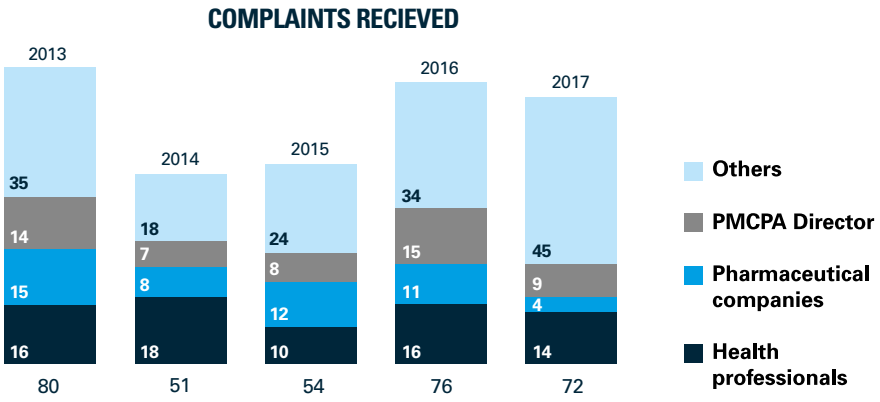
NUMBER 99 February 2018

CODE OF PRACTICE REVIEW

PMCPA | Prescription Medicines Code of Practice Authority

The Prescription Medicines Code of Practice Authority (PMCPA) was established by The Association of the British Pharmaceutical Industry (ABPI) to operate the ABPI Code of Practice for the Pharmaceutical Industry independently of the ABPI. The PMCPA is a division of the ABPI which is a company limited by guarantee registered in England & Wales no 09826787, registered office 7th Floor, Southside, 105 Victoria Street, London SW1E 6QT.

COMPLAINTS IN 2017



In 2017 the PMCPA received 72 complaints, compared with 76 in 2016. There were 54 complaints in 2015, 51 in 2014 and 80 complaints in 2013.

There were 77 cases to be considered in 2017, compared with 100 in 2016 and 66 in 2015. The number of cases usually differs from the number of complaints because some complaints involve more than one company and others, for a variety of reasons, do not become cases at all.

The number of complaints from health professionals in 2017 (14) was more than the number from pharmaceutical companies (both members and non-members of the ABPI) (4). In addition, there were 7 complaints from anonymous health professionals. The more complex cases considered by the Authority are generally inter-company complaints which often raise a number of issues.

Nine complaints were nominally made by the Director, of which 6 arose from voluntary admissions by companies, a substantial decrease on 2016, when there were 13 voluntary admissions. Two arose from criticism in the media and the publication of a study looking at disclosure of clinical trial details led to another.

There were 5 complaints made by employees/ex-employees. One complaint was made by a pharmaceutical physician, 9 were made by a consultant to a company and 4 complaints were from members of the public.

There were 17 anonymous complaints in addition to the 7 from anonymous health professionals. One was from an anonymous employee and one was from an anonymous ex-employee.

The details will be included in the PMCPA 2017 Annual report to be published in due course.

MHRA HOT TOPICS – REVIEW OF THE YEAR 2017

In February 2018 the Medicines and Healthcare products Regulatory Agency (MHRA) published its annual report for 2017 and held a webinar. 'Delivering High Standards in Medicines Advertising Regulation' focussed on highlights of the 2017 Annual Report as well as looking at the wider picture.

Continued overleaf...

PUBLIC REPRIMAND FOR PHARMAMAR

PharmaMar has been publicly reprimanded by the Code of Practice Appeal Board for failing to make any meaningful effort to undertake a thorough investigation and to provide evidence to support its position in relation to being found in breach of the Code for the promotion of Yondelis (trabectedin) for an unlicensed indication. Such an approach raised grave concerns about the importance attached to compliance and self-regulation by the company (Case AUTH/2979/9/17).

In Case AUTH/2979/9/17 the Panel ruled breaches of the Code including Clause 2 as PharmaMar was responsible for a Meeting Highlights document from the 13th annual conference of the British Sarcoma Group (BSG) that promoted Yondelis (trabectedin) for an unlicensed indication. The Panel was extremely concerned about the conduct of senior employees and the lack of procedures for certification and it reported PharmaMar to the Appeal Board.

On consideration of that report the Appeal Board considered that this case raised serious concerns about PharmaMar's processes and Code knowledge. The Appeal Board queried how such a fundamental failure of compliance on what should be well understood principles of the Code could occur. The Appeal Board considered that PharmaMar's investigation into this issue was wholly inadequate. The Appeal Board considered that the level of Code expertise within the company appeared to be very poor given the fundamental errors and the company's apparent lack of preparation for the report.

The Appeal Board also decided to require an audit of PharmaMar's procedures in relation to the Code and to require PharmaMar to issue a corrective statement to all attendees to the BSG conference and its organisers.

Full details of Case AUTH/2979/9/17, including a corrective statement, can be found on the PMCPA website.

CODE OF PRACTICE TRAINING

Training seminars on the Code of Practice, run by the Prescription Medicines Code of Practice Authority and open to all comers, are held on a regular basis in central London.

These full day seminars offer lectures on the Code and the procedures under which complaints are considered, discussion of case studies in syndicate groups and the opportunity to put questions to the Code of Practice Authority.

For dates of the Code of Practice Seminars in 2018 please see the PMCPA website.

Short training sessions on the Code or full day seminars can be arranged for individual companies, including advertising and public relations agencies and member and non member companies of the ABPI. Training sessions can be tailored to the requirements of the individual company.

For further information regarding any of the above, please contact Nora Alexander for details (020 7747 1443 or nalexander@pmcpa.org.uk).

HOW TO CONTACT THE AUTHORITY

Our address is:
Prescription Medicines Code of Practice Authority
7th Floor, Southside, 105 Victoria Street, London SW1E 6QT

www.pmcpa.org.uk

Telephone: 020 7747 8880

Copies of the Code of Practice for the Pharmaceutical Industry and of this Review can be obtained from Lisa Matthews (020 7747 8885 or lmatthews@pmcpa.org.uk).

Direct lines can be used to contact members of the Authority.

Heather Simmonds: 020 7747 1438
Etta Logan: 020 7747 1405
Tannyth Cox: 020 7747 8883
The above are available to give informal advice on the application of the Code of Practice.

The Authority rather than the ABPI is the contact point for information on the application of the Code.

ABPI DIGITAL AND SOCIAL MEDIA WORKSHOP

Members of the Compliance Network were invited to an ABPI workshop held in January 2018 on the challenges and opportunities of digital communications and social media.

Around 140 people from member companies, working across communications, digital, medical and compliance attended the workshop.

The purpose of the workshop was to understand the opportunities for the pharmaceutical industry to use social channels and digital communication. In addition, the current PMCPA guidance was discussed as well as the ABPI Code of Practice.

Case-studies from an agency social media lead, a member company and the PMCPA were presented. This was followed by a lively Q and A and breakout sessions to identify possible changes to the ABPI Code and PMCPA Digital Guidance.

The feedback received will inform further work in this challenging area to help companies understand the impact of the ABPI Code on digital communication.

Anyone is welcome to contact the PMCPA with suggestions or comments.

ABPI EXAMINATIONS FOR REPRESENTATIVES

The ABPI Code of Practice (Clause 16.3) requires representatives (defined in the Code as a representative calling upon members of the health professions and other relevant decision makers in relation to the promotion of medicines) to take an appropriate examination within one year of starting employment as a representative in the promotion of medicines to prescribers, and to pass it within two years.

Despite regular reminders to candidates to book early, the number of requests for extensions to the time allowed to either sit or pass an appropriate examination has increased. It appears that representatives are still not entering for the examinations, or allowing for re-sits, early enough to ensure that they can pass the examination by the end of the second year. It is important that pharmaceutical companies ensure that the requirements in the Code are met.

Information on the requirements of Clause 16 of the ABPI Code of Practice is on the PMCPA website.

You can find more information about the ABPI exams on the ABPI website.

Requests for an extension have to be made to the Director of the PMCPA by completing a form on the PMCPA website.

MHRA HOT TOPICS – REVIEW OF THE YEAR 2017

(Continued from cover)

Review of the Year

There were fewer complaint investigations in 2017 (155) v 2016 (171), which continued a long term downward trend. The two companies that opted out of the PMCPA complaint procedure in 2014 stated that they continued to comply with the ABPI Code requirements. They continued to be monitored by the MHRA, which was still vetting all advertising for one of them.

