to promote a medicine in the absence of its marketing authorization.

On discovery of this matter, Roche immediately tried to stop the mailing being posted. The matter was escalated to senior management and an investigation was undertaken to understand the root cause. Roche contacted the PMCPA for guidance as to what it could do to mitigate the risk of providing incorrect information to health professionals. The company also informed the Medicines and Healthcare products Regulatory Agency (MHRA).

Roche stated it was with deep regret that it acknowledged responsibility for the actions of the third party agency which acted on its behalf. The company voluntarily admitted breaches of Clauses 3.1, 9.1, 14.1 and 2.

Roche explained that the marketing authorization for Perjeta was expected in the first week of March. The mailing at issue was due to be sent after the marketing authorization was received, but as it was sent beforehand it clearly constituted promotion prior to the grant of a marketing authorization.

Roche explained that following artwork and proof approval of the job bag, it was company practice to print mailings with stock sent in parallel to the mailing house and to Roche for final certification. The mailing house had to await confirmation of certification from Roche before it distributed the mailing. This process was not followed and the mailing was distributed before the mailing house received this confirmation.

In failing to manage the effective implementation of this process and in acknowledgement of the human error of the mailing house, Roche accepted that it had failed to maintain high standards.

Given the seriousness of a breach of Clause 3, Roche considered that these actions risked reducing confidence in the industry and as such understood that a breach of Clause 2 might be a conclusion in this matter.

RESPONSE

Roche stated that the mailing with envelope (ref RXUKPERT00040c) and reply-paid card (RPC) (ref RXUKPERT00040d) were developed as part of a launch campaign for Perjeta, a new medicine for HER2-positive breast cancer, which at the time had not received its marketing authorization. The intended audience was oncologists, nurses and pharmacists with an interest in breast cancer.

The materials were certified on 18 January 2013 for submission to the MHRA for pre-vetting. As the pre-vetting materials were provided electronically, the materials were certified as PDFs specifically for the MHRA and watermarked 'MHRA draft'; this was to avoid confusion with the final production materials. The MHRA notified Roche on 24 January that it did not require any amendment to the mailing.

Roche's standard operating procedure (SOP) on approval and certification stated that permission to proceed to print was provided following the approval of a proof. Following notification from the MHRA, print production was commenced so that the mailing, envelope and RPC could be certified in their final forms. The reason for a full print run, rather than producing a small number of digital copies for certification, was that differences could occur between digital copies and those produced in a print run and as such they might not represent the final form.

Mailings (promotional or non-promotional) were printed and sent in parallel to Roche for final certification and to the mailing house for collation and labelling. The mailing house had to wait for email confirmation of final certification before it started the distribution process. There was a comprehensive contract between Roche and the mailing house and a standard agreed production process in place at the mailing house to confirm the mutual obligations of the two parties. Specific clauses highlighted the importance of ensuring compliance with the Code and respective legal obligations.

Clause 1.1 of the contract stipulated, *inter alia*, that for each project the parties would establish a project confirmation. Further, clause 2.1 stated that for each project, Roche would place a project brief with the agency. For the Perjeta mailing, in error on the part of Roche, no project confirmation was developed. There was also no formal brief, although an informal brief was provided by Roche to the mailing house in December 2012 which resulted in the mailing house providing Roche with some estimates.

An email on 17 January 2013 from Roche to the mailing house provided further detail of the project and included a postscript enquiry as to the latest date the material at issue needed to be with the mailing house in order to be distributed on 19 February – when it was anticipated that the marketing authorization for Perjeta would have been granted. Roche noted, however, that both the contract and agreed production process at the mailing house required that materials could only be released following confirmation from Roche of certification. A purchase order was raised on 22 January representing the official authorization by Roche for the agency to commence work on the project.

As part of the routine communication between Roche and the mailing house, a telephone call on 21 February confirmed receipt of the materials, review of the final mailing list and expected next steps. This call was returned 2 hours later, with the information that the mailing had been sent in error. An account of the telephone conversation was provided.

The promotional mailing for Perjeta was sent to 2,634 UK health professionals. Although the mailing had not been amended since it was certified for MHRA pre-vetting, it was not certified in its final hard copy form before it was distributed.

On discovery of this issue, Roche immediately tried to prevent the mailing entering the UK postal system. The matter was appropriately escalated to senior management. Roche contacted the PMCPA for guidance as to what it could do to appropriately mitigate the risk of providing incorrect information to health professionals and also contacted the MHRA.

An issues management group was instigated which consisted of senior UK managers and the respective heads of departments involved in the response. Evidence was gathered from the employee who originated the job and the third parties involved in the project.

A thorough stakeholder assessment was undertaken to ensure Roche had appropriately considered the possible routes of enquiry that might be initiated from the mailing. A plan of action for each stakeholder group was cross referenced with guidance provided by the PMCPA and confirmed by the issues management group.

Roche stated that a reactive statement and brief was certified and provided on 22 February (within 24 hours of the issue arising) for use by medical information, the supply chain customer service team and the communications department should any enquiries be received. Written briefs and reactive statements were certified and provided to field staff. These were emailed to all oncology field staff and a teleconference was convened with all field staff working in breast cancer to alert them to the brief and to direct them as to what to do if the matter was raised by a customer. This brief was reiterated in an email on 25 February to ensure appropriate direction was reinforced.

