CASE AUTH/2295/1/10

HOSPITAL CHIEF PHARMACIST v CEPHALON

Supply of Effentora

The chief pharmacist at an NHS trust complained about the provision of thirty boxes of Effentora (fentanyl citrate buccal tablets) by Cephalon. Effentora was indicated for the treatment of breakthrough pain (BTP) in adults with cancer who were already receiving maintenance opioid therapy for chronic cancer pain.

The complainant stated that a nurse working in the pain team had received from the goods receiving department thirty boxes of Effentora, a Schedule 2 controlled drug. All orders and deliveries of controlled drugs should be via the pharmacy department where auditable records were maintained in line with legal requirements.

This consignment had been initiated after a Cephalon representative met a local pain consultant. The consultant was unaware that her signature would be taken as an order, she thought she had only expressed an interest in the product.

Apart from serious breaches of UK regulations, which were being addressed elsewhere, the complainant alleged that this conduct breached the Code.

- ***No more than ten samples*** **– 30 boxes had been provided**
- ***Each sample must be marked*** **– Commercial packs with no other marking were provided**
- ***Narcotic drugs*** **– Effentora was a Schedule 2 controlled drug subject to ordering/storage and prescribing restrictions**
- ***Provision within hospitals must comply with hospital requirements*** **– The hospital requirements, supported by local guidelines, stated clearly that samples and free stock must not be left within the trust.**
- ***Supply as an inducement to prescribe*** **– The complainant attached emails which stated that Effentora was supplied as an inducement to prescribe and 'assist [Cephalon] with moving forward with a formulary application'.**

This was not the provision of stock since the consultant concerned was not authorized to purchase medicines on behalf of the trust and if they were for her private work they should not have been supplied to the trust.

There was significant risk in the company's conduct since this supply was not traceable and could easily have been misappropriated, also the supply was of short dated stock and patients might have inadvertently been given out-of-date medicines.

The detailed submission from Cephalon is given below.

The Panel noted that from the complaint it appeared that the consignment of Effentora was addressed such that it was delivered to a nurse in the pain team and not sent to the pharmacy department. The complainant also stated that the consultant was unaware that her signature would be taken as an order. In this regard the Panel noted that the request form provided by Cephalon headed 'Effentora Titration Stock Request' included a statement 'I can confirm that the above healthcare premises is licensed to receive and store controlled drugs and that the above named person is authorized to take delivery of the Effentora titration stock'. The form required the name of the person authorized to receive the delivery but not the signature of that person. The Panel queried whether the form in question had been signed as submitted by Cephalon given that the requesting consultant's name had been written in block capitals. The Panel noted that the person named as being authorized to receive delivery was not the person to whom the Effentora was delivered. There was no indication on the stock request form of exactly what had been requested or dispatched.

The Panel did not consider that the provision of Effentora met the definition of a sample as stated in the supplementary information to the Code. Further, Effentora was a Schedule 2 controlled drug and thus could not be provided as a sample. Thirty packs had been provided rather than the ten permitted for samples. The Panel did not consider that the packs provided were titration packs. The company had provided standard packs of the two lowest strengths of Effentora which it submitted were usually required to determine a patient's optimal dose. In the Panel's view a titration pack, as defined in the Code, was one pack which contained various strengths of a medicine, rather than standard packs of different strengths given for the purpose of titration. In the Panel's view the Effentora had been provided as free stock. The Panel ruled no breach of those clauses of the Code which related only to samples as defined in the Code.

The Panel noted the complainant's submission that the pain consultant was not authorized to order on behalf of the hospital trust and that the hospital requirements clearly stated that samples and free stock must not be left within the trust. This requirement was further supported by local guidelines. However the Panel noted that the