At the webinar the MHRA referred to its strong support of self regulation and in addition details of the MHRA work on prevetting and cases considered by the MHRA. The PMCPA presented on the role of self regulation and recent cases.

CASE AUTH/2951/4/17

CONSULTANT PHYSICIAN v SANOFI

Promotion of Toujeo

A consultant physician complained about promotion of Toujeo (insulin glargine) by Sanofi. The material at issue presented the outcome of Bailey *et al* 2016 and claimed that Toujeo provided more stable and more evenly distributed steady-state pharmacokinetic/pharmacodynamic (PK/PD) profiles compared with insulin degludec in type 1 diabetes. The interpretation of this data was that Toujeo in clinical practice would significantly reduce the incidence of hypoglycaemia particularly at night in patients with type 1 diabetes. If true this would be a significant clinical benefit.

The complainant stated that he was concerned that Sanofi had over interpreted the data and so he contacted the author of the study who noted that there were two studies comparing Toujeo and Tresiba (insulin degludec marketed by Novo Nordisk). The Sanofi study (Bailey *et al*) investigated 'within-day variability' the fluctuation of the metabolic effect in a treatment interval of 24 hours which (in absolute terms) was lower at a dose of 0.4U/kg, however, no differences were seen at 0.6U/kg. The other study, Heise *et al* investigated day-to-day variability and showed a significantly lower day-to-day variability for Tresiba. Heise *et al* also investigated within-day variability and came to a different conclusion comparing relative within-day variability (fluctuations corrected for the overall metabolic effect) which was higher for Tresiba than for Toujeo.

The author noted that both studies had some limitations however, Heise *et al* had a considerably higher statistical power as it enrolled more patients and did three clamps with either insulin in each individual. The author stated that further analyses was required to better understand the differences between the two studies.'

From this response the complainant considered that the promotional material at issue was at best, significantly incomplete and at worst, intentionally misleading in that it had only selectively quoted from the data.

The detailed response from Sanofi is given below.

The Panel noted that Bailey *et al* was a double-blind cross-over study to compare the steady state pharmacodynamic and pharmacokinetic profiles of Toujeo-300 and degludec-100 with two fixed once-daily dosing regimens (0.4U/kg and 0.6U/kg) in type 1 diabetics over 24 hours. The study authors concluded that Toujeo-300 resulted in less within day variability of the glucodynamic profile vs degludec-100 at a dose clinically relevant for type 1 diabetics (0.4U/kg/day). At the 0.4U/kg dose 6 hour fractions of glucodynamic activity were more evenly distributed over 24 hours with Toujeo-300 versus degludec-100. An overall more stable and more evenly distributed insulin exposure for Toujeo vs degludec-100 over 24 hours was observed in steady state at both dose levels (0.6U/kg/day and 0.4/kg/day). The within day variability of the glucodynamic profile with Toujeo-300 at the 0.6U/kg daily dose was not statistically significant vs degludec. The study authors noted that the potential clinical implications of these findings for people on basal insulin therapy should be evaluated in a larger clinical study.

The Panel noted that whether the presentation of data from a clamp study was acceptable under the Code in relation to any implied clinical benefit depended on the individual circumstances of each case. Care should be taken with such data so as not to mislead as to its significance. The Panel noted the study authors' caveats about the potential clinical implications set out above.

The Panel noted that the data in question was shown to the complainant on an iPad; it was described as the 'Latest Data app' and referenced Bailey *et al* and Bergenstal *et al* (2017) but that two studies were cited only became apparent on close examination. That claims about the PK and PD profile and a reduction in hypoglycaemia were referenced to different studies was not immediately obvious and in the Panel's view the design of the page was such that a reader was invited to link the reduction in hypoglycaemic risk with the flatter and more evenly distributed PK and PD profile. Similar concerns applied to the presentation of data throughout the app.

In the Panel's view, the design and layout of the app was such that readers would associate the findings in Bailey *et al* with the clinical claims about hypoglycaemia. The Panel considered that the material was misleading in this regard as alleged; it implied that the reduction in hypoglycaemic risk was unequivocally attributable to the product's PD and PK profile and that was not so and thus not capable of substantiation. Breaches of the Code were ruled.

The Panel also noted the complainant's allegation that the material was incomplete and misleading as it had selectively quoted from the data. The Panel queried whether the allegation was sufficiently clear: it might be construed as stating that it was not clear that the 0.6U/kg data from Bailey *et al* was not statistically significant, that the daily variation data from Heise *et al* was more clinically relevant and ought to have been included or that its secondary endpoint data of within-day variability ought to have been included or indeed that all of the data from Heise *et al* ought to have been part of the latest data app. The Panel noted that the complainant bore the burden of proof.

The Panel noted the comments made by an author of Bailey *et al* to the complainant: that while Bailey *et al* showed that within-day variability was lower for Toujeo at a dose of 0.4U/kg, no differences were seen at a dose of 0.6U/kg and that Heise *et al* investigated day-to-day variability. According to the complainant the author explained that Heise *et al* showed a significantly lower day-to-day variability for Tresiba but in relation to within-day variability came to a different conclusion (fluctuations corrected for the overall metabolic effect) which was higher for Tresiba than for Toujeo. The Panel noted the author's comment to the complainant about the within-day variability data from Heise *et al* and Bailey *et al* which the Panel considered appeared to be consistent.*

The Panel noted Sanofi's detailed submission about the differences between the two studies and why in its view they were not directly comparable. Sanofi had considered that it would not be able do justice to the discussion of the Heise *et al* study in its promotional material in this instance and could in fact risk confusing readers because in its view Bailey *et al* and Heise *et al* were not directly comparable.

The Panel considered that in principle it was not unacceptable to refer to discrete study results so long as the material overall complied with Code. Context including the nature and purpose of the material was relevant. The Panel noted the author's comment to the complainant about the data in Bailey *et al* and Heise *et al* in relation to within-day variability which the Panel considered were similar.* It also noted its comments above about the nature of the allegation. Noting these points, the Panel did not consider the material incomplete or misleading as alleged and ruled no breach of the Code.

The Panel noted its comments and rulings above with regard to the iPad app at issue and links to clinical benefit. The Panel reviewed the accompanying briefing material and training provided to the representative. The training document when referring to Bailey *et al* stated 'Understand the clinical information on the variability at duration of action data for Toujeo; translate into customer interactions, to strengthen your in call performance'. The following page listed bullet points under the heading 'Commercial relevance' including: 'What are the 3 claims out of this paper - product features?' and 'What are the clinical benefits for your customers and patients? The briefing document presented Bailey *et al* and Bergenstal *et al,* side by side without stating that the results of Bailey *et al* could not be extrapolated to the clinical benefits seen in Bergenstal *et al*. The Panel noted that it was accepted by Sanofi that the representative in question had linked Bailey *et al* to a decreased incidence of hypoglycaemia. The Panel considered that encouraging representatives to identify clinical benefits from Bailey *et al* and failing to instruct them to exercise caution in this regard meant that the material was such that it advocated a course of action likely to breach the Code. A breach of the Code was ruled.

The Panel noted its comments and rulings above and considered that Sanofi had failed to maintain high standards. A breach of the Code was ruled.

[* See post publication note at end of case report]

A consultant physician and community diabetes specialist complained about promotional material for Toujeo (insulin glargine) produced by Sanofi. The material at issue (ref SAGB.TJO.16.12.1140(1)a March 2017) was derived from an abstract (Bailey *et al* 2016) published by the American Diabetes Association entitled 'Insulin glargine 300U/ml [Toujeo] provides more stable and more evenly distributed steady-state PK/PD [pharmacokinetic/pharmacodynamic] profiles compared with insulin degludec in type 1 diabetes'. Toujeo was for the treatment of diabetes mellitus in adults.

COMPLAINT

The complainant noted that Bailey *et al* showed the glucose infusion rate to maintain blood glucose during an insulin clamp following injection of 0.4 units of Toujeo or insulin degludec. The study as presented suggested that there was less variability within the 24 hour period using Toujeo than with insulin degludec and a slightly longer duration of action. The interpretation of this data was that Toujeo in clinical practice would significantly reduce the incidence of hypoglycaemia particularly at night in patients with type 1 diabetes. If true this would be a significant clinical benefit.

