CASE AUTH/3324/3/20

EMPLOYEE v GEDEON RICHTER

Publication of data and approval of materials/activities

An employee of Gedeon Richter (UK) Ltd complained about a number of compliance issues within the company.

The detailed response from Gedeon Richter is given below.

1 Alleged data cover-up

The complainant alleged that there was a plan to conceal patient safety data. Details were provide including that a study for Levosert (levonorgestrel – a intrauterine device (IUD) for contraception) had never been published, and there was no plan to publish it, to purposefully avoid disclosure of anaesthetic use for insertions of Levosert. The complainant alleged that this was also reported to a member of UK staff who had not acted upon it.

The Panel considered that any allegation that patient safety data had been concealed was extremely concerning.

The Panel noted Gedeon Richter's submission that its only responsibility was to present the study as part of the documentation to the authorities during the marketing authorization process which it had done. Gedeon Richter referred to the relevant public domain data regarding the study on the Food and Drug Administration (FDA) website where safety was reported. The Panel noted that the clinical review published on the website had a completion date of 23 February 2015 and included reference to the study in question.

The Panel noted Gedeon Richter's submission that there had never been any 'cover-up' and all regulatory requirements regarding making data available in the public domain had been met and there was the usual access to all of the data including, importantly, the safety data.

In the Panel's view, the complainant had not discharged his/her burden of proof to show that the study had not been disclosed or that safety data had been concealed by Gedeon Richter and that this had been done with the knowledge of UK staff. The Panel therefore ruled no breaches of the Code including Clause 2.

2 Alleged refusal to learn from previous complaints

The complainant stated that he/she had been made aware of a complaint in December 2019 and of previous serious breaches of the Code. To the complainant's knowledge, no new measures had been implemented to prevent future breaches.

The Panel noted that Gedeon Richter had not been informed of the outcome of its consideration of Case AUTH/3273/10/19 when the complaint was made in Case AUTH/3324/3/20. There was no requirement under the Constitution and Procedure for the company to take action until notified of the Panel's ruling in a case.

The Panel noted Gedeon Richter's submission regarding the actions taken to look at ways to improve the company's processes when it received the complaint in Case AUTH/3273/10/19. In addition, the company submitted that it had instigated a detailed corrective and preventative action (CAPA) plan which included a review of the actions taken in order to make further improvements as necessary.

In the Panel's view, the complainant had not discharged his/her burden of proof to show that no new measures had been implemented to prevent future breaches of the Code as alleged. Further given the position of its consideration of Case AUTH/3273/10/19 there was no requirement for Gedeon Richter to do so. The Panel ruled no breaches of the Code including Clause 2.

3 Training materials

The complainant submitted that some of the International Osteoporosis Foundation website had been directly copied and pasted into a training slide deck: Key Account Manager (KAM) introduction to osteoporosis. The material was referenced, but some slides had been taken as a screenshot and inserted directly into the training slide deck. This meant the slide had not been created by the Gedeon Richter employee but had been copied and pasted directly.

The complainant alleged that materials had not been updated/reviewed or re-approved.

The Panel noted Gedeon Richter's submission that its analysis showed that two training items had been created, reviewed, approved and certified but unfortunately had been used by medical during training outside of their approval dates. The Panel ruled breaches of the Code as acknowledged by Gedeon Richter.

The Panel noted Gedeon Richter's summary of its training materials referred to by the complainant. It appeared that all of the materials had been re-certified or withdrawn within the two-year period as required by the Code. The Panel therefore ruled no breaches of the Code including Clause 2.

4 Internal company meeting

The complainant submitted that in a presentation to the entire company, a global member of staff used a slide deck which had not been approved (either before or after the meeting) and without any references. The complainant alleged that a request for the slide deck and references to be provided before the meeting was ignored.

The Panel noted that a presentation regarding Terrosa (teriparatide) for the treatment of osteoporosis given by a global colleague at an internal cycle-meeting, attended by the whole sales force as well as most of the UK head-office staff had not been certified as required. The Panel ruled a breach of the Code as acknowledged by Gedeon Richter.

According to Gedeon Richter the global colleague provided the slides at very short notice which meant that there was no time to place them in the approval system. The Panel was concerned that prior to the meeting Gedeon Richter decided to proceed as the team would benefit educationally from the session. The Panel considered that Gedeon Richter had failed to maintain high standards and a breach of the Code was ruled.

The Panel did not consider that the complainant had provided evidence to show on the balance of probabilities that the lack of reference was in relation to a published study or that the particular internal presentation at issue was one that fell within the scope of the clause of the Code that required clear references be given in relation to published studies and therefore ruled no breaches of the Code including Clause 2.

5 Global advisory board meeting

The complainant submitted that a meeting took place in Germany. One UK health professional was invited to attend the standalone meeting. The meeting included four Gedeon Richter employees (three commercial, one medical) and four health professionals. The complainant queried whether the meeting was truly advisory in nature. The meeting consisted of a promotional presentation from a global marketing employee focused on the sales and marketing strategy of the business, followed by a session where the health professionals were asked for their opinion on anabolic therapies.