hospital guidelines provided by the complainant did not refer to free stock. The local document 'Working with the Pharmaceutical Industry' stated 'Samples should not be available for patients/carers, nor should any direct promotional activity, including providing details of direct supply activities be made available'. It was further stated that samples could be left with appropriate practitioners for personal use only. Such samples must not be used for patients. The arrangements reflected the requirements of the Code with regard to the need for a signed request and that no more than 10 samples could be provided in the course of a year. Appendix I of the document asked representatives to adhere to eight guidelines. It stated that samples could be left in pharmacy, and that no samples could be left with other trust staff. Samples must not be used in clinical practice without appropriate, prior authorization. The document 'Working with the Pharmaceutical Industry' referred to the basis upon which purchasing decisions should be made but did not identify who should make the decision. Contrary to the complainant's submission the Panel did not consider that the published hospital policy was clear about the provision of free stock. Samples were specifically mentioned; it was unclear as to what was envisaged by 'direct supply activities'. The Panel queried whether the trust's definition of 'sample' was the same as that given in the Code – particularly when, according to the trust, samples could not be used for patients. No specific mention was made in the trust guidelines about the supply of controlled medicines. Nonetheless the Panel considered that when providing free stock it was beholden upon the representative to make specific enquiries to ensure that its provision complied with hospital requirements irrespective of the status of the health professional involved. This was even more important when controlled drugs were being supplied. That the hospital guidelines did not mention free goods or the provision of controlled drugs did not mean that there were no relevant requirements. The Panel did not accept Cephalon's submission that it was entitled to rely on the status and knowledge of the relevant doctor. The provision of Effentora as free stock to the pain clinic did not comply with hospital requirements and thus a breach of the Code was ruled. This ruling was appealed by Cephalon.

The Appeal Board noted that the hospital guidelines included the term 'samples' but not the term 'free stock'. The term 'samples' had not been defined. The Appeal Board noted that the guidelines would have been written by hospital staff and in that regard it appeared that their use of the term 'samples' might not be the same as the use in the Code. It was possible that some hospital staff would view the term 'samples' as all embracing. Nonetheless it was not for the Appeal Board to second guess what the guidelines meant. The Appeal Board considered that as the hospital guidelines did not refer to 'free stock' the supply of Effentora could not have breached them. No breach of the Code was ruled.

The representative had facilitated the provision of free stock for a Schedule 2 controlled drug contrary to hospital requirements and had failed to maintain high standards in this regard. Breaches of the Code were ruled.

The Panel considered that the provision of a Schedule 2 controlled drug without sufficient controls fell short of competent care and brought discredit upon and reduced confidence in the pharmaceutical industry. A breach of Clause 2 was ruled which was upheld on appeal by Cephalon.

The chief pharmacist at a NHS trust complained about the provision of thirty boxes of Effentora (fentanyl citrate buccal tablets) by Cephalon UK Limited. Effentora was indicated for the treatment of breakthrough pain (BTP) in adults with cancer who were already receiving maintenance opioid therapy for chronic cancer pain.

COMPLAINT

The complainant stated that the local hospital pharmacy department was contacted by a nurse working in the pain team at the trust concerned that she had received from the goods receiving department thirty boxes of Effentora, a Schedule 2 controlled drug subject to control under the Misuse of Drugs regulations. All orders and deliveries of controlled drugs should be via the pharmacy department where auditable records were maintained in line with legal requirements.

This consignment had been initiated after a visit by a Cephalon representative to a pain consultant within the trust. The consultant was unaware that her signature would be taken as an order – although she had no authority to place such an order on behalf of the trust – and thought that this was an expression of interest in the product.

Apart from serious breaches of the Misuse of Drugs regulations, which were being addressed elsewhere, the complainant alleged that this conduct breached Clause 17 of the Code.

- *17.2 No more than ten samples* – The consultant was provided with 30 boxes of the medicine
- *17.5 Each sample must be marked* – They were supplied as commercial stock in commercial packaging with no other marking
- *17.6 Narcotic drugs* – Effentora was a Schedule 2 controlled drug subject to ordering/storage and prescribing restrictions
- *17.8 Provision within hospitals must comply with hospital requirements* – The hospital requirements stated clearly that samples and free stock must not be left within the trust. This was further supported by the local guidelines (copies of each were provided)

- 17*.12 Supply as an inducement to prescribe* – The complainant attached emails which clearly stated that Effentora was supplied as an inducement to prescribe and 'assist [Cephalon] with moving forward with a formulary application'. This clearly contravened the hospital and local primary care trust (PCT) guidelines referred to above.

It could not be argued that this provision was stock as ordered since the consultant concerned was not authorized to purchase medicines on behalf of the trust and if the tablets were for her private work they should not have been supplied to the trust.

There was significant risk in the company's conduct since this supply was not traceable and could easily have been misappropriated and found its way onto the streets, also the supply was of short dated stock and the consultant might have inadvertently supplied out-of-date medicines to a patient.