The complainant stated that because he was concerned about this data, particularly what he considered to be over interpretation, he contacted the author of the study who replied:

> 'The variability issue is a bit confusing as there are two studies comparing Toujeo and Tresiba (insulin degludec marketed by Novo Nordisk). [Bailey *et al*] investigated "within-day variability" which is just another term for the fluctuation of the metabolic effect in a treatment interval of 24 hours which (in absolute terms) was lower at a dose of 0.4U/kg, however, no differences were seen at 0.6U/kg. [Heise *et al*] was recently published and investigated day-to-day variability which I think is what you are interested in most. It showed a significantly lower day-to-day variability for Tresiba as you might have expected. [Heise *et al*] also investigated within-day variability and came to a different conclusion comparing relative within-day variability (fluctuations corrected for the overall metabolic effect) which was higher for Tresiba than for Toujeo.
>
> Both studies have some limitations as the metabolic effect of 0.4U/kg did not always keep blood glucose during the clamp at target levels (which is a pre-requisite to get meaningful glucose infusion rates as parameter for metabolic action). However, [Heise *et al*] had a considerably higher statistical power as it enrolled more patients and did three clamps with either insulin

in each individual. We are waiting for [Bailey *et al*] to be published, but will probably do further analyses to better understand the differences between the two studies.'

From this response the complainant considered that the promotional material at issue was at best, significantly incomplete and at worst, intentionally misleading in that it had only selectively quoted from the data.

The complainant was concerned that other health professionals who might not have the expertise to investigate these claims further would be misled by this material.

When writing to Sanofi, the Authority asked it to bear in mind the requirements of Clauses 7.2, 7.4, 9.1 and 15.9 of the Code.

RESPONSE

Sanofi stated that its investigation of the complaint identified a call made to the complainant on 4 April 2017 by a representative who was accompanied by his/her area sales manager. Both individuals had submitted reports of their recollection of the call.

The material used in the call was presented from the representative's iPad. A copy of the material at issue was provided. The material had only just been released for use – secondary care representatives were recently trained on the new data and a copy of that training and the briefing document to accompany the material was provided. Given the training provided and the briefing document, Sanofi did not believe that its actions had breached Clause 15.9.

Sanofi explained that Bailey *et al* was a double-blind, cross-over euglycemic clamp study which compared the steady-state PD and PK profiles of insulin glargine-300 with that of insulin degludec-100, in two parallel cohorts, with two fixed once-daily dosing regimens in type 1 diabetics. The study results were presented according to the pre-specified study endpoints and study objectives as officially communicated (clinical.trial.gov) when the study started and before the study results.

The study discussed the PK/PD data of both medicines under a 30 hour clamp at the end of each treatment period and concluded that insulin glargine provided more stable and more evenly distributed steady state PD and PK profiles at a daily dose of 0.4 U/kg, compared with insulin degludec in type 1 diabetics. The poster had been presented at various high quality international and national scientific meetings including Diabetes Technology Society (2016), Advanced Technologies and Treatments for Diabetes (2017) and Association of British Clinical Diabetologists (2017).

The approved Sanofi promotional material was based on discussion from Bailey *et al* and accurately reflected the discussion and conclusion of that study. It included the study design which clearly stated it was conducted to assess variability over 24 hours and informed the reader that this was a euglycemic clamp study and conducted consistent with general gold standard methodology. In addition to results at 0.4U/kg daily dose which favoured insulin glargine 300 unit/ml, it also highlighted that the within-day fluctuation of metabolic activity at doses of 0.6U/kg numerically favoured glargine U300 but the difference vs insulin degludec did not reach statistical significance. Also, it did not refer or suggest any connection between less variability and/or flatter profile and incidence of hypoglycaemia. Bailey *et al* was not designed to measure hypoglycaemia.

Sanofi stated that the material did not comment on the recent Heise *et al* study. Sanofi acknowledged that whilst the title of the two studies might appear similar, the two could not be compared as both looked at different endpoints and used different methodology and study design. The primary endpoint in Bailey *et al* was to assess 'within variability' (fluctuation of the smoothed glucose infusion rate (GIR) curve over 24 hours) with insulin glargine 300 and insulin degludec 100. Whereas the primary endpoint with Heise *et al* was to assess 'between days variability' with insulin glargine-300 and insulin degludec-100. Heise *et al*, however, included within day variability assessment as a secondary endpoint. Injections in Bailey *et al* were given during the morning whilst in Heise *et al* injections were administered in the evening. Bailey *et al* looked at both the pharmacokinetics and pharmacodynamics of the two insulins, whilst Heise *et al* assessed only their pharmacodynamics. Furthermore a smoothing factor of 0.25 was applied to individual GIR curves in Heise *et al* whereas in Bailey *et al* a smoothing factor of 0.15 was applied. All the above differences could potentially lead to different results and thus in Sanofi's view the two studies were designed differently and could not be directly compared. In addition, since Sanofi was not close to the intimate details of the design and statistical plan of Heise *et al* and the analysis in both studies was widely considered as complex therefore it was considered, in this instance, that Sanofi would not be able do justice to discussion of Heise *et al* in this promotional material and in fact could risk confusing the recipient. Sanofi noted that full data from Heise *et al* was in the public domain and accessible to all health professionals, therefore they could form their own opinions on the outcomes of both studies. Sanofi had not attempted to restrict health professionals' opinion on PK/PD data of insulin glargine-300 and insulin degludec-100 to Bailey *et al* only and had no intention of directly or indirectly linking its outcomes with hypoglycaemia.

In conclusion, Sanofi considered that the discussion in its promotional material was neither incomplete nor misleading. The comparisons were accurate, balanced, fair, and based on up-to-date data. Sanofi denied breaches of Clauses 7.2 or 7.4.

As stated above, the investigation into the complaint had included obtaining reports from both the representative and his/her manager regarding the call made to the complainant. The following exert was from the representative's report:

'Firstly, I outlined where the Bailey data was presented, who the main author was, and co-author. I also stated that it had been presented as a poster at the [American Diabetic Association] in Boston in October 2016.

I then went through the study objective and design stating that it was a euglycaemic clamp study and finally the endpoint of the study which I stated was within-day variability.

I was asked about the number of patients in the study which I stated was 48, run in two parallel cohorts at the 0.4 and 0.6U/kg.

I presented him the data showing the PK/PD data for both products. I spoke about mimicking endogenous insulin and asked which line best represented that profile. [The complainant] took the iPad and scrutinised the data, after which he commented that he had expected the lines to be the other way round. He also commented that both products had similar tail off points which was something else he wasn't expecting to see. I stated that this data had bought the two insulins a lot closer than was first thought.

[The complainant] stated that he knew the author very well and that he would telephone him to question the results.

I stated that as a result of the lower PK/PD profile of Toujeo you would expect to see a lower incidence of hypos in type 1 patients.'

The representative then went on to present the other study in the material.

Whilst the initial report from the manager did not mention the representative linking the PK/PD data and a lower risk of hypoglycaemia in type 1 patients, upon asking for clarification the manager stated *'he did talk about "reduced fluctuations may result in a more predictable glucose profile and less hypoglycaemia"'.*

Sanofi concluded upon considering the statements made by the representative carefully in conjunction with reviewing the materials, training and briefing documents, that the representative had acted outside of the training and briefing provided when he/she linked the PK/PD data presented and a potential clinical outcome. As such Sanofi admitted a breach of Clause 15.2 as the representative had failed to maintain high standards.

As a result of the investigation into this complaint, senior managers met to discuss what action should be taken. In the case of the individual concerned disciplinary action had been commenced, which would be progressed using the company's usual disciplinary process. In addition, everyone who had already been briefed on the new material had received a second briefing (copy provided) to reinforce the correct use of the material. Sanofi considered this was a preventative action as it had no evidence to suggest that other representatives had made such incorrect claims.

In conclusion, Sanofi did not consider that it had breached the Code in relation to the clauses specified. However, it did consider that the representative in question had not maintained high standards; the individual and hence the company had breached Clause 15.2.

Further comments from the complainant

In response to a question raised by the Panel the complainant stated that he was shown the data on a laptop as stated by Sanofi and was also offered follow-up printed material which he declined. The complainant stated that Sanofi's submission that he took the iPad and scrutinised the data, after which he commented that he had expected the lines to be the other way round was correct.

Further comments from Sanofi

In response to a request for further information from the Panel about, *inter alia*, the complainant's reference to an abstract Sanofi stated that the Bailey *et al* data was not included in any of its printed material and no printed material was made available to the complainant during the call.