The Panel had some concern about the ratio of Gedeon Richter staff to advisors and queried whether gaining the advisors advice and involvement in a promotional symposium was a legitimate business question for an advisory board. The papers referred to the meeting as an advisory board working group meeting. The Panel noted that the agenda included four topics, the experience following the launch of Terrosa (a biosimilar medicine) across Europe. The minutes noting that clinical experience among the working group members had been limited due to reimbursement issues and limitations on prescribing. The second topic was a discussion about guidelines in osteoporosis. These two topics were covered in a session of an hour. The third topic was a two hour session on the organisation of a pan-European event focussed on the early initiation of anabolic treatment and the final topic was 30 minutes on Teriparatide, combination and sequential therapies.

The Panel noted that the complainant had provided no evidence with regard to the appropriateness of the attendees. The Panel noted Gedeon Richter's submission that contrary to the complainant's allegation, there was no presentation on the sales and strategy for the product and no global marketing director attended the advisory board. The Panel noted however that a marketing manager was listed as attending. Whilst the Panel had some concerns about the advisory board in question it did not consider that the complainant had shown on the balance of probabilities that the advisory board was unacceptable as alleged. Based on the allegation the Panel ruled no breaches of the Code including Clause 2.

6 Use of the word 'unique'

The complainant noted that an e-detail aid for a new hormone replacement therapy (HRT) spray (Lenzetto (oestradiol)) was currently undergoing approval and described the

product as 'unique'. The final signatory had advised that the product should not be described as such but he/she was over-ruled by the UK company directors whose view was that the decision to use the word 'unique' in relation to the spray delivery was appropriate.

The Panel noted that Gedeon Richter had provided a copy of the final item for the Lenzetto e-detail aid demonstrating certification. The Panel noted Gedeon Richter's submission that Lenzetto had not been determined as superior to other HRT formulations; 'unique' was used to describe the fact that it was currently the only HRT with a spray design and that this was an accurate, balanced, fair, objective and unambiguous representation of the product delivery. The complainant had not provided any evidence to the contrary and the Panel therefore ruled no breaches of the Code including Clause 2.

An employee of Gedeon Richter (UK) Ltd complained about a number of compliance issues within the company including an alleged plan to conceal patient safety data. The complainant submitted that due to previous lack of response to colleagues involved in a whistleblowing case on patient safety, he/she had no confidence that Gedeon Richter would respond to his/her complaint and ultimately protect patient safety.

Gedeon Richter submitted that the complaint came from a disgruntled ex-employee and hoped the PMCPA would consider this context when appraising not only the content of the complaint itself, but also its response. The complaint contained numerous inaccuracies and allegations which were not true which highlighted that the complainant was not fully party to all of the facts – much of the complaint was based on hearsay and the complainant's own erroneous assumptions.

1 Alleged discovery of data cover-up plan

COMPLAINT

The complainant alleged that there was a plan to conceal patient safety data. The complainant was informed on further questioning, that Medicines360 originally performed the two-handed inserter study for Levosert (levonorgestrel – a intrauterine device (IUD) for contraception) in the US, and that a different named pharmaceutical company then purchased the marketing authorisation. Later down the line, Gedeon Richter purchased the marketing authorization in the EU and the named pharmaceutical company wanted to conceal the section in patient safety data in the study, where there was clear evidence of more anaesthetic being used than it wanted to have published; therefore the study had never been published, and there was not a plan to publish it, to purposefully avoid disclosure of anaesthetic use for insertions of Levosert. It had also come to the complainant's attention that this was also reported to a member of the UK medical staff, who had not, to his/her knowledge, acted upon it.

When writing to Gedeon Richter, the Authority asked it to consider the requirements of Clauses 2, 9.1 and 13.1.

RESPONSE

Gedeon Richter was extremely unhappy about the allegation that there had been a plan to conceal patient safety data. The company strongly refuted that it would act in this manner; not

only with regards to the study in question, but also with regards to any other study with which the company was directly or indirectly involved. This was an entirely false allegation for which there was no foundation whatsoever.

Gedeon Richter understood that the obligation regarding publication lay with the sponsor of the study ie Medicines360 and that Gedeon Richter's only responsibility was to present the study as part of the documentation to the authorities during the marketing authorization process (based on the provisions of Medicines Directive). Gedeon Richter submitted that it had fulfilled its obligations in that regard.

Gedeon Richter referred to the link to the relevant public domain data on the Food and Drug Administration (FDA) website. The FDA requested the inserter study prior to initial approval. Safety was reported in that FDA document.

With regard to the complainant's comments about the use of anaesthetic, Gedeon Richter stated that its very clear position was that the use of local anaesthetic when a Levosert device was being fitted should be based on the individual patient's needs and what she was comfortable with. There was huge variability in how individual patients tolerated pain and discomfort and what they found acceptable. Furthermore, patients could also vary from day-to-day in terms of their pain levels and tolerability. Gedeon Richter had neither claimed, nor had it supported claims that Levosert required either more or less anaesthetic than other IUDs. This was an area of clinical discussion between the patient and the health professional fitting the device. Gedeon Richter stated that it did not have (nor had it sought) evidence to prove that Levosert had any advantage in this respect. The company's only advice in this regard was to recommend the use of over-the-counter pain relief approximately 30 minutes before an appointment to fit Levosert; and that patients also discussed pain relief with their health professional at the appointment itself.