As emails suggested that this was not a one-off incident, since it referred to 'another of these [free of charge] FOC Effentora orders', the complainant had told all chief pharmacists in the area and all members of the area purchasing consortium about her concerns.

When writing to Cephalon the Authority asked it to respond in relation to Clauses 2, 9.1 and 15.2 in addition to those clauses cited by the complainant.

RESPONSE

Cephalon stated that it had written to the complainant to apologise for what was an extremely unfortunate set of misunderstandings.

However, Cephalon noted that the consultant who completed the stock request form was not only an experienced consultant pain physician, familiar with the management requirements of controlled medicines, but was also the chair of the local medicines management committee and had signed the trust's guidelines for representatives. Given the physician's roles and experience the company considered this was an appropriately senior level of staff for the representative to have interacted with.

Clause 17 concerned the distribution of samples. The supplementary information to Clause 17 clearly identified a sample as a small supply of a medicine provided to health professionals so that they might familiarise themselves with it and acquire experience in dealing with it. The supplementary information further stated that titration packs, free goods and bonus stock provided to pharmacists and others were not samples and that titration packs were packs containing various strengths of a medicine for the purposes of establishing a patient on an effective dose.

Cephalon believed the complainant had misunderstood the nature of the stock provided to the hospital and the sub-clauses within the Code. While Cephalon did not wish to minimise the complainant's obvious concerns, it respectfully suggested that Clauses 17.2, 17.5 and 17.6 did not apply to titration stock and therefore denied any breach of these clauses.

The stock of Effentora requested by the pain consultant was solely for the purposes of titration and was provided free of charge in response to a signed request for titration stock. Effentora typically had to be titrated to the optimal maintenance dose. The packs were provided expressly for this purpose and not as samples for the purpose of familiarisation. Indeed, only the two lowest strengths of Effentora were provided which were usually required to determine an optimal dose for a given patient, there being five strengths in total.

However, the complainant made points that warranted further comment.

Cephalon recognised the concern that the consultant in question was unaware that her signature would be taken as an order. This was indeed an unfortunate situation; however, the company had made every attempt on the one-page form to indicate the situation clearly. The form was clearly entitled 'Effentora Titration Stock Request'. The person placing the order was required to indicate who was authorized to receive the delivery in the section 'Name of person authorized to receive the **delivery**:' (emphasis added). Immediately beneath the space for the name, telephone number and email address of the person authorized to receive delivery, was the statement 'Delivery on', thus again indicating that a delivery of stock was the outcome of completing the form. Finally, the lower half of the page required the person requesting the titration stock to complete the following declaration, 'I can confirm that the above healthcare premises is licensed to receive and store controlled drugs and that the person named above is authorized to take delivery of the Effentora titration stock'. The consultant signed and dated the form immediately beneath this statement.

Hence, the form signed was clearly not an expression of interest but an order form for titration stock.

Cephalon was aware of the controls on Schedule 2 medicines with regard to ordering and storage, which were the applicable elements here. With this consideration, following a small number of requests from health professionals for titration stock of Effentora, it was deemed necessary to have a formal titration stock request form to ensure appropriate control (a copy was provided). Any health professional that made a request then was obliged to complete obligatory information that highlighted and accounted for these restrictions. The consultant signed the form on which the location for delivery was stated.

The hospital requirements and locality guidelines

enclosed with the complaint were not clear that free stock was not to be left within the trust. However, the form ensured that the person and place nominated to receive the titration stock was authorized to do so. This aligned with any hospital policy that should be known by the requesting health professional. The consultant, as chair of the local medicines management committee, signed the guidelines regarding pharmaceutical representatives and could, therefore, reasonably be expected to be aware of all applicable policies within the trust including the individual hospital requirements regarding place of delivery of controlled medicines. Hence, Cephalon acted in good faith that the use of the request form by the requesting consultant was consistent with local guidelines.

With reference to the alleged breach of Clause 17.8, which referred to supply of medicines and samples complying with individual hospital requirements, Cephalon therefore took reasonable precautions regarding compliance with individual hospital requirements by gaining the consultant's prior approval and signature.

Cephalon regretted the circumstances of the complaint and the misunderstanding; however it believed it acted reasonably and in good faith and therefore asserted no breach of Clause 17.8.