Sanofi also stated that the FAQ handler mentioned in the Winning with Toujeo training slide deck (ref SAGB.TJO.17.02.0144ad) did not exist. According to Sanofi there was a plan to produce a FAQ document but it had not been produced at the time that the original complaint was received. It was decided that a written FAQ document was not sufficient and that field teams required a more in depth briefing of the data. This occurred by way of the updated representative briefing material which was submitted with the original response.

PANEL RULING

The Panel noted the complainant's allegation that the material used by the representative based on Bailey *et al* (2016) suggested that there was less variability within a 24 hour period and a slightly longer duration of action with Toujeo compared with degludec insulin which was interpreted to mean that the use of Toujeo in clinical practice would significantly reduce the incidence of hypoglycaemic episodes, especially at night, and that this over interpreted the data. The complainant, noting the study author's comments, also alleged that the material was incomplete or intentionally misleading.

The Panel noted that Bailey *et al* was a double-blind cross-over euglycemic 30 hour clamp study comparing the steady state pharmacodynamic and pharmacokinetic profiles of Toujeo-300 and degludec-100 with two fixed once-daily dosing regimens(0.4U/kg and 0.6U/kg) in type 1 diabetics over 24 hours. The study authors concluded that Toujeo-300 resulted in less within day variability of the glucodynamic profile versus degludec-100 at a dose clinically relevant for type 1 diabetics (0.4U/kg/day). At the 0.4U/kg dose 6 hour fractions of glucodynamic activity were more evenly distributed over 24 hours with Toujeo-300 versus degludec-100. An overall more stable and more evenly distributed insulin exposure for Toujeo versus degludec-100

over 24 hours was observed in steady state at both dose levels (0.6U/kg/day and 0.4/kg/day). The within day variability of the glucodynamic profile with Toujeo-300 at the 0.6U/kg daily dose was not statistically significant versus degludec. The study authors noted that the potential clinical implications of these findings for people on basal insulin therapy should be evaluated in a larger clinical study.

The Panel noted that whether the presentation of data from a clamp study was acceptable under the Code in relation to any implied clinical benefit depended on the individual circumstances of each case. Care should be taken with such data so as not to mislead as to its significance. The Panel noted the study authors' caveats about the potential clinical implications set out above.

The Panel noted that both parties agreed that the data in question was in a digital format shown to the complainant on the representative's iPad. It was also agreed that the complainant had held the iPad to scrutinise the data. The material in question was described as the 'Latest Data app'. It appeared from the material provided by Sanofi that this app was one of seven autonomous apps available for representatives to use with health professionals on their iPads. The Panel noted that the app in question referenced two studies, Bailey *et al* and Bergenstal *et al* (2017). The Panel queried whether the data from these studies was sufficiently differentiated in the app. It was only on close examination that it was apparent that the data was referenced to two separate studies. For example, the first page headed 'Latest data' featured two prominent adjacent highlighted boxes. The first box was prominently headed 'PK/PD profile' which was described as a flatter and more evenly distributed insulin profile versus Lantus and insulin degludec. The Lantus data within this box was referenced to Bergenstal *et al* and the degludec data to Bailey *et al*. The adjacent box read 'Reducing hypoglycaemic risk vs. Lantus in adults with type 1 diabetes' and was referenced to Bergenstal *et al*. That the claims were referenced to different studies was not immediately obvious and in the Panel's view the design of the page was such that a reader was invited to link the reduction in hypoglycaemic risk with the flatter and more evenly distributed PK and PD profile. Similar concerns applied to the presentation of data throughout the app. The uniform design meant that it was not always immediately clear which study the data derived from. The Panel did not have sight of the original app but on the printed copy it appeared that after the first page described above pages 2-7 cited Bergenstal *et al*, pages 8-10 cited Bailey *et al*, and after a reproduction of the first page (page 11) pages 12 and 13 cited Bergenstal *et al*. Page 12 bore prominent headline claims: 'Reducing hypoglycaemic risk in adults with type 1 diabetes' and showed the annualised risk of nocturnal and severe hypoglycaemia including a relative risk reduction of 55% of Toujeo versus Lantus and the bold strapline 'In people with T1 DM Toujeo was associated with significantly lower annualised rates of nocturnal or severe hypoglycaemic events than Lantus'. The Panel noted that a health professional would normally be taken through the app by a representative but noted that it must nonetheless be capable of standing alone with regard to the requirements of the Code. The Panel also noted that the complainant had held the iPad to independently scrutinise the data.

In the Panel's view, the design and layout of the app, particularly the first page headed 'Latest Data', was such that readers would associate the findings in Bailey *et al*, a clamp study, with the clinical claims about hypoglycaemia. The Panel noted the study authors' caveats in this regard. The Panel also noted Sanofi's submission that Bailey *et al* did not refer to or suggest any connection between less variability or a flatter profile and the incidence of hypoglycaemia and it was not designed to measure this. The Panel considered that the material was misleading in this regard as alleged; it implied that the reduction in hypoglycaemic risk was unequivocally attributable to the product's pharmacodynamic and pharmacokinetic profile as seen in Bailey *et al* and that was not so. Further, such an implication was not capable of substantiation. A breach of Clauses 7.2 and 7.4 were ruled.

The Panel also noted the complainant's allegation that the material was incomplete and misleading as it had selectively quoted from the data. The Panel queried whether the allegation was sufficiently clear: it might be construed as stating that it was not clear that the 0.6U/kg data from Bailey *et al* was not statistically significant, that the daily variation data from Heise *et al* was more clinically relevant and ought to have been included or that its secondary endpoint data of within day variability ought to have been included or indeed that all of the data from Heise *et al* ought to have been part of the latest data app. The Panel noted that the complainant bore the burden of proof.

The Panel noted the comments made by an author of Bailey *et al* to the complainant: that while Bailey *et al* showed that within-day variability was lower for Toujeo at a dose of 0.4U/kg, no differences were seen at a dose of 0.6U/kg and that a recently published study (Heise *et al*) investigated day-to-day variability. According to the complainant the author explained that Heise *et al* showed a significantly lower day-to-day variability for Tresiba but in relation to within-day variability came to a different conclusion (fluctuations corrected for the overall metabolic effect) which was higher for Tresiba than for Toujeo. The Panel noted the author's comment to the complainant about the within-day variability data from Heise *et al* and Bailey *et al* which the Panel considered appeared to be consistent.*

The Panel noted Sanofi's detailed submission about the differences between the two studies and why in its view they were not directly comparable. Sanofi had considered that it would not be able do justice to the discussion of Heise *et al* in its promotional material in this instance and could in fact risk confusing readers because in its view Bailey *et al* and Heise *et al* were not directly comparable.

The Panel considered that in principle it was not unacceptable to refer to discrete study results so

long as the material overall complied with Code. Context including the nature and purpose of the material was relevant. The Panel noted the author's comment to the complainant about the data in Bailey *et al* and Heise *et al* in relation to within-day variability which the Panel considered were similar.* It also noted its comments above about the nature of the allegation. Noting these points, the Panel did not consider the material incomplete or misleading as alleged and ruled no breach of Clause 7.2.

The Panel noted its comments and rulings above with regard to the iPad app at issue and links to clinical benefit. The Panel reviewed the accompanying briefing material and training provided to the representative. The training document (ref SAGB.TJO.17.02.0144ad) when referring to Bailey *et al* stated 'Understand the clinical information on the variability at duration of action data for Toujeo; translate into customer interactions to strengthen your in call performance'. The following page listed bullet points under the heading 'Commercial relevance including: 'What are 3 claims out of this paper-product features?' and 'What are the clinical benefits for your customers and patients?'. The briefing document (ref SAGB.TJO.16.12.1140(1)b) presented the two studies, Bailey *et al* and Bergenstal *et al*, side by side without stating that the results of Bailey *et al* could not be extrapolated to the clinical benefits seen in Bergenstal *et al*. The Panel noted that it was accepted by Sanofi that the representative in question had linked Bailey *et al* to a decreased incidence of hypoglycaemia. The Panel considered that encouraging representatives to identify clinical benefits from Bailey *et al* and failing to instruct representatives to exercise caution in this regard meant that the material was such that it advocated a course of action likely to breach the Code. A breach of Clause 15.9 was ruled.

The Panel noted its comments and rulings above and considered that Sanofi had failed to maintain high standards. A breach of Clause 9.1 was ruled.