Gedeon Richter submitted that this was not a patient safety issue; it was an issue of pain management at the time that the device was inserted. Gedeon Richter submitted that it hoped it had explained its reasons for not making claims around this area. This could also be further substantiated by the study under discussion which would not provide adequate evidence to make a claim regarding anaesthetic use.

In relation to the study in question, Gedeon Richter referred to the detailed summary section in and provided a copy of the core components of the Clinical Study Report (CSR). To avoid confusion, Gedeon Richter therefore referred to two documents; its own summary of the study, highlighting key points, as requested by the PMCPA, as well as, separately, the core components of the CSR. Gedeon Richter's own summary gave an overview of the study and then focussed on the parts relevant to the complaint.

Gedeon Richter stated that it could not comment on the detail of individual discussions that had taken place between Gedeon Richter global and the other named pharmaceutical company before Levosert was available to the UK affiliate. Gedeon Richter was not party to these high-level discussions which took place a number of years ago. However, Gedeon Richter had spoken to its global colleagues and they had stated that they were aware of the study results when entering the licence agreement with the other named pharmaceutical company and when becoming the marketing authorization holders of the product in the EU. Gedeon Richter noted that by this point the study report had already been incorporated into the clinical trial database (CTD) documentation for Levosert, as well as interpreted in the clinical modules. Gedeon

Richter stated categorically that there had never been any 'cover-up' between the companies jointly or individually. Gedeon Richter could not comment further as the complainant's allegations on this point had no foundation.

Gedeon Richter stated that, in summary, all regulatory requirements regarding making data available in the public domain had been met and there were the usual accesses to all of the data including, importantly, all of the safety data. Correct process had been followed in all regards.

Furthermore, the company noted that it did have access to, and oversight of, all the relevant clinical trial data, pertaining to Levosert.

In conclusion, Gedeon Richter strongly refuted a breach of Clauses 2, 9.1 and 13.1. The company had maintained high standards in addition to its obligations in disclosing clinical trial details. Accordingly, Gedeon Richter strongly believed that there were no grounds to constitute a breach of Clause 2.

Finally, and in response to the allegation that a member of the UK medical staff had known about this information but not acted upon it, a conversation was recalled by the member of staff but with the complainant no patient safety issue was identified. The complainant was asked to discuss any queries with a colleague in the global medical affairs unit. Had the complainant reported back a patient safety issue, then the medical department would have taken that very seriously and acted accordingly. Gedeon Richter hoped the detail provided above clearly demonstrated that there was not a safety concern to be addressed, or a 'cover-up' and publication obligations had very clearly been met from all parties.

PANEL RULING

The Panel considered that any allegation that patient safety data had been concealed was extremely concerning.

The Panel noted Gedeon Richter's submission that the obligation regarding publication lay with the sponsor of the study ie Medicines360 and that Gedeon Richter's only responsibility was to present the study as part of the documentation to the authorities during the marketing authorization process which it had done. Gedeon Richter referred to the relevant public domain data regarding the study on the Food and Drug Administration (FDA) website where safety was reported. The Panel noted that the clinical review published on the website had a completion date of 23 February 2015 and included reference to the study in question.

The Panel noted that the study in question (ref M360-L104) was a Phase 1, multi-centre study to assess the performance of a two-handed LNG20 Intrauterine System Inserter for Levosert. The study, originally performed by Medicines360, was carried out in 6 sites in the US and completed in March 2014. A secondary endpoint of the study included adjunctive procedures needed for IUS placement including cervical anaesthesia. Local anaesthesia was used prophylactically for 44 (44.0%) subjects during IUS placement. Local anaesthesia was more likely to be used for nulliparous (52.6 %) than parous (32.6 %) subjects. One site used topical benzocaine spray for all 15 of their subjects. Two sites used cervical block with lidocaine for 39 of their combined 40 subjects. Three sites used no cervical anaesthesia for their combined 45 subjects. All cervical anaesthesia was used prophylactically with none being applied out of clinical necessity (ie, procedure-elicited). Pain scores using a VAS scale of 0 to 100 were used

after sounding, after IUS placement, and before IUS removal to assess the 24 hours prior to removal. However, the study did not control for prophylactic use of pain medications or local cervical anaesthesia, thereby confounding interpretation of the VAS pain scores.

The material provided by Gedeon Richter stated that because of the limitations of a small number of participants (n=100) and short study duration (24 hours) and the notable findings for the THI inserter, it was reasonable that more safety data should be collected post-approval with a formal agreed method and a recommendation was made regarding a post marketing surveillance study.

The Panel noted that Clause 13.1 required that companies disclose details of clinical trials in accordance with the Joint Position on the Disclosure of Clinical Trial Information via Clinical Trial Registries and Databases and the Joint Position on the Publication of Clinical Trial Results in the Scientific Literature.

The Panel noted Gedeon Richter's submission that there had never been any 'cover-up' between the companies jointly or individually and all regulatory requirements regarding making data available in the public domain had been met and there was the usual access to all of the data including, importantly, all of the safety data.

The Panel noted that the complainant bore the burden of proof. In the Panel's view, the complainant had not discharged his/her burden of proof to show that the study had not been disclosed or that safety data had been concealed by Gedeon Richter and that this had been done with the knowledge of its medical director. The Panel therefore ruled no breach of Clauses 13.1 and 9.1 and consequently no breach of Clause 2.

