CASE AUTH/3014/1/18

ANONYMOUS, NON-CONTACTABLE HEALTH PROFESSIONAL v GW PHARMACEUTICALS

Promotion of Epidiolex

An anonymous, non-contactable complainant, who described him/herself as a health professional, alleged that GW Pharmaceuticals had promoted Epidiolex (cannabidiol) at a meeting in January 2018 before the medicine had been granted a marketing authorization.

The complainant alleged that the GW Pharmaceuticals exhibition stand displayed Epidiolex material and that a named employee introduced the medicine as a new treatment for paediatric patients with Dravet Syndrome and patients with Lennox-Gastaut Syndrome and stated that the medicine had been licensed by the European Medicines Agency (EMA) and would soon be available in the UK. The complainant had since found out that Epidiolex had not been approved by the EMA; the information from GW Pharmaceuticals was misleading.

The detailed response from GW Pharmaceuticals is given below.

The Panel noted that when the meeting was held, Epidiolex did not have a marketing authorization although licences had been applied for in the EU and US. GW Pharmaceuticals had submitted that it expected a decision from the European Commission for Epidiolex in mid-2019.

The Panel noted that the named GW Pharmaceuticals employee stated that the company's presence at the meeting comprised a small medical booth staffed by him/her and another member of the UK medical team. The booth was intended to provide a non-promotional presence to demonstrate the company's commitment to research and development, its corporate awareness as a pharmaceutical development company, non-product specific disease awareness, and information on GW Pharmaceuticals' main research activities including cannabinoid medicines. Copies of the materials available at the booth were provided; none mentioned Epidiolex by name. The Panel noted that it was an accepted principle under the Code that a product could be promoted without its name ever being mentioned.

Photographs of the exhibition stand showed material including the infographics that were striking and very prominently placed and thus highly visible to delegates visiting the stand. The material discussed various aspects of Dravet Syndrome and Lennox-Gastaut Syndrome and highlighted that current therapeutic options were inadequate. Material for Lennox-Gastaut Syndrome stated 'Up to 80% of patients are refractory to anti-epileptic drug therapy' and that for Dravet Syndrome stated 'Only 16% of patients experience complete resolution in their seizures. All seizure types extremely resistant to treatment'. In the Panel's view, these statements would, on the balance of probabilities, solicit questions about the company's pipeline products. A leaflet entitled 'A World leader in the development of cannabinoid medicines' discussed GW Pharmaceuticals' commitment to cannabinoid treatments. The final page gave more details describing the cannabinoid development pipeline by indication under investigation and phase of clinical study. Seven neuroscience pipeline indications were listed and it was stated that Dravet Syndrome and Lennox-Gastaut Syndrome had completed Phase 3 trials. It was further stated that the company's 'lead cannabinoid' had received orphan drug designation in these indications. The Panel noted that whilst Epidiolex was not named, sufficient information about it was given such that it was indirectly identified and on the balance of probabilities the material would solicit questions about the company's 'lead cannabinoid'.

In the Panel's view, the cumulative effect of the material, including the reference to the company's 'lead cannabinoid', meant that the exhibition stand promoted a medicine prior to the grant of its marketing authorization. Breaches of the Code were ruled including a breach of Clause 2.

The Panel noted that the materials had a promotional appearance and considered that they went beyond disease awareness information and/or non-promotional information about the company and its research interests.

The Panel noted the complainant's comments about statements allegedly made by the named employee ie that Epidiolex was a new treatment for paediatric patients with Dravet Syndrome and patients with Lennox-Gastaut Syndrome and that it had been licensed by the EMA and would soon be available in the UK. GW Pharmaceuticals denied that such comments had been made. The Panel noted that it was often impossible in complaints based on one party's word against the other to determine precisely what had happened. The complainant had the burden of proving his/her complaint on the balance of probabilities. The complainant was non-contactable and it was not possible to ask him/her for further information. The Panel had to make a ruling on the evidence before it.

The Panel noted its comments above about responses to unsolicited enquiries and also the statement of the company employee manning the booth in relation to training, the nature of queries received at the exhibition stand, and whether he/

she would have responded as alleged. The Panel also noted the detailed briefing for staff to use at conferences in response to unsolicited requests advising that discussions with health professionals must be reactive and in response to the requested information. Staff were advised to narrowly tailor the response to the level of the question posed. The company's report on interactions at the conference did not closely mirror the complainant's allegation. In relation to the alleged comments made at the exhibition stand, it was impossible to determine where the truth lay and the Panel accordingly ruled no breach of the Code.