*** Post publication note**

Following publication of the original case report, the PMCPA received information from a third party that Heise *et al* 2016 showed that Tresiba had both a lower-day-to-day and within-day variability than Toujeo contrary to the information provided by the complainant. The Panel had not had sight of Heise *et al* 2016. The case report was updated and the third party advised that it was not possible to change the Panel's ruling which was due to a number of factors not only the complainant's reference to the within-day variability data from Heise *et al*. The third party was also advised that it could make its own complaint if it wished.

Complaint received **6 April 2017**

Case completed **12 September 2017**

Post publication note added January 2018

MEDIA/DIRECTOR v BAUSCH & LOMB

Promotion of Emerade

A letter published in The Pharmaceutical Journal entitled 'Superior Shelf-Life of Emerade (adrenaline)' July 2017 was critical of claims made by Bausch & Lomb UK.

In accordance with Paragraph 6.2 of the Constitution and Procedure the matter was taken up as a complaint under the Code. The author of the letter was contacted and was willing to be treated as the complainant.

In the letter at issue, the complainant stated that he/she went into anaphylactic shock after being stung by a wasp and his/her general practitioner suggested that he/she carry an adrenaline auto-injector pen. Emerade was chosen because in addition to having a higher and more realistic dose (500mcg) it had a 30 month shelf-life compared with only 18 months for EpiPen. However, the best the local pharmacist could supply was an Emerade pen with a 13-month shelf-life.

The complainant explained that he/she had exchanged emails with Bausch & Lomb and alleged that '…they just make a big song and dance about how superior in terms of shelf-life [there] product is over Epipen'. The complainant considered that it was nothing more than noise and expected an ethical company to do better.

In response to a request for any additional information from the case preparation manager the complainant provided a time-line of the circumstances which led to the publication of his/her letter in the Pharmaceutical Journal. This included his/her correspondence with Bausch & Lomb (12 January 2017) to ask how to obtain Emerade with a full 30 months shelf-life. As no progress was made the complainant decided to resolve the situation publicly and wrote to the Editor of the Pharmaceutical Journal on 31 January 2017. The letter was published in July 2017.

The complainant stated that whilst writing to the Authority in late August 2017 he/she did a search to look at Bausch & Lomb's claims again because he/she had thrown away the original documentation where 30 months' shelf-life was claimed. To the complainant's surprise the search produced a document headed 'Patient information: Important information for patients using Emerade solution for injection in prefilled pen notification'. A copy was provided and was dated 20 January 2017.

The document stated that the claimed shelf-life of Emerade was to be reduced from 30 months to 18 months from February 2017. The complainant was surprised and equally puzzled how this statement tied up with the note at the end of his/her letter in the Pharmaceutical Journal where the Editor stated 'Bausch & Lomb declined to comment on the allegations made in this letter'. The complainant stated that it sounded like the right hand of Bausch & Lomb did not actually know what the left hand was doing or had done 6 months previously.

The complainant stated that since Bausch & Lomb had changed its shelf-life claims to something more realistic there was little point in pursuing his/her complaint further. The complainant stated that what was clearly wrong had been put right or at least the complainant hoped so because he/she didn't know whether the pharmacist would now be able to get hold of a product with a shelf-life of even 18 months. 13 months was the best he/she could manage last time. It was also unclear to the complainant how patients are or were supposed to know that things had changed. Nobody from Bausch & Lomb contacted the complainant not even when he/she complained publicly. The complainant stated that whilst it was still slightly messy, he/she didn't think there was enough justification for continuing to make a complaint and hoped that the Authority agreed that the obvious and sensible thing to do now was nothing.

The case preparation manager noted Paragraph 15.1 of the Constitution and Procedure that a complainant can withdraw the complaint up until the time that the response is received from the company. As Bausch & Lomb's response had already been received the matter could not be withdrawn.

The detailed response from Bausch was given below.

The Panel noted that the complainant's letter in the Pharmaceutical Journal criticised claims made by Bausch & Lomb about the 30 month shelf-life of Emerade.

No specific materials were identified and the Panel noted the complainant's submission that he/she had thrown away the original documentation where 30 months' shelf-life was claimed. The Panel was unsure what material the complainant had received or which materials had been seen by the complainant's GP or pharmacist.

The Panel noted Bausch & Lomb's submission that prior to 18 January 2017, Emerade had a 30 month shelf-life at the point of manufacture and it used the same wording consistently across its promotional materials, ie 30 months shelf-life at time of manufacture and it did not promote to the public. Bausch & Lomb provided a leavepiece which claimed that with a shelf-life at production of 30 months, Emerade had a 12 month longer shelf-life at production than Jext (18 months) and Epipen (18 months). The leavepiece was certified on 6 January 2016.

The Panel further noted Bausch & Lomb's submission that on 18 January 2017 a variation was approved to amend Emerade's shelf-life to 18 months from date of manufacture and all materials were amended to reflect this. A promotional item provided by Bausch & Lomb with June 2017 as the date of preparation did not include any claims regarding shelf-life. The Panel also noted Bausch & Lomb's submission that the variation to the marketing authorisation on this point was as a consequence of stability testing and was not related to supply to the market as inferred by the complainant.

The Panel noted Bausch & Lomb's submission that the shelf-life was assigned at the point of manufacture. Following product manufacture, there were further processes that needed to be completed prior to Emerade reaching the UK market. The Panel noted Bausch & Lomb's submission that this delay also applied to products with an 18 month shelf-life from manufacture.

The Panel accepted that the complainant was frustrated by his inability to obtain the product with a longer shelf-life as evidenced by the published letter. The Panel, however, did not consider that the complainant had shown, on the balance of probabilities, that claims and information regarding the shelf-life at production provided by Bausch & Lomb was not factual nor presented in a balanced way and was not capable of substantiation. The Panel ruled no breach of the Code.

A letter published in The Pharmaceutical Journal entitled 'Superior Shelf-Life of Emerade' July 2017 was critical of claims made by Bausch & Lomb UK Ltd about Emerade (adrenaline).

In accordance with Paragraph 6.2 of the Constitution and Procedure the matter was taken up as a complaint under the Code. The author of the letter, was contacted and was willing to be treated as the complainant.

COMPLAINT

In the letter at issue, the complainant stated that he/she went into anaphylactic shock after being stung by a wasp last summer. Upon recovering his/her general practitioner suggested that he/she carry an adrenaline auto-injector pen and together they chose Emerade. Emerade was chosen over EpiPen because in addition to having a higher and more realistic dose (500mcg) it had a 30 month shelf-life compared with only 18 months for EpiPen. However, the best the local pharmacist could supply was an Emerade pen with a 13-month shelf-life and the pharmacist was unable to obtain one with a longer shelf-life.

The complainant explained that he/she had exchanged emails with Bausch & Lomb and alleged that '…they just make a big song and dance about how superior in terms of shelf-life [their] product is over Epipen'. The complainant considered that it was nothing more than noise and expected an ethical company to do better.

In a subsequent letter to the Authority the complainant explained that in practical terms his/her inability to get hold of the product with the claimed shelf-life meant that he/she now had the trouble of getting a repeat prescription almost 18 months before needed and more importantly that the NHS would have to fork out another £50 or so prematurely.

In response to a request for any additional information from the case preparation manager to support his/her case, the complainant provided a time-line of the circumstances which led to the publication of his/her letter in the Pharmaceutical Journal. In early August the complainant was stung by a wasp and had a severe anaphylactic reaction. His/her general practitioner prescribed Emerade 500mcg. This preparation was chosen rather than EpiPen because the dose was in line with the BNF recommendations, and the makers, Bausch& Lomb, claimed it had a shelf-life of 30 months.

The complainant stated that his/her pharmacist dispensed the product on 4 August 2016 with an expiry date of 19 September 2017; a remaining shelf-life of 13 months and not the 30 months as claimed by Bausch & Lomb. The complainant complained to the pharmacist who agreed to try to find a replacement product which fitted the claims. The complainant kept the originally dispensed product in case he/she was stung again. Over the next few months the pharmacist tried on several occasions to find a replacement and failed.

By January 2017 the complainant was exasperated by the situation and wrote to Bausch & Lomb (12 January 2017) to ask how to obtain Emerade with a full 30 months shelf-life. The complainant provided his/her correspondence with Bausch & Lomb and noted that no progress was made and so he/she decided that a more productive way to resolve the situation would be to ask some questions publicly and where better than the Pharmaceutical Journal.

The complainant's records showed that he/she wrote to the Editor on 31 January 2017 but the letter was not actually published until months later in July 2017.