2 Alleged refusal to learn from previous complaints

COMPLAINT

The complainant stated that he/she had been made aware of a complaint in December 2019 that the Richter Resource Centre website had inappropriate promotion both to patients and health professionals and the website had been found to be live without prescribing information. The complainant was also aware of previous serious breaches of the Code. To the complainant's knowledge, no new measures had been implemented to prevent future breaches of the Code; for example, no new standard operating procedures (SOPs) or guidance issued for either the company, or any third party agency, to follow that would ensure future content and company websites displayed appropriate information.

When writing to Gedeon Richter, that Authority asked it to consider the requirements of Clauses 2 and 9.1.

RESPONSE

Gedeon Richter submitted that the complainant was clearly referring to Case AUTH/3273/10/19 and in March 2020 when Gedeon Richter was notified of this complaint, Case AUTH/3273/10/19 had not yet been the subject of a determination by the Panel.

Gedeon Richter noted that its cross-functional team immediately began to look at ways to improve the company's processes as it began to write the response to the complaint; not only in

relation to the clauses of the Code which it might have breached, but also in relation to the 'spirit of the Code' – how could Gedeon Richter prevent any such errors in future and how could it improve its materials more generally speaking focusing on improving educational content and also taking a more balanced view of the disease areas it portrayed (not only on websites, but other materials too). Gedeon Richter submitted that it acted quickly and spent a good deal of time looking at comprehensive improvements and learnings – this occurred both when the complaint was received and beyond. Gedeon Richter did not wait until it had submitted its response to the PMCPA, let alone for the PMCPA's reply.

Gedeon Richter noted that the complainant had stated that to his/her knowledge no new measures had been implemented to prevent future breaches of the Code. Gedeon Richter hoped the PMCPA would agree that to refer to the absence of new measures, one would need a detailed oversight of all company activities in that regard. It was difficult to prove the absence of something, and it was wholly incorrect in relation to this complaint. In addition to the many improvements, Gedeon Richter had instigated a detailed corrective and preventative action (CAPA) (copy provided). Gedeon Richter referred to the detailed actions as described. Gedeon Richter had also detailed in the CAPA a date in October 2020 to review actions and make further improvements as necessary.

Additionally, an update to one of the key relevant SOPs related to promotional materials was a work in progress (copy provided) and Gedeon Richter hoped that that provided clear evidence of its actions and improvements.

Finally, on 5 May 2020 the company's signatory sent out a briefing document to all those involved in copy approval.

Gedeon Richter believed the actions it had taken were comprehensive.

Gedeon Richter noted that the complainant had provided incorrect information about the Richter Resource Centre website. The error with the website was indeed the inclusion of the prescribing information in the opening page and therefore 'potential promotion to the public' (inadvertently). It was not omission of the prescribing information as had been stated.

Gedeon Richter stated that as the PMCPA recalled; it acted quickly to not only acknowledge errors, but it also took the relevant website down within 24 hours of receipt of the complaint. Gedeon Richter simultaneously internally spoke about improving the clarity and navigational properties of the website, as well as making the content more balanced with regard to the disease areas the company covered. All of the above had been progressed.

Gedeon Richter very strongly denied breaches of Clauses 2 and 9.1. The company hoped its actions would counteract the complainant's false allegations. Gedeon Richter stated that it constantly sought to improve its processes – and ultimately the materials it provided to patients and health professionals.

PANEL RULING

The Panel noted that Gedeon Richter had not been informed of the outcome of its consideration of Case AUTH/3273/10/19 when the complaint was made in Case AUTH/3324/3/20. There was no requirement under the Constitution and Procedure for the company to take action until notified of the Panel's ruling in a case.

The Panel noted Gedeon Richter's submission regarding the actions taken to look at ways to improve the company's processes when it received the complaint in Case AUTH/3273/10/19. In addition, the company submitted that it had instigated a detailed corrective and preventative action (CAPA) plan which included a review of the actions taken in order to make further improvements as necessary. An update to one of the relevant SOPs related to promotional materials was a work in progress and in May 2020 a briefing document was sent to all those involved in copy approval which provided details regarding Case AUTH/3273/10/19 and reminded staff of the need to include the generic name of a medicine immediately adjacent to the brand name at its first mention so that the error was not repeated.

In the Panel's view, the complainant had not discharged his/her burden of proof to show that no new measures had been implemented to prevent future breaches of the Code as alleged. Further given the position of its consideration of Case AUTH/3273/10/19 there was no requirement for Gedeon Richter to do so. The Panel ruled no breach of Clauses 9.1 and 2.

3 Training materials

COMPLAINT

The complainant submitted that some of the International Osteoporosis Foundation website had been directly copied and pasted into a training slide deck: Key Account Manager (KAM) introduction to osteoporosis (ref UK/TERR/0619/0105). The material was referenced, but some slides had been taken as a screenshot and inserted directly into the training slide deck. This could be ascertained by clicking on the slide deck and the window appeared as a whole image inserted to be used as one slide per screenshot. This meant the slide had not been created by the Gedeon Richter employee but had been copied and pasted directly.

The complainant alleged that materials had not been updated/reviewed or re-approved, materials created for training employees on Levosert; date of creation: 2017. Including UK/LEV/0417/0029 – slide deck. Levosert training modules 1-4, dated March 2017, Esmya Module 1 dated March 2017, which were not currently being reviewed for update.