With specific reference to the alleged breach of Clause 17.12, ie that the titration stock was supplied as an inducement to prescribe, the consultant made the request, as discussed above, and would be reasonably held accountable for appropriate supply of titration stock under hospital and local PCT guidelines, No sample was provided, rather, as clearly noted on the request form, titration stock was requested – a presentation of the two lowest strengths of Effentora that were usually required to place patients on a stable dose. The Effentora summary of product characteristics (SPC) made specific recommendations for the titration and use of specific tablet strengths, as part of risk management. Titration was required in all patients, and the consultant requested titration stock to assist in the initial administration to find a suitable maintenance dose for a very limited number of patients.

As the titration stock was clearly provided on request, it could not be held that supply was an inducement to prescribe. The request came from a person responsible, as chair of the local medicines management committee, for local hospital and PCT guidelines regarding formulary applications. There would still remain the stage of formal evaluation through a formulary submission that evaluated the evidence and other medicines that could also be used. There was no commitment by either the consultant or Cephalon to an ongoing supply of Effentora titration stock that could influence the recommendation by a formulary review panel.

In addition, the Appeal Board had previously ruled that an inducement must relate to the provision of an incentive for the individual (Case AUTH/2095/2/08). It was difficult to see what benefit the individual derived from the supply of titration to stock delivered to the hospital and therefore the company believed that it was not possible for any inducement to have occurred.

Cephalon therefore asserted that no sample was provided and no inducement to prescribe was present and therefore that there was no breach of Clause 17.12.

Based on the points made above, Cephalon believed it had acted to maintain high standards. Cephalon identified the need to produce a request form to ensure appropriate controls and gained a signature regarding supply and place of supply from a person who would reasonably be assumed to be aware of local trust policies and procedures regarding delivery of narcotic titration stock. Although Cephalon implemented appropriate controls as above, when it first became aware of the circumstances in this case it immediately suspended the ability for health professionals to request titration stock pending review of the process and resolution of this complaint. Cephalon also arranged for immediate removal of the titration stock from the hospital as requested by the pharmacy department. Cephalon denied a breach of Clause 9.1.

The representative involved had responded to a request from the health professional and was only involved in forwarding the form completed by the consultant to Cephalon head office, which arranged supply based on the details provided on the form. Cephalon took the information provided in good faith that it represented appropriate authorization to request and take delivery of the titration stock. The representative had interacted at the time with the same clinician who signed the pharmaceutical company representatives' guidelines for the trust. Cephalon denied a breach of Clause 15.2.

Overall, Cephalon believed that the availability of titration stock on the request of a limited number of health professionals was appropriate and was consistent with the titration steps required to use Effentora appropriately.

Given that Cephalon believed it had not therefore breached Clauses 9, 15 or 17 in that it reacted to a request for titration stock appropriately, did not provide a sample as an inducement to prescribe and acted on good faith following receipt of an order form signature from someone who would reasonably be assumed to be conversant with local trust policies, it did not believe that its actions had brought the industry into disrepute. Cephalon denied a breach of Clause 2.

With respect to the question regarding any documents sent with the titration stock, other than the logistics documentation, no further documentation was provided. The titration stock

contained the obligatory regulatory document within the box, such as the patient information leaflet. As requests for titration stock had been received via representatives, no briefing other than provision of a request form was considered necessary.

PANEL RULING

The Panel noted that from the complaint it appeared that the consignment of Effentora was addressed such that it was delivered to a nurse in the pain team and not sent to the pharmacy department. The complainant also stated that the consultant was unaware that her signature would be taken as an order. In this regard the Panel noted that the request form provided by Cephalon headed 'Effentora Titration Stock Request' included a statement 'I can confirm that the above healthcare premises is licensed to receive and store controlled drugs and that the above named person is authorized to take delivery of the Effentora titration stock'. The form required the name of the person authorized to receive the delivery but not the signature of that person. The Panel queried whether the form in question had been signed as submitted by Cephalon given that the requesting consultant's name had been written in block capitals. The Panel noted that the person named as being authorized to receive delivery was not the person to whom the consignment of Effentora was delivered. There was no indication on the stock request form of exactly what had been requested or dispatched.