An anonymous, non-contactable complainant who described him/herself as a health professional alleged that GW Pharmaceuticals had promoted Epidiolex (cannabidiol) before the grant of its marketing authorization.

COMPLAINT

The complainant explained that he/she had attended the British Paediatric Neurology Association (BPNA) meeting on 5 January 2018 where GW Pharmaceuticals had had an exhibition stand with Epidiolex materials. A named medical representative introduced Epidiolex as a new treatment for paediatric patients with Dravet Syndrome and patients with Lennox-Gastaut Syndrome. The representative stated that Epidiolex had been licensed by the European Medicines Agency (EMA) and would soon be available for UK prescribers.

The complainant stated that he/she had since found out that Epidiolex had not been approved by the EMA, the application was only submitted in December 2017, and the medicine would not be available until the application process had been completed.

The complainant considered that the information from GW Pharmaceuticals was misleading and promoted an unlicensed medicine.

The complainant provided photographs of some of the material available on the exhibition stand, cited a press release about the submission of the marketing authorization published on GW Pharmaceuticals' website and provided a website address for the conference in question.

When writing to GW Pharmaceuticals, the Authority asked it to consider the requirements of Clauses 2, 3, 7.2, 9.1 and 15.2.

RESPONSE

GW Pharmaceuticals submitted that the complainant's allegations were entirely unfounded; the company flatly denied any wrong-doing or impropriety on its part or that of its representatives. GW Pharmaceuticals understood the difficulty in investigating and responding to this type of anonymous complaint, but it was comfortable that the complaint had no basis. The named individual, was a highly experienced, qualified, eminently sensible and conscientious medical affairs professional and had satisfied the company that he/she had not made the alleged statement. He/she was fully aware of the Code and his/her responsibilities under it. His/her account was also backed by contemporaneous records of interactions with health professionals with whom he/she interacted at the BPNA conference and his/her summary of that meeting, as well as briefing materials on which he/she was well-trained. A number of factual issues and inconsistencies in language in the complaint led the company to suspect that it was unfounded or fabricated, that the complainant might have been mistaken or that the complaint had resulted from a misunderstanding.

GW Pharmaceuticals provided a detailed statement from the named individual in question and after careful enquiry it was satisfied that, along with his/her professional background and experience, he/she had through the company and its third party partner, received appropriate and comprehensive briefing and training in order to enable him/her to represent GW Pharmaceuticals to high standards of ethical conduct in compliance with the Code.

The named individual had provided a rigorous and detailed account of the events which occurred at the BPNA conference over 3-5 January 2018, backed by robust supporting materials, including a number of contemporaneous records of his/her interactions with health professionals. GW Pharmaceuticals had complete trust in his/her account of events and thus supported him/her in refuting the allegations. GW Pharmaceuticals noted in particular that the named individual recorded instances where health professionals requested information on the development status of products. As indicated in the statement, he/she responded appropriately and provided detailed accounts of having done so. GW Pharmaceuticals noted in particular that in a summary of the meeting he/she made shortly afterwards which indicated that '[health professionals] still thinking [Epidiolex] available in mid 2018. We are disappointing customers' expectations'. This clearly indicated that he/she and GW Pharmaceuticals were consistently telling health professionals that Epidiolex would be available later than many of them expected. The named individual also recalled an earlier incident in which a third-party health professional stated that Epidiolex would be available in 2018 to which he/she took prompt action to correct this mistaken position.

GW Pharmaceuticals stated that it had also taken particular care to re-assess and review, in the context of the complaint, all relevant material, procedures, processes, instructions, briefing and training which might pertain to the alleged events, including anything which might have resulted in a representative making the alleged statement in error. The company had also reviewed the employee's account of events and of any instructions he/she received. Further, the company had reviewed all the materials which were available or displayed on the stand, including photographic evidence of the same. All of this material, where relevant, was provided.

GW Pharmaceuticals submitted that it had never, implicitly or directly, promoted or encouraged the promotion of any unlicensed medicine, including

Epidiolex. Indeed, it went to particular lengths to ensure that the alleged claims would not happen even by reason of genuine error; in that regard it referred to its standard responses to enquiries on cannabidiol.

GW Pharmaceuticals submitted that the materials displayed on the stand were disease awareness information and/or genuine non-promotional information about the company and its research interests.