When writing to Gedeon Richter, the Authority asked it to consider the requirements of Clauses 2, 9.1, 14.1 and 14.5 (in relation to the requirement to re-certify at intervals of no more than 2 years).

RESPONSE

Gedeon Richter listed the material relevant to the allegation as follows:

a) Terrosa training – Introduction to Osteoporosis – UK/TERR/0619/0105 (incorrectly called 'KAM introduction to osteoporosis' by the complainant).
b) Levosert MAM Training slides April 2017 – UK/LEV/0417/0029
Minimal use – by a medic for training.
c) Levosert training modules Module 1 (June 2017) (Re-approval 1) – UK/LEV/0617/0041
d) Levosert training modules Module 2 (July 2019) – UK/LEV/0617/0041a(1)
e) Levosert training modules Module 3 (June 2017) – UK/LEV/0617/0041b
f) Levosert Training Module 4 v2 – UK/LEV/0617/0041d

g) Gynaecology – MED ED – Richter Resource Centre – Module 1 About Uterine Fibroids – UK/GYN/1216/0108.

Gedeon Richter submitted that marketing and medical personnel were originators of training materials and those materials were reviewed and approved by commercial and medical.

The requested details of the relevant training materials were provided as were the SOPs and copies of the relevant SPCs and details of updates to them. Gedeon Richter submitted that the analysis showed that two training items had been created, reviewed, approved and certified but unfortunately used by medical during training outside of their approval dates. There were three key SOPs, identified which outlined a clear process to be followed. Gedeon Richter believed, on analysing of its internal materials, that these SOPs were followed but had twice not prevented the use of materials beyond their approval dates. To capture these non-conformances, a CAPA had been opened to address the deficiencies. Accordingly, for the two training items, Gedeon Richter accepted it had breached Clauses 9.1 and 14.1.

PANEL RULING

The Panel noted Gedeon Richter's submission that its analysis showed that two training items including the Levosert Training Module 4 v2 (ref UK/LEV/0617/0041d) had been created, reviewed, approved and certified but unfortunately had been used by medical during training outside of their approval dates. The Panel noted that it could not identify the second item from the information provided by Gedeon Richter. The Panel ruled a breach of Clauses 14.1 and 9.1 in relation to the two items referred to by Gedeon Richter as acknowledged by Gedeon Richter.

The Panel noted Gedeon Richter's summary of its training materials referred to by the complainant. It appeared that all of the materials had been re-certified or withdrawn within the two-year period as required by Clause 14.5. The Panel therefore ruled no breach of Clause 14.5 and consequently no breach of Clause 9.1.

The Panel noted its rulings and comments above but did not consider that the particular circumstances of this case were such as to warrant a breach of Clause 2 which was a sign of particular censure. No breach of Clause 2 was ruled.

4 Internal company meeting

COMPLAINT

The complainant submitted that in a presentation to the entire company, a global marketing employee used a slide deck which had not been approved (either before or after the meeting) and without any references. The complainant alleged that a request for the slide deck and references to be provided before the meeting was ignored. The complainant submitted that it was normal practice for the global headquarters employees who presented slides to UK employees, to ignore guidance on compliant approval of materials being presented to the company and they continued to send materials created outside the UK without appropriate references.

When writing to Gedeon Richter, the Authority asked it to consider the requirements of Clauses 2, 7.6 (if the material was promotional), 9.1 and 14.1.

RESPONSE

Gedeon Richter stated that the meeting in question was an internal cycle-meeting, attended by the whole sales force as well as most of the UK head-office staff. The meeting covered many different topics and included a general company update; a cultural survey update; updates on various Gedeon Richter products (including Esmya and Levosert) as well as a disease area presentation on osteoporosis and guidelines for treatment of osteoporosis. The agenda also covered some sessions on Gedeon Richter's newest product at the time, ie Terrosa (teriparatide) for the treatment of osteoporosis. One of the company's global medical colleagues attended the meeting as an expert on Terrosa; he/she had been closely involved in the development of the product and overseen launches in other countries. Gedeon Richter considered that all of those factors would bring educational value and insights to the team, as well as potentially learnings from other countries. The global colleague's participation was also designed to allow a more interactive question and answer session; with questions cross-functionally, including from the sales team.

Gedeon Richter's materials for such meetings were copy-approved and referenced in accordance with SOP COM001 which set out the process for review, approval and certification of promotional and non-promotional materials. Gedeon Richter adhered to this SOP in all but highly exceptional cases, and in these cases it very carefully weighed-up and discussed any exceptions. For the presentation in question (copy provided) the global colleague provided the slides at very short notice which was a far from ideal and meant that there was no time to place them in the approval system. On balance, Gedeon Richter considered that the team would benefit educationally from the session and also viewing the slides on the product, this non-conformance would, however, be captured in a CAPA.

Gedeon Richter's agreed actions included a medical review, which was completed and a clear understanding that, as the slides had not been certified, they would not be given out to anyone in the company. Gedeon Richter could only re-iterate that this was a highly unusual circumstance for the UK company, and the timelines were not in its favour on this occasion (the slides were received the day before the presentation). Gedeon Richter's materials were almost without exception subject to a very high level of review including very rigorous referencing checks, where needed, and it ordinarily used two certifiers – a medical and commercial signatory. Gedeon Richter was taking proactive steps to ensure that such a presentation, that had not been through its formal approval, did not recur.