A reactive email and letter were generated to respond to any RPCs received from the mailing. The issues management group monitored the responses received from RPCs, medical information requests and product requests through the customer care group. Eight queries had been received to date.

A formal recall was initiated to ensure internal staff and agencies confirmed destruction or return of any remaining mailings. Field staff were instructed on what to do if a customer directly returned a mailing or the RPC.

Copies of all these documents were submitted.

Roche submitted that its investigation confirmed that although approval processes had been followed up to the point of distribution of the mailing, there were a number of contractual requirements between Roche and the mailing house that were not met in relation to the placing of a project confirmation and a formal brief; processes had not been followed by either the Roche employee involved or the mailing house. Communication had been received from the mailing house which identified that the mailing was released before certification because production staff failed to gain the required confirmation of certification in advance of distribution. In addition, Roche acknowledged the lack of a signed project confirmation form or formal brief and the failure for either side to confirm a target mailing date following enquiries regarding print and delivery requirements. Roche had taken steps with both its employee and the mailing house to address the failure to follow documented procedure.

The conclusion of the investigation was that human error and failure to follow agreed process led to the distribution of the mailings.

It had been recognized, and demonstrated by this incident, that sending materials to a third party for packing and distribution ahead of final certification exposed the company to a level of risk, despite agreed processes and contracts.

A group had been convened to review the internal process for mailings, although no formal change to the SOP would be made until the outcome of this case had been received. It was proposed that the internal process should be amended to ensure that, as with other printed materials, mailings, must be quarantined in the company's warehouse facilities and only released to a mailing house when they had been certified.

With regard to the requirements of Clause 3.1, Roche noted that the marketing authorization for Perjeta had not been received when the mailing was sent and Roche accepted that it had thus unwittingly promoted a medicine prior to the grant of its marketing authorization. An electronic form of the material had been certified as part of the MHRA pre-vetting process and, although the content had not changed, Roche accepted that the final form of the hard-copy mailing had not been certified in breach of Clause 14.1.

In failing to fully manage this process and in acknowledgement of the human error of the mailing house involved in this matter (acting on Roche's behalf) and of a Roche employee, Roche accepted that it had failed to maintain high standards at all times, in breach of Clause 9.1.

Given the seriousness of a breach of Clause 3.1 and with no dispute of the fact that this matter constituted promotion prior to the grant of marketing authorization, Roche considered these actions had risked reducing confidence in the industry and as such understood that a breach of Clause 2 would be a conclusion in this matter.

Roche reiterated that it was committed to the appropriate use of medicines and protecting patient safety and that it strove to maintain high standards in the ethical promotion of its medicines. As such, the company and its employees understood the strict requirements of UK medicines regulations and the Code not to promote a medicine in the absence of a marketing authorization.

Roche was committed to ensuring that such an issue could not happen again.

PANEL RULING

The Panel noted that the Perjeta mailing at issue had been distributed before Roche had received the marketing authorization which permitted the medicine's sale or supply. Copies of the mailing had been sent to the mailing house before it had been certified. The mailing house should have waited for confirmation from Roche that the material had been certified before it distributed the mailing. The Panel noted, however, that in an email to the mailing house a Roche employee had asked 'In order to hit the target list on 19th Feb – when do you need the material?' There was no indication in the email that the date of 19 February was subject to confirmation.

The Panel noted Roche's submission that there was a contract between Roche and the mailing house and a standard agreed production process in place at the mailing house. Clause 1.1 of the contract required the parties to establish a project confirmation; a template project confirmation form was provided which required a project overview and timeframes to be stipulated. Clause 2.1 of the contract required Roche to place a project brief with the agency. There was, however, no project confirmation between the company and its agency for the mailing at issue and no formal project brief - although the Panel noted Roche's submission that emails between the company and the mailing house constituted an informal brief.

The Panel noted that a Perjeta mailing had been sent to health professionals before the product had been granted a marketing authorization. A breach of Clause 3.1 was ruled. The mailing was sent before it had been certified. A breach of Clause 14.1 was ruled.

The Panel noted that the mailing appeared to have been sent in error due to a combination of poor

communication, lack of a project confirmation, no formal brief and human error. In the Panel's view high standards had not be maintained. A breach of Clause 9.1 was ruled.

The Panel noted Roche's submission that in the light of the events above, it had proposed that mailings would no longer be sent to mailing houses ahead of certification; they would instead be quarantined in the company's warehouse until they had been approved for release. The Panel agreed with Roche's acknowledgement that sending uncertified material to a mailing house exposed the company to the risk of the material being distributed ahead of time.

In the Panel's view, companies must be extremely careful to ensure that material for medicines which were awaiting authorization were not distributed before the relevant marketing authorization had been received. Given the seriousness with which promotion before the grant of a marketing authorization was viewed, Roche's failure to follow set procedures and its reference to a mailing date without making it abundantly clear that the date was subject to confirmation, the Panel considered that the company, by promoting an unlicensed medicine had brought discredit upon, and reduced confidence in, the pharmaceutical industry. A breach of Clause 2 was ruled.

Complaint received **27 February 2013**

Case completed **27 March 2013**