Finally, GW Pharmaceuticals outlined significant concerns about the language used in the complaint, which it considered questioned its credibility. The named individual had identified a number of elements in what he/she was alleged to have said that made little sense and that an experienced medical affairs professional would never state, including that the product was authorized, that the EMA had authorized it and that it would be available to patients soon. The named individual explained that he/she knew that the product was not authorized and that a determination on whether to authorize would not be made until 2019 and that as reflected in the briefing and stand materials, the Commission, not the EMA, approved medicines, and there would be a delay between approval and access by patients in the UK. Indeed, the National Institute for Health and Care Excellence (NICE) intended to subject cannabidiol to its standard single technology appraisal (STA) process, which would most likely extend the date for routine access by patients in England and Wales well beyond its likely approval in 2019.

GW Pharmaceuticals noted the complainant's allegation that the company had a manned exhibition stand with Epidiolex materials. The materials, however, only referred to cannabidiol by its non-proprietary name; the brand name was not used at all. This was reflected in the company's briefing and training materials.

GW Pharmaceuticals noted that the complainant provided a direct quotation of what the named individual was alleged to have stated but did so in a seemingly implausible manner. The allegation was that he/she introduced Epidiolex as a new treatment, yet there was no introduction to, or presentation on, cannabidiol. Those manning the booth reacted to requests and questions from health professionals. The named individual would simply not have stated this in conversation with a health professional, because it was not a natural expression when responding to an unsolicited request.

Finally, GW Pharmaceuticals stated that the complainant seemed to have used extensive knowledge of medicines advertising law and the Code to construct a complaint covering all the elements that the PMCPA would look for when seeking to identify inappropriate pre-approval promotion of a medicine, ie:

- Involvement of sales representatives in medical information activities – by suggesting that the named individual was a representative, the complainant had implied that GW Pharmaceuticals had manned a medical stand with sales staff. The named individual was not a representative. GW Pharmaceuticals noted that the complainant had referred to a 'medical representative', a term typically used by those with extensive familiarity with the Code eg the supplementary information to Clause 16.3.

  GW Pharmaceuticals doubted whether a genuine health professional would be aware of this terminology, or indeed the distinction between a medical representative and a generic representative.

- Use of a product's brand name pre-approval – the complainant alleged that the stand materials and statements referred to cannabidiol by its brand name, Epidiolex. That was clearly incorrect to the extent it related to the stand materials, and GW Pharmaceuticals denied that the named individual ever stated that.

- Alleged pre-authorization and misleading advertising – the complaint also seemed carefully constructed to suggest that GW Pharmaceuticals had engaged in both illegal pre-approval *and* misleading advertising of Epidiolex, which again suggested familiarity with medicines advertising law and the manner in which the Panel considered cases.

The above led GW Pharmaceuticals to query whether the complainant was genuinely a health professional attendee at the stand.

GW Pharmaceuticals stated that it considered that the complaint was unmerited and implausible and that the Panel should dismiss it. However, the company also appreciated that the anonymity of the complainant and paucity of evidence in support of what was in effect one person's word, presented the Panel particular difficulties in adjudicating this matter. In this regard, GW Pharmaceuticals noted that when adjudicating complaints involving conflicting claims, the appropriate standard to be used was the 'balance of probabilities'. In that regard, GW Pharmaceuticals referred to cases in UK law and to two previous cases under the Code (Case AUTH/2572/1/13 and Case AUTH/2824/2/16).

GW Pharmaceuticals submitted that its version of events was more probable than that put forward by the complainant. Indeed, given the substantial evidence provided and careful assessment of the materials at issue and relevant events, GW Pharmaceuticals did not consider that the complainant had discharged the burden of proof on the balance or probabilities assessment. In conclusion, GW Pharmaceuticals submitted that it was impossible on a common sense view to find against the company on the basis of the simple statement put forward by the complainant, given its flaws and the weight of contradictory evidence and material submitted by the company.

With regard to approval certificates for the materials in question, GW Pharmaceuticals submitted that as it was non promotional it did not require certification. The supplementary information to

Clause 14.3 required that other material which was not promotional *per se*, such as corporate advertising should be examined to ensure that it did not contravene the Code. GW Pharmaceuticals confirmed that it had undertaken such examination and found all applicable material at issue was compliant.

GW Pharmaceuticals therefore denied any breaches of the Code, including of Clauses 3, 7.2, 9.1, 15.2 and 2.