Gedeon Richter provided a copy of the training materials that it had formally used to train the team and submitted that they were of a high standard; they had been extensively reviewed and certified as was its usual practice; Gedeon Richter referred to the Terrosa training modules 1-4.

Gedeon Richter stated that the UK and global teams (based in Hungary) worked very closely together across many functions of the business, eg medical, marketing, pharmacovigilance, product quality complaints and regulatory. Close liaison with its Hungarian counterparts was integral to the UK business, indeed Hungary led the organisation on a number of the functions mentioned above. Overall, the UK and global teams worked very well together and the UK had made concerted efforts to build and strengthen this relationship over time. Gedeon Richter frequently drew upon global expertise in terms of its products because in a number of cases the global medical staff had worked on certain products since inception and this was an invaluable source of information for Gedeon Richter.

However, on rare occasions, the global teams had not met Gedeon Richter's UK timelines required, for example, referencing of slides and submitting slide-decks for review. This was an area Gedeon Richter continued to work on, and it had made good progress to that effect. Gedeon Richter frequently referred to Code requirements for certification of materials and considered that the global team was more cognisant of its UK obligations than it might have been in the past. This was an ongoing process which Gedeon Richter took very seriously. On occasions that the UK had received inadequately referenced training materials from the global team, it had reverted to making its own training materials – again it referred to the Terrosa training modules. These had been shared with other countries as an example of how comprehensive the UK training materials were. Gedeon Richter had received much positive feedback in relation to these modules and its teams were very well trained as a result of them.

Gedeon Richter recognised there were shortcomings which meant that, in this instance, and in relation to Paragraph 4, it had breached Clauses 9.1 and 14.1. However, it noted that this did not accurately reflected its training materials, processes, and SOPs.

PANEL RULING

The Panel noted that a presentation regarding Terrosa (teriparatide) for the treatment of osteoporosis given by a global colleague at an internal cycle-meeting, attended by the whole sales force as well as most of the UK head-office staff had not been certified as required. The Panel ruled a breach of Clause 14.1 as acknowledged by Gedeon Richter.

According to Gedeon Richter the global colleague provided the slides at very short notice which meant that there was no time to place them in the approval system. The Panel was concerned that prior to the meeting Gedeon Richter decided to proceed as the team would benefit educationally from the session and also viewing the slides on the product and captured this failure to certify in a CAPA. The Panel considered failure to certify the global colleague's presentation meant that Gedeon Richter had failed to maintain high standards and a breach of Clause 9.1 was ruled.

The Panel noted that Clause 15.9 required that companies must prepare detailed briefing material for medical representatives on the technical aspects of each medicine which they will promote and that such briefing material must comply with the relevant requirements of the Code and, in particular, was subject to the certification requirements of Clause 14. Briefing material must not advocate, either directly or indirectly, any course of action which would be likely to lead to a breach of the Code.

The Panel noted that Clause 7.6 required that clear references must be given when promotional material referred to published studies. The Panel noted the complainant's allegation that the global marketing employee used a slide deck without any references.

The Panel noted that the presentation referred to by the complainant included details of the pivotal efficacy/safety study of Forsteo (teriparatide), (the innovator product) but provided no references. The Panel was unclear as to whether the study was published and no information in this regard had been provided by either party. The Code required all material to be capable of substantiation but references were only required by the Code in limited circumstances. Further, the presentation was used internally and in the Panel's view whether references were required on internal presentations which referred to published studies would depend on the circumstances.

The Panel did not consider that the complainant had provided evidence to show on the balance of probabilities that the lack of reference was in relation to a published study or that the particular internal presentation at issue was one that fell within the scope of Clause 7.6 of the Code. The Panel therefore ruled no breach of Clause 7.6.

The Panel noted its rulings and comments above but did not consider that the particular circumstances of this case were such as to warrant a breach of Clause 2 which was a sign of particular censure. No breach of Clause 2 was ruled.

5 Global advisory board meeting

COMPLAINT

The complainant submitted that a meeting took place in Germany. One UK health professional was invited to attend the standalone meeting (not associated with an international conference attendance). The meeting included four Gedeon Richter employees (three commercial, one medical) and four health professionals. In that regard, the complainant queried whether the meeting was truly advisory in nature. The meeting consisted of a promotional presentation from a global marketing employee focused on the sales and marketing strategy of the business, followed by a session where the health professionals were asked for their opinion on anabolic therapies.

When writing to Gedeon Richter, the Authority asked it to consider the requirements of Clauses 2, 9.1 and 23.1.

RESPONSE

Gedeon Richter submitted that it was not aware of any advisory board which took place in Germany. It was clear that the complainant had referred to an advisory board which took place in Vienna, Austria. This was another error by the complainant.