The Panel noted that the complainant considered that the packs of Effentora had been provided as samples whilst Cephalon maintained that they were titration stock. The supplementary information to Clause 17, 'Definition of Sample', defined each term. A sample was a small supply of a medicine provided to health professionals so that they might familiarise themselves with it and acquire experience in dealing with it; titration packs were packs containing various strengths of a medicine for the purpose of establishing a patient on an effective dose.

The Panel did not consider that the provision of Effentora met the definition of a sample given in the Code. Further, Effentora was a Schedule 2 controlled drug and thus could not be provided as a sample under Clause 17.6. Thirty packs had been provided rather than the ten permitted for samples under Clause 17.2. The Panel did not consider that the packs provided were titration packs. The company had provided standard packs of the two lowest strengths of Effentora which it submitted were usually required to determine a patient's optimal dose. In the Panel's view a titration pack, as defined in the Code, was one pack which contained various strengths of a medicine, rather than standard packs of different strengths given for the purpose of titration. The Effentora SPC stated that the initial dose should be 100mcg titrating upwards as necessary. The product was available in a range of tablet strengths (100mcg-800mcg). In the Panel's view Cephalon had provided 30 packs of Effentora, a Schedule 2 controlled medicine, as free stock. The Panel ruled no breach of Clauses 17.2, 17.5 17.6, and 17.12 as these related to samples as defined in the Code.

The Panel noted the complainant's submission that the pain consultant was not authorized to order on behalf of the hospital trust and that the hospital requirements clearly stated that samples and free stock must not be left within the trust. This requirement was further supported by local guidelines. However the Panel noted that the hospital guidelines provided by the complainant did not refer to free stock. Representatives were reminded that the trust had a drugs guide and formulary. Promotional activities which conflicted with the recommendations of the formulary would not be tolerated. The local document 'Working with the Pharmaceutical Industry' stated 'Samples should not be available for patients/carers, nor should any direct promotional activity, including providing details of direct supply activities be made available'. It was further stated that samples could be left with appropriate practitioners for personal use only. Such samples must not be used for patients. The arrangements reflected the requirements of the Code with regard to the need for a signed request and that no more than 10 samples could be provided in the course of a year. Appendix I of the document asked representatives to adhere to eight guidelines. It stated that samples could be left in pharmacy, and that no samples could be left with other trust staff. Samples must not be used in clinical practice without appropriate, prior authorization. The document 'Working with the Pharmaceutical Industry' referred to the basis upon which purchasing decisions should be made but did not identify who should make the decision. Contrary to the complainant's submission the Panel did not consider that the published hospital policy was clear about the provision of free stock. Samples were specifically mentioned; it was unclear as to what was envisaged by 'direct supply activities'. The Panel queried whether the trust's definition of 'sample' was the same as that given in the Code – particularly when, according to the trust, samples could not be used for patients. No specific mention was made in the trust guidelines about the supply of controlled medicines. Nonetheless the Panel considered that when providing free stock it was beholden upon the representative to make specific enquiries to ensure that its provision complied with hospital requirements irrespective of the status of the health professional involved. This was even more important when controlled drugs were being supplied. That the hospital guidelines did not mention free goods or the provision of controlled drugs did not mean that there were no relevant requirements. The Panel did not accept Cephalon's submission that it was entitled to rely on the status and knowledge of the relevant doctor. In that regard the Panel noted that the document 'Working with the Pharmaceutical Industry' and its Appendix I appeared to have been signed off by someone other

than the consultant in question. The provision of Effentora as free stock to the pain clinic did not comply with hospital requirements and thus a breach of Clause 17.8 was ruled. This ruling was appealed.

The representative had facilitated the provision of free stock for a Schedule 2 controlled drug contrary to hospital requirements and had failed to maintain high standards in this regard. Breaches of Clauses 9.1 and 15.2 were ruled.

The Panel considered that the provision of a Schedule 2 controlled drug without sufficient controls fell short of competent care and brought discredit upon and reduced confidence in the pharmaceutical industry. A breach of Clause 2 was ruled. This ruling was appealed.

APPEAL BY CEPHALON

Cephalon submitted that the Panel's rulings in respect of Clauses 2 and 17.8 did not accurately reflect the factual circumstances in which Effentora was supplied to the pain clinic. As regards the breach of Clause 17.8, Cephalon was unclear as to which of the local guidelines it had breached.