FURTHER INFORMATION FROM GW PHARMACEUTICALS

GW Pharmaceuticals had continued to investigate the matter beyond the submission date of the response above. When GW Pharmaceuticals was advised of the second complaint (Case AUTH/3024/3/18) it again immediately investigated the matter independently of the ongoing investigation in this case. GW Pharmaceuticals considered that rather than two unrelated incidents, leading to separate complaints by unrelated complainants, the complaints were entirely fabricated by the same individual. GW Pharmaceuticals gave further, confidential background information about the suspected complainant and the events which led to the submission of his/her complaints.

PANEL RULING

The Panel noted that the anonymous complainant had, as set out in the introduction to the Constitution and Procedure, the burden of proving his/her complaint on the balance of probabilities. Anonymous complaints were accepted and, like all complaints, judged on the evidence provided by the parties. The Panel also noted that as the complainant was non-contactable it was not possible to ask him/her for further information.

The Panel noted the complainant's concern that GW Pharmaceuticals had promoted Epidiolex at the 2018 BPNA prior to the grant of its marketing authorization. The complainant's concerns covered both the materials on the exhibition stand and what he/she alleged was said by a company representative at the exhibition stand.

The Panel noted that when the meeting was held on 3-5 January 2018, Epidiolex did not have a marketing authorization although a licence had been applied for in the EU and US. The Panel noted GW Pharmaceuticals' submission that it currently expected a decision from the European Commission for Epidiolex in mid-2019. The company briefing on its standard responses for enquiries about Epidiolex (EU version 1.0, June 2017) stated that it was difficult to anticipate if, or when Epidiolex would be approved although the Panel noted that this document pre-dated the submission of the application for a marketing authorization.

The Panel noted that according to a press release dated 29 December 2017, the proposed indications in the EMA marketing authorization application for Epidiolex were as adjunctive treatment for seizures associated with Lennox-Gastaut Syndrome and Dravet Syndrome, each forms of childhood onset epilepsy. Orphan designation had been granted for these proposed indications. In addition, the press release stated that orphan designations had been granted for West Syndrome and Tuberous Sclerosis Complex.

The Panel noted that although Clause 3 prohibited the promotion of a medicine prior to the grant of its marketing authorization, the Code permitted companies to undertake certain limited activities with regard to unlicensed medicines. GW Pharmaceuticals had not argued that any of the material and activities at issue constituted the legitimate exchange of medical and scientific information during the development of a medicine. The Panel noted that Clause 1.2 and its supplementary information permitted companies to respond in certain circumstances to unsolicited enquiries about a medicine including those without a marketing authorization; such responses should, *inter alia*, not go beyond the orbit of the original enquiry and the company should be satisfied that the enquiry was truly unsolicited.

The Panel noted that in a signed statement, the named GW Pharmaceuticals employee at the exhibition stand stated that the company's presence at the BPNA conference comprised a small medical booth staffed by him/her and another member of the UK medical team. According to GW Pharmaceuticals, the exhibition booth was intended to provide a non-promotional presence that demonstrated the company's commitment to research and development, its corporate awareness as a pharmaceutical development company, non-product specific disease awareness, and information on GW Pharmaceuticals' main research activities including cannabinoid medicinal products. GW Pharmaceuticals provided copies of the materials available at the booth; none mentioned Epidiolex by name. The Panel noted that it was an accepted principle under the Code that a product could be promoted without its name ever being mentioned.

An annotated photograph of the exhibition stand provided by GW Pharmaceuticals showed a table on which two infographics and five stacks of three leaflets were clearly displayed. An exhibition panel to the left of the table, headed 'GW Pharmaceuticals' depicted a photograph of a parent and child and referred the reader to the corporate website.

Two A3 infographics on Dravet Syndrome and Lennox-Gastaut Syndrome were each placed at the front of the table on the right-hand side. In the Panel's view, their location and striking design was such that they would have been highly visible to delegates visiting the stand. Each discussed age of onset of disease, prevalence, diagnosis, seizure types, aetiology, mortality rate and costs/economic burden. Each highlighted that current therapeutic options were inadequate. That for Lennox-Gastaut Syndrome stated 'Up to **80%** of patients are r**efractory to anti-epileptic drug therapy**'. That for Dravet Syndrome stated 'Only **16%** of patients experience complete resolution in their seizures. All

seizure types **extremely resistant to treatment**'. In the Panel's view, these statements on materials at a pharmaceutical company exhibition stand would, on the balance of probabilities, solicit questions about the company's pipeline/other products.