One UK health professional attended the advisory board in Vienna arranged by Gedeon Richter's global colleagues with support from the UK affiliate. The meeting arrangements were approved in line with Gedeon Richter's UK SOPs and certified via its Advisory Board Meeting Approval Form which listed the *bona fide* business questions which were addressed. The advisory board included four health professionals and four members of the Gedeon Richter team (the meeting minutes and a detailed breakdown of delegates titles was provided). The cross-functional medical and marketing team worked to jointly facilitate discussions as per the agenda. The UK company's role was to facilitate the attendance of the UK health professional in a compliant manner. The four health professionals were selected as experts in managing osteoporosis and were either professors or doctors. They were selected from specific countries (UK, Spain, Slovenia and Austria) which had vastly varying environments for the use of teriparatide for osteoporosis (Terrosa was the company's biosimilar teriparatide which was launched in August 2019). The markets ranged from restricted access of the product to fully available – this, Gedeon Richter believed was a good representation of the European environment for the product. The experts were also selected to provide guidance on the product usage and on guidelines in the very different marketplaces of their own countries.

The key output of the advisory board was that Gedeon Richter should focus its efforts to try to get anabolic treatment used earlier in the treatment pathway, this was provided in the meeting minutes. This was something the company would focus on moving forwards. Advisors were also asked to provide expert guidance on developing an agenda and content for a promotional symposium which would have been held in June 2020 but was cancelled/postponed due to Covid-19. The symposium would factor in the different landscape for the product in Europe and all four advisors had agreed to participate in it. Finally, advisors were asked for their views about the possible future usage of the product; their advice was that they would like the product used for glucocorticoid-induced osteoporosis and that the company explore clinical trials for longer term usage. The company would explore both recommendations as part of the long-term plan for the product.

- Contrary to the complainant's allegation, there was no presentation on the sales and strategy for the product and no global marketing director attended the advisory board. The agenda was the only item presented at the advisory board – all discussion revolved around the agenda items. There was no marketing presentation despite the complainant's assertion. The agenda content was certified as part of Gedeon Richter's advisory board approval. No formal attendee feedback was sought. Copies of the invitation, agenda, SOP and guidance, advisory board approval form, minutes from the meeting and the signed agreement were provided.

The UK health professional received an honorarium (details provided)which was within Gedeon Richter's fair market value for maximum daily rate. As a UK affiliate, Gedeon Richter fully supported the global advisory board with the participation of one UK health professional.

- Clause 9.1 – Gedeon Richter believed high standards had been met – a thorough appraisal process of the advisory board was performed and all arrangements were certified accordingly.
- Clause 23.1 – Gedeon Richter believed the use of appropriate consultants for the advisory board was in line with Clause 23.1. The health professionals had supplied consultancy services within contractual agreements with the company at fair market values as demonstrated by the UK agreement example provided.
- Clause 2 – as described above, a thorough and rigorous review process was upheld by the team at Gedeon Richter and the final signatories. The advisory board, led by the global Gedeon Richter team, was truly advisory in nature; the UK health professional's involvement was certified. No promotional slides were presented as alleged by the complainant. The use of advisors for the meeting, Gedeon Richter believed, was proportionate and not excessive. Gedeon Richter believed that high standards had been met and that this advisory board did not discredit, or reduce confidence in, the pharmaceutical industry.

Gedeon Richter denied breaches of Clauses; 23.1, 9.1 and 2.

PANEL RULING

The Panel noted that the complainant queried whether the advisory board was truly advisory in nature. The Panel noted that it included four Gedeon Richter employees (three commercial, and one medical) and four health professionals. The slides listed another member of Gedeon Richter staff but no details were provided regarding the role of this person.

The Panel noted that it was acceptable for companies to pay health professionals and others for relevant advice. Nonetheless, the arrangements for such meetings had to comply with the Code, particularly Clause 23. To be considered a legitimate advisory board the choice and number of participants should stand up to independent scrutiny; each should be chosen according to their expertise such that they would be able to contribute meaningfully to the purpose and expected outcomes of the advisory board. The number of participants should be limited so as to allow active participation by all. The agenda should allow adequate time for discussion. The number of meetings and the number of participants should be driven by need and not the invitees' willingness to attend. Invitations to participate should state the purpose of the advisory board meeting, the expected advisory role and the amount of work to be undertaken. If an honorarium was offered it should be made clear that it was a payment for such work and advice. Honoraria must be reasonable and reflect the fair market value of the time and effort involved.

The Panel had some concern about the ratio of Gedeon Richter staff to advisors and queried whether gaining the advisors advice and involvement in a promotional symposium was a legitimate business question for an advisory board. The papers referred to the meeting as an advisory board working group meeting. The Panel noted that the agenda included four topics, the experience following the launch of Terrosa (a biosimilar medicine) across Europe. The minutes noting that clinical experience among the working group members had been limited due to reimbursement issues and limitations on prescribing. The second topic was a discussion about guidelines in osteoporosis. These two topics were covered in a session of an hour. The third topic was a two hour session on the organisation of a pan-European event focussed on the early initiation of anabolic treatment and the final topic was 30 minutes on Teriparatide, combination and sequential therapies.

The Panel noted that the complainant had provided no evidence with regard to the appropriateness of the attendees. The Panel noted Gedeon Richter's submission that contrary to the complainant's allegation, there was no presentation on the sales and strategy for the product and no global marketing director attended the advisory board. The Panel noted however that a senior international marketing employee was listed as attending. Whilst the Panel had some concerns about the advisory board in question it did not consider that the complainant had shown on the balance of probabilities that the advisory board was unacceptable as alleged. Based on the allegation the Panel ruled no breach of Clauses 23.1 and consequently no breach of Clause 9.1 and Clause 2.