Cephalon did not accept that there were serious breaches of the Misuse of Drugs regulations as alleged by the complainant. This had essentially underpinned the Panel's ruling of a breach of Clause 2.

Cephalon submitted that the legal basis for the supply and possession of controlled drugs in the UK was governed by the Misuse of Drugs Act 1971 Sections 4 and 5 of which established a general prohibition on the supply and possession of controlled drugs. Section 7 gave power to the Secretary of State to make secondary legislation. The regulations were made under Section 7 of the act and provided that the Secretary of State might issue licences authorizing the production, supply and possession of controlled drugs.

Cephalon noted that in this case, Effentora was manufactured in the US with the finished product being shipped to Cephalon's distributor in the UK. Distribution of Cephalon's branded products in the UK was subject to a distribution agreement and a technical agreement setting out the obligations of the contracting parties with particular reference to compliance with the applicable laws and regulations. In this case, the distributor was contractually required to keep written/electronic records sufficient to track the purchase and sale of product lots. In addition, it was required under the technical agreement to supply products to the approved sites and *bona fide* recipients of the products (see below).

Cephalon submitted that as regulation 10(1)(a) authorized registered medical practitioners to possess Schedule 2 controlled drugs for the purposes of their work, the hospital consultant was authorised to hold controlled drugs for the purposes of administering pain relief to patients in her care.

Cephalon submitted that regulation 14(2) provided that where a controlled drug was supplied otherwise than on a prescription or by way of administration by a practitioner (defined under Section 37 of the act to include a doctor) the supplier was permitted to supply the controlled drug if he had received a written requisition which:

- was signed by the person to whom the drug was supplied;
- stated the name, address and profession or occupation of the recipient; and
- specified the purpose for which the drug supplied was required and the total quantity to be supplied.

Cephalon noted the Effentora Titration Stock Request form was completed by the consultant, a senior physician in the hospital, and an authorized practitioner within the meaning of the act and the regulations to hold and administer controlled drugs. The consultant declared in the request form that the hospital was licensed to receive and store controlled drugs. As it was evident from the title of the request form, the requested supply of Effentora was intended for dose titration.

Cephalon submitted that although the quantity of Effentora was not expressly recorded on the request form, the other requirements set out in regulation 14(2) were essentially met. According to the representative's records the consultant had requested 10 boxes of 4 x 100 micrograms and 20 boxes of 4 x 200 micrograms of Effentora tablets for dose titration. A copy of the representative's notes and a signed witness statement from the representative was provided.

Whilst Cephalon accepted that there had been a technical breach of regulation 14, it did not accept that there were serious breaches of the regulations, as alleged by the complainant and included as part of the reasoning of rulings made by the Panel. This allegation would ordinarily mean that Cephalon had had no regard to the regulatory requirements for the supply of controlled drugs in the UK. This did not reflect the facts of this case.

Cephalon submitted that the Panel, however, correctly noted that the person authorized to receive the delivery of the Effentora titration stock the consultant was not the person to whom the consignment was actually delivered. As described above, following an agreement between Cephalon and its distributor, the distributor was solely responsible for the distribution of Cephalon's products to customers in response to orders placed by Cephalon's representatives. Regrettably, the distributor's failure to deliver the titration stock to the authorized practitioner, the consultant, was a breach of its obligations under that agreement.

Cephalon submitted that in this case, the intended recipient was clearly the consultant as an authorized practitioner under regulation 10(1)(a) and the named signatory on the request form as she would be undertaking the dose titration on her patients. Cephalon noted that although the consultant did not receive the titration stock herself, the delivery was received and signed for by a specialist nurse working in her offices.

Cephalon submitted that it had instructed its distributor to remove the titration stock from the hospital immediately on receipt of the complaint and that it was thoroughly investigating its breach of the applicable requirements. Cephalon submitted that it had acted responsively and responsibly in the course of the supply of a stock of Effentora to the consultant and the subsequent retrieval of the delivery from the hospital after the company was made aware of the complaint. Therefore, with the existing procedures and contractual arrangements in place for the distribution of Effentora in line with the current industry standards, Cephalon was troubled that these activities could properly and proportionately be characterised as bringing discredit upon or reducing confidence in the pharmaceutical industry in the context of Clause 2.