A leaflet entitled 'Early–Onset Epilepsy Syndromes: Facts and Figures' reproduced the two aforementioned infographics on Lennox-Gastaut Syndrome and Dravet Syndrome. It also included two further infographics on Infantile Spasms and Tuberous Sclerosis Syndrome. These further infographics also implied that current therapy was inadequate; 'Most cases are **resistant** to anti-epileptic medications **45%** have intractable seizures after 3 years follow-up' (Infantile Spasms) and '63% of patients have refractory seizures' (Tuberous Sclerosis Complex). The Panel considered that its comments above in relation to the A3 infographics applied to this leaflet.

A leaflet entitled 'A World leader in the development of cannabinoid medicines' discussed GW Pharmaceuticals' commitment to cannabinoid treatments. The final page gave more details describing the cannabinoid development pipeline by indication under investigation and phase of clinical study. Seven neuroscience pipeline indications were listed. Dravet Syndrome and Lennox-Gastaut Syndrome had completed Phase 3 trials. Tuberous Sclerosis was shown as halfway through Phase 3 trials and infantile spasm halfway through Phase 2. A highlighted box beneath discussed the scale of the Phase 3 clinical development programmes with Dravet Syndrome and Lennox-Gastaut Syndrome and noted that the company's 'lead cannabinoid' had received orphan drug designation in these indications. The Panel noted that whilst Epidiolex was not named, sufficient information about its proposed indications, clinical development and orphan status was given such that it was indirectly identified and on the balance of probabilities the material would solicit questions about the company's 'lead cannabinoid'.

A fifth item was a glossary of cannabinoid terms. The Panel noted its concerns about the materials set out above. The Panel also noted that the materials had a promotional appearance. The Panel considered that the materials went beyond disease awareness information and/or non-promotional information about the company and its research interests as asserted by GW Pharmaceuticals.

In the Panel's view, the cumulative effect of highlighting the specific conditions for which it was anticipated the product would be licensed (as opposed to a more general discussion of paediatric epilepsy), deficiencies of current therapeutic options for the proposed indications in the infographics and discussing the Phase 3 clinical development program including referring to the company's 'lead cannabinoid', meant that the exhibition stand promoted a medicine prior to the grant of its marketing authorization. A breach of Clause 3.1 was ruled. High standards had not been maintained; a breach of Clause 9.1 was ruled.

The Panel noted that promoting a product prior to the grant of its marketing authorization was listed in the supplementary information to Clause 2 as an activity likely to give rise to a breach of that Clause. The Panel noted its comments and rulings above and considered that GW Pharmaceuticals had brought discredit upon and reduced confidence in the pharmaceutical industry and a breach of Clause 2 was ruled.

The Panel noted the complainant's further allegation about comments that he/she alleged were made by a named company representative at the stand, namely that Epidiolex was introduced as a new treatment for paediatric patients with Dravet Syndrome and patients with Lennox-Gastaut Syndrome and that it had been licensed by the EMA and would soon be available in the UK. GW Pharmaceuticals denied that such comments had been made. The Panel noted the difficulty in dealing with complaints based on one party's word against the other; it was often impossible in such circumstances to determine precisely what had happened. The introduction to the Constitution and Procedure stated that a complainant had the burden of proving their complaint on the balance of probabilities. The complainant was non-contactable and it was not possible to ask him/her for further information. The Panel had to make a ruling on the evidence before it.

The Panel noted its comments above about responses to unsolicited enquiries and Clause 1.2 of the Code and its supplementary information. The Panel also noted the signed statement of the company employee manning the booth in relation to training, the nature of queries received at the exhibition stand, and whether he/she would have responded as alleged. The Panel also noted the detailed briefing to medical affairs staff to use at conferences in response to unsolicited requests. The briefing pre-dated the submission of the company's marketing authorization application to the EMA and advised that discussions with health professionals must be reactive and in response to the requested information. Staff were advised to narrowly tailor the response to the level of the question posed. The company's report on interactions at the conference did not closely mirror the complainant's allegation. In relation to the alleged comments made at the exhibition stand, it was impossible to determine where the truth lay and the Panel accordingly ruled no breach of Clauses 15.2, 9.1, 7.2, 3.1 and 2.

Complaint received **24 January 2018**

Case completed **22 November 2018**