The complainant stated that whilst writing to the Authority in late August 2017 he/she did a google search to look at Bausch & Lomb's claims again because he/she had thrown away the original documentation where 30 months' shelf-life was claimed. To the complainant's surprise the search produced a document dated 30 January 2017 headed 'Patient information: Important information for patients using Emerade solution for injection in prefilled pen notification'. A copy was provided and was dated 20 January 2017.

The document stated that the claimed shelf-life of Emerade was to be reduced from 30 months to 18 months from February 2017. The complainant was surprised and equally puzzled how this statement tied up with the note at the end of his/her letter in the Pharmaceutical Journal where the Editor stated 'Bausch & Lomb declined to comment on the allegations made in this letter'. The complainant

stated that it sounded like the right hand of Bausch & Lomb did not actually know what the left hand was doing or had done 6 months previously.

The complainant stated that since Bausch & Lomb had changed its shelf-life claims to something more realistic there was little point in pursuing his/her complaint further. The complainant stated that what was clearly wrong had been put right or at least the complainant hoped so because he/she didn't know whether the pharmacist would now be able to get hold of a product with a shelf-life of even 18 months. 13 months was the best he/she could manage last time. It was also unclear to the complainant how patients are or were supposed to know that things had changed. Nobody from Bausch & Lomb contacted the complainant not even when he/she complained publicly. The complainant stated that whilst it was still slightly messy, he/she didn't think there was enough justification for continuing to make a complaint and hoped that the Authority agreed that the obvious and sensible thing to do now was nothing.

The case preparation manager noted Paragraph 15.1 of the Constitution and Procedure that a complainant can withdraw the complaint up until the time that the response is received from the company. As Bausch & Lomb's response had already been received the matter could not be withdrawn.

In writing to Bausch and Lomb attention was drawn to the requirements of Clauses 7.2 and 7.4.

RESPONSE

Bausch & Lomb stated that as members of the ABPI it took compliance with the Code seriously. Bausch & Lomb submitted that in relation to the complaint, the marketing authorisation holder (MAH) had not breached Clauses 7.2 and 7.4 for the following reasons:

- The clock on expiry started once the chemical compound was manufactured. Subsequently further in-process checks and qualified person (QP) release would need to be performed hence no stock could be made available to the market at 30 months. This was a process, in alignment with all other AAIs and pharmaceutical manufacturers. The marketing authorisation holder could also confirm that it had not received any other complaints of shorter shelf-life following the launch of Emerade.

- The same wording about Emerade's 30 month shelf life was used, consistently ie 30 months at time of manufacture.

- As with all products, the marketing authorisation holder had no control of the supply chain once it left the warehouse.

- The marketing authorisation holder communicated that prior to 18 January 2017 it had a 30 month shelf-life at the point of manufacture for Emerade. Subsequently, the marketing authorisation holder's promotional materials were reviewed as part of a previous complaint, Case AUTH/2796/9/15. The PMCPA ruled no breach of Clauses 7.2 and 7.4.

- On 18 January 2017 a variation was approved to amend Emerade shelf-life to 18 months from date of manufacture and all materials were amended accordingly to reflect this.

- Bausch & Lomb further submitted that it did not promote directly to patients.

Bausch & Lomb concluded that for the reasons above it disagreed that there had been a breach of Clauses 7.2 and 7.4 in this instance.

In response to a request for further information from the case preparation manager, Bausch & Lomb stated that the new summary of product characteristics (SPC) was developed for the application of the variation on 21 September 2016 but was not used until the approval of that variation on 18 January 2017. The old SPC was the one used prior to the final approval.

Bausch & Lomb stated that it had no further comment as it had already stated its position that the 30 month shelf-life was from the date of manufacture and it had no direct control over the supply chain. This was a similar situation with all auto injector manufacturers. The current shelf-life stated was 18 months from manufacture.

In response to the complainant's follow-up letter relating to his/her concerns regarding the claims made prior to the change in shelf-life from 30 months to 18 months, Bausch & Lomb submitted that its material was accurate regarding shelf-life and was consistent with the SPC. Bausch & Lomb submitted that the marketing authorisation holder assigned the 30 months shelf-life at the point of manufacture. Following finished product manufacture, there were further processes that needed to be completed prior to Emerade reaching the UK market.

Bausch & Lomb submitted that it continued to work extensively with its wholesalers to move stock around its depots to keep it as fresh as possible but this could not be achieved at pharmacy level, as the marketing authorisation holder had no control over these consignments.

Bausch & Lomb noted that in September 2016, the marketing authorisation holder submitted a variation on the shelf-life to reduce it to 18 months. This was not related to supply to the market as the complainant inferred but as a consequence of stability testing. Bausch & Lomb submitted that as per regulations it was unable to discuss any proposed changes to an SPC or product variation until full approval to do so and could not misrepresent the current status in its promotional materials. Therefore, the best it could do was advise the complainant that there was stock in the market with a shelf-life of 24 months which the company was aware of as it was his/her question. Bausch & Lomb submitted that arguably some more dialogue could have explained in greater detail the production and release process but the complainant became persistent in his/her request for a pen with a 30 months shelf-life ignoring any explanation the

company was trying to provide. Bausch & Lomb noted that as stated in the complainant's letter, there was a more important reason for the choice of the physician to recommend Emerade as an adult male over 60kgs according to the BNF required a 500mcg dose which could only be found in Bausch & Lomb's range.

Bausch & Lomb submitted that issues with supply chain affected all pharmaceutical products in that manner as a wholesaler would sell stock into the market at up to 6 months as per the Healthcare Distributors Association gold standards of distribution. However, this was not such an issue with a monthly course of treatment perhaps as it was with a product that most likely would not be used in its shelf-life. As to the complainant's request as to where he/she could obtain a product with an 18 months shelf-life, it was an impossible request as per the previous explanation as there was the same 2 to 3 month requirement to complete manufacture prior to release to market. This was consistent with regulations on stating shelf-life in the product dossier and SPC.

PANEL RULING

The Panel noted that the complainant wrote a letter to the Editor of the Pharmaceutical Journal on 31 January 2017 criticising claims made by Bausch & Lomb about the 30 month shelf-life of Emerade. The letter was not published until July 2017.

No specific materials were identified. The Panel noted the complainant's submission that he/she had thrown away the original documentation where 30 months' shelf-life was claimed. The Panel was unsure what material the complainant had received. It appeared that the complainant was a doctor but the Panel was unsure if he/she was a medical doctor that might have received materials directed at health professionals or materials directed to patients who had been prescribed Emerade. The complainant stated that such claims were taken into account when his/her GP decided to prescribe Emerade, rather than EpiPen. It was not known which materials had been seen by the complainant's GP or, indeed, his/her pharmacist.

The Panel noted Bausch & Lomb's submission that prior to 18 January 2017, Emerade had a 30 month shelf-life at the point of manufacture and it used the same wording consistently across its promotional materials, ie 30 months shelf-life at time of manufacture and it did not promote to the public. The Panel noted Bausch & Lomb's submission about Case AUTH/2796/9/15. Bausch & Lomb provided a leavepiece (ref EME-UK-601-002DA) which included a section comparing the shelf-life of Emerade versus Jext and Epipen. The leavepiece claimed that with a shelf-life at production of 30 months, Emerade had a 12 month longer shelf-life at production than Jext (18 months) and Epipen (18 months). The leavepiece was certified on 6 January 2016.

The Panel further noted Bausch & Lomb's submission that on 18 January 2017 a variation was approved to amend Emerade's shelf-life to 18 months from date of manufacture and all materials were amended to reflect this. A promotional item provided by Bausch & Lomb (ref EME-UK-1706-004DA) with June 2017 as the date of preparation did not include any claims regarding shelf-life. The Panel also noted Bausch & Lomb's submission that the variation to the marketing authorisation on this point was as a consequence of stability testing and not related to supply to the market as inferred by the complainant.

The Panel noted Bausch & Lomb's submission that the marketing authorisation holder assigned the shelf-life at the point of manufacture. Following product manufacture, there were further processes that needed to be completed prior to Emerade reaching the UK market. The Panel noted Bausch & Lomb's submission that this delay also applied to products with an 18 month shelf-life from manufacture.

The Panel accepted that the complainant was frustrated by his inability to obtain the product with a longer shelf-life as evidenced by the published letter. The Panel, however, did not consider that the complainant had shown, on the balance of probabilities, that claims and information regarding the shelf-life at production provided by Bausch & Lomb was not factual nor presented in a balanced way and was not capable of substantiation. The Panel ruled no breach of Clauses 7.2 and 7.4.