Cephalon submitted that the request form was intended for the ordering of titration stock only and it was not used for sample requests. Furthermore, supply of titration stock in response to a legitimate request made by a doctor to undertake dose titration, was consistent with the Effentora SPC Section 4.2 of which stated:

'Effentora should be individually titrated to an "effective" dose that provides adequate analgesia and minimises undesirable effects. In clinical studies, the effective dose of Effentora for BTP was not predictable from the daily maintenance dose of opioid. Patients should be carefully monitored until an effective dose is reached.

The initial dose of Effentora should be 100 micrograms, titrating upwards as necessary through the range of available tablets strengths ….

Method of titration

During titration, if adequate analgesia is not obtained within 30 minutes after the start of administration of a single tablet, a second Effentora tablet of the same strength may be used.

If treatment of a BTP episode requires more than one tablet, an increase in dose to the next higher available strength should be considered to treat the next BTP episode.

During titration, multiple tablets may be used: up to four 100 micrograms or up to four 200 micrograms tablets may be used to treat a single episode of BTP during dose titration according to the following schedule ...'

Cephalon submitted that the consultant requested a supply of the lowest two strengths of Effentora for dose titration in patients under her care (Sections 2 and 6.5 of the SPC referred). Five strengths of Effentora were authorized for supply to the UK market: 100; 200; 400; 600 and 800 micrograms. No specific titration pack (containing a smaller amount of tablets) was authorized under the terms of the existing Effentora marketing authorization. Indeed, the pack size provided (4 tablets per pack) was currently the only pack size commercially available in the UK. The amount supplied to the consultant would typically be sufficient to titrate four or five patients up to an effective maintenance dose for pain relief. Patients would generally be maintained at a higher strength than 200mcg per dose. However, the amount given to each patient during titration and maintenance was individualised according to that patient's clinical response as assessed by the treating physician. Cephalon supplied the approved pack size of Effentora as free stock for the specific purpose of dose titration, and not as samples, in response to the consultant's bona fide request for the same.

Cephalon submitted that the consultant was an experienced pain consultant familiar with the management requirements of controlled drugs; the medicines management committee chair; the clinician responsible for developing the Guidelines for drug company representatives; and was authorized under regulation 10(1)(a) to possess Schedule 2 controlled drugs for the purposes of administering pain relief to the patients under her control. In the circumstances, it appeared appropriate for Cephalon's representative to have met the consultant and processed her order for the requested Effentora titration stock.

Cephalon was unclear as to which hospital guidelines it had breached. Three documents had been provided. Cephalon submitted that although none of this guidance appeared to deal with the issue of free stock, it had respectfully asked the Authority to identify the particular hospital requirements and specific guidelines which Cephalon was alleged to have breached. This was important not only to ensure that the ruling reflected the facts of the case, but also help Cephalon to implement appropriate corrective and remedial action.

Moreover, Cephalon requested guidance from the Authority on how to address compliance with Clause 17.8 in circumstances where the individual hospital requirements were unclear and unspecific, such as in this case in relation to the provision of free stock. Cephalon submitted that the Code did not provide guidance on how a company should ensure compliance with hospital policy. In these circumstances, Cephalon submitted that it was not unreasonable for the company representative to approach a senior staff member of the hospital who ought to be able to advise or direct the company representative, where appropriate, to the relevant personnel to provide guidance on the local drug

policy requirements for, and expectation on provision of medicines.

Cephalon accepted that although there had been a technical breach of the Misuse of Drugs regulations, this could not be properly characterised as serious given the facts of this case. Cephalon respectfully requested that the Appeal Board consider the facts and amend the language used to characterise the breach accordingly.

As regards the ruling of a breach of Clause 2, as explained above Cephalon submitted that it had acted responsively and responsibly; it immediately retrieved the delivered stock as soon as it knew about the complaint subject to the company's internal investigation. Distribution of Cephalon's branded products was governed by distribution and technical agreements requiring its distributor to comply with the applicable laws and regulations during product distribution. Given these facts, the company queried whether the activities described could properly or proportionately be characterised as bringing discredit upon or reducing confidence in the pharmaceutical industry in the context of Clause 2.

Cephalon submitted that its fulfilment of the consultant's order comprised the provision of free stock for the specific purpose of dose titration (consistent with both the terms of the marketing authorization and the SPC) and could not be treated as the provision of samples. Accordingly, Cephalon did not consider that there had been a breach of Clause 17.8. Cephalon requested clarification of the specific hospital guidelines which it had breached.