6 Use of the word 'unique'

COMPLAINT

The complainant noted that an e-detail aid for a new hormone replacement therapy (HRT) spray (Lenzetto (oestradiol)) was currently undergoing approval and described the product as 'unique'. The final signatory had advised that the product should not be described as such but he/she was over-ruled by the UK directors who had instructed the team to have the e-detail aid annotated with a comment to the effect that the decision to use the word 'unique' in relation to the spray delivery was appropriate.

When writing to Gedeon Richter, the Authority asked it to consider the requirements of Clauses 2, 9.1, 14.1 and 7.2.

RESPONSE

Gedeon Richter provided a copy of the Lenzetto sales aid at issue and noted that use of the word 'unique' had been heavily debated during the development of the material. Marketing and medical, in addition to Gedeon Richter's contract signatories had assessed the terminology and considered it to be accurate and fairly represent the product. Gedeon Richter referred to Clause 7.10 and, following its own research to confirm that there were no other HRT spray products, it collectively agreed that the product had a clearly defined special feature and the phrase 'unique spray design' could be used with extra supporting text to reinforce this point. Gedeon Richter noted that Lenzetto had not been determined as superior to other HRT formulations; 'unique' was used to describe the fact that it was currently the only HRT with a spray design. Gedeon Richter considered that this was an accurate, balanced, fair, objective and unambiguous representation of the product delivery.

Gedeon Richter referred to the highlighted section from the sales aid outlined by the complainant.

Gedeon Richter submitted that it was simply not true that signatories were over-ruled or that materials were issued without formal certification. The marketing, medical and final signatories met regularly to discuss jobs but also met *ad hoc* to discuss specific jobs, such as the material now at issue. That process was fully collaborative – when reviewing the wording for the sales aid Gedeon Richter included all the above functions. With the material at issue, Gedeon Richter had consulted the Code, debated the wording, refined the wording and, as a team, agreed the wording. There was no over-ruling of final signatories by UK company directors – Gedeon Richter was proud of its cross-functional working and categorically disagreed with the complainant's account. In fact, there was no discussion between the 'company directors' and the final signatory about the use of the word 'unique'; the final signatory's decision was final. Gedeon Richter provided copies of the sales aid, the approval document, documents detailing comments on previous version of the sales aid and a copy of the Lenzetto SPC.

Addressing the clauses identified:

- Clause 9.1 – Gedeon Richter believed high standards had been met – a thorough review process was performed by its UK medical and commercial signatories and the final item was reviewed and certified by its medical signatory.
- Clause 14.1 – Gedeon Richter had provided a copy of the final item demonstrating certification by its nominated UK signatory.
- Clause 7.2 – Gedeon Richter believed the features of Lenzetto had been represented accurately, fairly and unambiguously, summarising up-to-date evaluations of the available evidence; the claims were valid and not misleading.
- Clause 2 – as described above, the material went through a thorough and rigorous review process by the Gedeon Richter team and the final signatory. Gedeon Richter did not believe that the material or the review process brought discredit upon, or reduced confidence in, the pharmaceutical industry.

Gedeon Richter thus denied breaches of Clauses 9.1, 14.1, 7.2 and 2.

PANEL RULING

The Panel noted Gedeon Richter's submission that it was simply not true that signatories were over-ruled or that materials were issued without formal certification. The Panel noted that Gedeon Richter had provided a copy of the final item for the Lenzetto e-detail aid demonstrating certification by its nominated UK signatory. The Panel therefore ruled no breach of Clause 14.1 and 9.1.

The Panel noted that Clause 7.10 stated that promotion must encourage the rational use of a medicine by presenting it objectively and without exaggerating its properties. Exaggerated or all-embracing claims must not be made and superlatives must not be used except for those limited circumstances where they relate to a clear fact about a medicine. Claims should not imply that a medicine or an active ingredient has some special merit, quality or property unless this can be substantiated. The supplementary information stated that care needed to be taken with the use of 'unique'. Although 'unique' may sometimes be used to describe some clearly defined special feature of a medicine, often it may simply imply a general superiority. In such instances it is not possible to substantiate the claim as the claim itself is so ill defined.

Clause 7.2 which had been raised with the company stated, *inter alia*, that information, claims and comparisons must be accurate, balanced, fair, objective and unambiguous and must be based on an up-to-date evaluation of all the evidence and reflect that evidence clearly. They must not mislead either directly or by implication, by distortion, exaggeration or undue emphasis. The Panel noted Gedeon Richter's submission that following its own research it confirmed that there were no other HRT spray products and therefore Lenzetto had a clearly defined special feature and the phrase 'unique spray design' could be used with extra supporting text to reinforce this point. The Panel further noted Gedeon Richter's submission that Lenzetto had not been determined as superior to other HRT formulations; 'unique' was used to describe the fact that it was currently the only HRT with a spray design and that this was an accurate, balanced, fair, objective and unambiguous representation of the product delivery. The complainant had not provided any evidence to the contrary and the Panel therefore ruled no breach of Clauses 7.2 and 9.1.

The Panel noted its comments and rulings above and consequently ruled no breach of Clause 2.

Complaint received **2 March 20**

Case completed **4 February 2021**