During its consideration of this case, the Panel noted Bausch & Lomb's submission that whilst the marketing authorisation holder submitted a variation on the shelf-life to reduce it to 18 months in September 2016, the company was unable to discuss any proposed changes to an SPC or product variation until full approval had been granted (which was on 18 January 2017) and could not misrepresent the current status in its promotional materials as per regulations. The Panel considered that, as acknowledged by Bausch & Lomb, it could have explained in greater detail the production and release process to the complainant. The Panel also queried why Bausch & Lomb had not written back to the complainant once approval was granted or when the document headed 'Patient information: Important information for patients using Emerade solution for injection in prefilled pen notification' and dated 20 January 2017 was published considering the complainant had first written to Bausch & Lomb on 12 January 2017. The Panel also queried whether it was appropriate to include claims about a 30 month shelf-life in materials when the company was aware of stability issues before the variation was granted. The Panel had no information about the stability issues. This was not the subject of complaint and the company had not been asked to respond to this point. The Panel asked that Bausch & Lomb be advised of its views in this regard.

Complaint received **8 August 2017**

Case completed **14 December 2017**

CASE AUTH/2972/8/17

ANONYMOUS, NON-CONTACTABLE HEALTHCARE JOURNALIST v UCB

UCB website

An anonymous, non-contactable complainant who stated that he/she was a healthcare journalist submitted a complaint about the UCB Pharma website. The complainant provided annotated screenshots. There were four allegations.

Firstly, the complainant alleged that the section labelled 'UCB's product list' stated that this information was 'specific to the UK'. However, it mentioned several products that were not part of UCB UK's portfolio.

The complainant alleged that inaccurate, misleading information about prescription only medicines was provided to the public (ie by placing on a website freely available to the public) and high standards had not been maintained.

The detailed response from UCB is given below.

The Panel noted UCB's submission that the available product list on its website was published as proactive reference information directed to a public audience. The Panel considered that the list in question was neither factual nor accurate and was thereby misleading. Breaches of the Code were ruled.

The Panel noted that the website listed 19 products that were no longer marketed by UCB but were, according to UCB, still available in the UK from other manufacturers. The Panel considered that, as acknowledged by UCB, its poor governance of the website meant that high standards had not been maintained and a breach was ruled.

Secondly, the complainant alleged that ten items were not recertified after two years, as required by the Code. High standards had not been maintained.

The Panel noted UCB's submission that in relation to the materials listed by the complainant posted in the 'Therapy area' section of its website, none had been re-certified after two years. The Panel ruled a breach of the Code in relation to each of the 10 items.

The Panel noted that a robust certification procedure underpinned self-regulation. The Panel considered that UCB's failure to review and re-certify material aimed at the public or patients meant that it had failed to maintain high standards. A breach of the Code was ruled.

The Panel noted that the educational materials listed had all been certified in advance between August and October 2012 and the Panel ruled no breach of the Code in this regard.

Thirdly, the complainant referred to three separate press releases on Briviact (brivaracetam) January 2016; July 2016, October 2016 and alleged that each had a 'black triangle' which was a requirement for promotional materials only (as required by Clause 4.10 of the Code). Press releases by definition should be non-promotional and hence would not require black triangles. The complainant pointed out that when one clicked on the links to read the press releases, the triangles actually appeared 'orange coloured!' The complainant alleged that high standards had not been maintained.

The Panel noted UCB's submission that the press releases were non-promotional and informed the intended audience of medical, trade and consumer journalists about the availability of Briviact (brivaracetam) in the NHS.

The Panel noted that material which related to a medicine and which was intended for patients taking a medicine which was subject to additional monitoring, an inverted black equilateral triangle must be included on it together with a statement about additional monitoring and reporting of side-effects. The Panel noted that contrary to the complainant's view, it was not only promotional material that required the inclusion of a black triangle. The Panel ruled no breach of the Code as it considered that the press releases were not specifically intended for patients taking the medicine.

The Panel considered that although there was no requirement to include the black triangle within press releases, its inclusion and accompanying explanatory text was, nonetheless, a prudent approach given the intended audience of medical, trade and consumer journalists and that it was likely that the journalists would ultimately disseminate the information to health professionals and members of the public.

The Panel noted that the inclusion of the inverted black triangle on press releases was not a Code requirement. In the Panel's view, it was a well-known and established symbol. Its appropriate use was an important part of medicines regulation. Thus, in the Panel's view, irrespective of the fact that its presence was not a Code requirement, the failure to publish the triangle in the correct colour across three press releases was, at the very least, inappropriate and might potentially cause confusion. The Panel also noted the complainant's comment that the company had not been meticulous or thorough enough to check whether the triangles were the required colour. High standards had not been maintained. A breach of the Code was ruled.

Finally, the complainant queried whether anyone at UCB checked and kept an eye on its website.

The Panel noted its rulings and comments above. The Panel noted the number of materials intended for patients which had not been correctly re-certified and the number of products that were incorrectly listed on its website. In the Panel's view, a robust certification procedure underpinned self-regulation. It was of concern that UCB only became aware of such matters on notification of the complaint rather than as a result of its own compliance oversight. The company's compliance failure in relation to these matters was compounded by the fact that they appeared to be longstanding; the earliest educational item was dated August 2012 and therefore ought to have been the subject of re-certification on two occasions. This was unacceptable, particularly in relation to materials directed at the general public including patients. No adequate explanation for the errors had been provided. The Panel considered that UCB's failure to review and re-certify materials aimed at the public or patients and the poor governance of its website which appeared to be longstanding meant that it had brought the industry into disrepute. A breach of Clause 2 was ruled.

An anonymous, non-contactable complainant who stated that he/she was a healthcare journalist submitted a complaint about the UCB Pharma Ltd website. The complainant provided annotated screenshots.

1 Product list

COMPLAINT

The complainant alleged that the section labelled 'UCB's product list' stated that this information was 'specific to the UK'. However, it mentioned several products that were NOT part of UCB UK's portfolio.

The complainant alleged that this was in breach of Clause 7.2 as information about medicines was inaccurate and misleading, Clause 26.2 as misleading information about prescription only medicines was provided to the public (ie by placing on a website freely available to the public) and Clause 9.1 as high standards had not been maintained.

The complainant provided the product list printed from UCB's website on 1 August 2017.

RESPONSE

UCB acknowledged that the product list available on the UCB UK website (www.ucbpharma.co.uk) was not up-to-date. From the list published on the website, products currently available from UCB in the UK were: Cimzia (Certolizumab pegol), Coracten (SR and XL) (Nifedipine), Dioctyl (Docusate sodium), Ethinyloestradiol (Ethinyloestradiol), Keppra (Levetiracetam), Neupro (Rotigotine), Nootropil (Piracetam), Moexipril hydrochloride, Tylex (Codeine phosphate hemihydrate), Vimpat (Lacosamide), Viridal (Alprostadil), Xyrem (Oxybate sodium), Xyzal (Levocetirizine dihydrochloride) and Zirtek (Cetirizine hydrochloride).

The products no longer marketed by UCB but available in the UK from other manufacturers were: Deponit (Glyceryl trinitrate), Olsalazine sodium, Elantan LA (Isosorbide mononitrate), Isosorbide Mononitrate Tablets (Isosorbide mononitrate), Isoket (Isosorbide dinitrate), Isoket Retard (Isosorbide dinitrate), and Minijets portfolio: Amiodarone Injection Minijet (Amiodarone hydrochloride), Atropine Injection BP Minijet (Atropine Sulphate), Calcium Chloride Injection Minijet (Calcium Chloride dehydrate), Epinephrine (Adrenaline) Injection Minijet (Adrenaline (Epinephrine hydrochloride), Furosemide Injection BP Minijet (Furosemide), Glucose Injection BP Minijet (Glucose), Lidocaine Hydrochloride Injection BP Minijet (Lidocaine), Magnesium Sulphate BP Minijet (Magnesium Sulphate), Morphine Sulphate Injection BP Minijet (Morphine Sulphate), Naloxone Hydrochloride Injection, Minijet (Naloxone), Sodium Bicarbonate Injection BP Minijet (Sodium Bicarbonate), Nitrocine (Glyceryl trinitrate) and Hydroxyzine hydrochloride.