Cephalon had suspended all activities relating to any requests for titration stock of Effentora made by any physician, pending the final outcome of the case.

COMMENTS FROM THE COMPLAINANT

There were no further comments from the complainant.

APPEAL BOARD RULING

The Appeal Board noted that Cephalon's representative had met the consultant and agreed to supply her with titration stock of Effentora. In an email the representative had stated that 'This will also assist us with moving forward with a formulary application, as to date they have had little experience of Effentora'. It thus appeared that Effentora was not on the hospital formulary. The consultant chaired the local medicines management committee. The free stock of Effentora was supplied such that it by-passed the hospital pharmacy department. The complainant had stated that 'The hospital requirements stated quite clearly that samples and free stock must not be left within the trust'. The Appeal Board noted, however, that the hospital guidelines provided by the complainant included the term 'samples' but not the term 'free stock'. The term 'samples' had not been defined in the hospital guidelines. The Appeal Board had some sympathy with the complainant in that it noted that the hospital guidelines would have been written by hospital staff and in that regard it appeared that their use of the term 'samples' might not be the same as the use in the Code. It was possible that some hospital staff would view the term 'samples' as all embracing. Nonetheless it was not for the Appeal Board to second guess what the hospital guidelines meant. Given that the hospital guidelines did not refer to 'free stock' the supply of Effentora could not have breached those guidelines. The Appeal Board thus ruled no breach of Clause 17.8. The appeal on this point was successful.

The Appeal Board was very concerned about the request form provided by Cephalon headed 'Effentora Titration Stock Request'. The form included a statement 'I can confirm that the above healthcare premises is licensed to receive and store controlled drugs and that the above named person is authorized to take delivery of the Effentora titration stock'. The form required the name of the person authorized to receive the delivery but not their signature; the form did not require the quantity of medicines being requested to be specified. The Appeal Board noted that the requesting consultant's name had been written in block capitals on the form and at the appeal, contrary to Cephalon's previous submission, its representatives agreed that the form had not been signed. The Appeal Board considered that the request form was woefully inadequate for the supply of a Schedule 2 controlled drug. In that regard the Appeal Board was concerned that Cephalon considered this only to be a technical breach of regulation 14(2). As far as the Code was concerned the Appeal Board viewed this as a serious matter.

The Appeal Board noted that a significant quantity (120 tablets) of Effentora had been supplied. The complainant stated that the delivery should have been via the pharmacy department where auditable records of receipt would be maintained. The Appeal Board considered that the delivery of the controlled drugs via the goods receiving department to a nurse in the pain team had the potential to expose individuals to risk or harm. The Appeal Board noted Cephalon's submission that the free stock had been provided in the context of assisting a formulary application ie not for possible use in the hospital consultant's private practice. The Appeal Board noted Cephalon's submission regarding the seniority of the consultant and her position on the local medicines management committee. The Appeal Board considered that in all cases, however, the responsibility under the Code for complying with individual hospital requirements regarding the provision of medicines and samples was with the pharmaceutical company and could not be devolved to the requesting health professional.

The Appeal Board considered that the provision of a Schedule 2 controlled drug without sufficient controls fell short of competent care and brought discredit upon and reduced confidence in the pharmaceutical industry. The Appeal Board upheld the Panel's ruling of a breach of Clause 2. The appeal on this point was unsuccessful.

During its consideration of the case the Appeal Board noted that the complainant stated that the consultant thought that she had expressed an interest in the product rather than her signature being taken as an order. However the Appeal Board was concerned that a hospital consultant had accepted the offer of a direct supply of a Schedule 2 controlled drug. The consultant had accepted a wholly inadequate order form which she had neither signed nor stated the quantity to be supplied. The Appeal Board decided that the complainant should be advised of these concerns and assurances sought from her that the matter would be thoroughly investigated in a proper way involving the chief executive and head of governance so as to ensure that any future supplies of controlled drugs, for hospital use, would be appropriately supplied. If such assurances were not forthcoming from the complainant then the Chairman and Director would contact the hospital's chief executive and head of governance directly.

Complaint received **25 January 2010**

Case completed **8 June 2010**