UCB acknowledged that this inaccuracy was an oversight and confirmed that the page had been removed from the website for further review. However, the only information available for each product was the brand name (if available), generic name and main indication, with a clickable link to the electronic medicines compendium (eMC) website. UCB recognised that in some instances the link was not working (resulting in no results returned from the eMC website), however, this did not constitute misleading information with respect to the safety of the product or success of the treatment (Clause 26.2). UCB had no intent to raise public interest in a medicine which would be available at a later stage or conversely medicines no longer available in the UK from UCB. UCB therefore refuted a breach of Clause 26.2. UCB also disagreed with the complainant that Clause 7.2 applied to the available product list on this website as the list was published as proactive reference information directed to a public audience, therefore covered under the requirement of Clause 26.2.

Nevertheless, considering that better oversight could have been maintained, UCB accepted a breach of Clause 9.1.

PANEL RULING

The Panel noted that Clause 26.2 stated that information about prescription only medicines which was made available to the public either directly or indirectly must be factual and presented in a balanced way. It must not raise unfounded hopes of successful treatment or be misleading with respect to the safety of the product. Statements must not be made for the purpose of encouraging members of the public to ask their health professional to prescribe a specific prescription only medicine.

The Panel noted that the supplementary information to Clause 26.2 allowed companies to make available reference information to provide a comprehensive

up-to-date resource on their websites or by way of a link from their website or by some other means. The primary purpose of reference information was to be a library resource for members of the public giving information relating to prescription only medicines which have marketing authorizations.

The Panel noted that as stated in the supplementary information to Clause 26.2 the requirements of Clause 7 relating to information (including Clause 7.2) also applied to information to the public. Clause 7.2 stated that Information, claims and comparisons must be, *inter alia*, accurate, balanced, fair and objective. They must not mislead either directly or by implication.

The Panel noted UCB's submission that the available product list on its website was published as proactive reference information directed to a public audience. The Panel considered that the list in question was neither factual as required by Clause 26.2, nor accurate as required by Clause 7.2 and the list in question was thereby misleading. Breaches of Clauses 7.2 and 26.2 were ruled accordingly.

The Panel noted that the website listed 19 products that were no longer marketed by UCB but were, according to UCB, still available in the UK from other manufacturers. The Panel considered that, as acknowledged by UCB, its poor governance of the website meant that high standards had not been maintained and a breach of Clause 9.1 was ruled.

During its consideration of this matter the Panel was concerned to note that in some instances the clickable links from the product list to the electronic medicines compendium (eMC) website were not working resulting in no results being returned from the eMC website. The Panel considered that if links were provided they should work and considered that this might be seen as another example of poor governance. The complainant had not directly raised this point. Nonetheless, the Panel requested that UCB be advised of its concerns.

2 Educational materials

COMPLAINT

The complainant alleged that materials on the website did not meet the certification requirements in the Code. The materials were:

1 Parkinson's disease factsheet – UK/12NE0077, September 2012
2 Parkinson's disease fast facts – UK/12NE0077a, August 2012
3 Epilepsy factsheet – UK/12VPE0061, October 2012
4 Epilepsy fast facts – UK/12VPE0061a, October 2012
5 Lupus factsheet – UK/12CI0090, October 2012
6 Lupus fast facts – UK/12CI0090, October 2012
7 Restless legs syndrome factsheet – UK/12NE0079, October 2012
8 Restless legs syndrome fast facts – UK/12NE0079a, October 2012
9 Rheumatoid Arthritis factsheet – UK/12CI00787, October 2012
10 Rheumatoid Arthritis fast facts – UK/12CI00787a, October 2012.

Clause 14.5 of the Code clearly stated that material which was still in use must be recertified at intervals of no more than two years to ensure that it continued to conform with the relevant regulations relating to advertising and the Code.

As such, all ten items were alleged to be in breach of Clause 14.5 as none had been recertified after two years, as required by the Code. Ten separate breaches of Clause 14.5 were alleged. Also, by failing to certify after 2014, the complainant alleged that UCB had failed to maintain high standards in breach of Clause 9.1.

In addition, the case preparation manager had cited Clause 14.3 of the Code.

RESPONSE

UCB submitted that in relation to the materials listed by the complainant posted in the 'Therapy area' section of the UCB website, it accepted a breach of Clause 14.5 as the material had not been re-certified after two years. UCB also accepted a breach of Clause 9.1, as the company had failed to maintain high standards. All the materials were immediately withdrawn from the website.

PANEL RULING

The Panel noted that Clause 14.5 required, *inter alia*, that material which was still in use must be recertified at intervals of no more than two years to ensure that it continued to conform with the relevant regulations relating to advertising and the Code. The Panel noted UCB's submission that in relation to the materials listed by the complainant posted in the 'Therapy area' section of its website, none had been re-certified after two years. The Panel ruled a breach of Clause 14.5 in relation to each of the 10 items listed by the complainant.

The Panel noted that a robust certification procedure underpinned self-regulation. The Panel considered that UCB's failure to review and re-certify material aimed at the public or patients meant that it had failed to maintain high standards. A breach of Clause 9.1 was ruled.

The Panel noted that Clause 14.3 required that certain items be certified in advance in a manner similar to that provided for by Clause 14.1. This included materials for the public or patients issued by companies which related to diseases or medicines but was not intended as promotion for those medicines. The Panel noted that the educational materials listed above had all been originally certified in advance between August and October 2012 and the Panel ruled no breach of Clause 14.3. That the original certification was lapsed was covered by the Panel's ruling of a breach of Clause 14.5 above.

3 Press releases

COMPLAINT

The complainant referred to three separate press releases on Briviact (brivaracetam) January 2016 – UK/15BRV0015b(1); July 2016 – UK/15BRV0015q,

October 2016 – UK/15BRV0015r and alleged that each had a 'black triangle' which was a requirement for promotional materials only (as required by Clause 4.10 of the Code). Press releases by definition should be non-promotional and hence would not require black triangles. The complainant pointed out that interestingly, when one clicked on the press release links to read the press releases, the triangles actually appeared 'orange coloured!' The complainant stated that this further confirmed his/her belief that UCB was either not well versed in the Code requirements or just not meticulous or thorough enough to check if the triangles were of the required colour. The complainant alleged that high standards had not been maintained.

When writing to UCB the Authority asked it to bear in mind the requirements of Clauses 14.3 and 26.3 of the Code in addition to Clause 9.1 which applied to the complainant's allegation that high standards had not been maintained.

RESPONSE

UCB submitted that the press releases were examined as per Clause 14.3 in a word format that was then subsequently used as PR material. In the examined version, in which the content was the same but the final layout different from that published on the website, the black triangle was the correct colour and adjacent to the first mention of the product. When the press release was published on the UCB UK website, the colour of the black triangle in the title changed to orange. UCB recognised that this inconsistency should have been detected and appropriate actions taken to remedy it. Following receipt of this complaint, the root cause of this technical issue had been identified and immediate remedial steps were underway to prevent this from happening in the future.

The complainant was also contesting the use of the black triangle in non-promotional material such as press releases, as it was not specifically mandated in Clause 4.10 of the Code. UCB submitted that the brivaracetam non-promotional press releases were directed to inform the intended audience of medical, trade and consumer journalists on the availability of Briviact (brivaracetam) in the NHS. As the intended audience were journalists familiar with the meaning of the black triangle, UCB considered it appropriate to include this with the following note:

> 'Note: ▼ The black triangle symbol applies to all new medicines and means that it is subject to additional monitoring by the European Medicines Agency. This allows for quick identification of new safety information. http://www.ema.europa.eu/ema/index.jsp?curl=pages/special_topics/document_listing/document_listing_000365.jsp.'

In addition, the use of the black triangle was noted by the MHRA when UCB submitted the initial version of job bag UK/15BRV00015b(1) as part of the national press release for vetting and this was not commented on as being inappropriate. Moreover, the press release was not intended for patients taking the medicine, therefore UCB did not accept that Clause 26.3 applied.

PANEL RULING

The Panel noted that the case preparation manager had raised Clause 14.3 and UCB had responded to this Clause in relation to the press releases. Noting the layout of the complaint, the Panel did not consider that the complainant's comment 'I wonder whether there is anyone in UCB who checked and kept an eye on its UK website' was a discrete allegation about the press releases. All of the allegations about specific materials were in indented paragraphs. The statement in question was a separate full paragraph which the Panel considered applied to the governance of the website generally rather than approval of the press releases. The Panel considered the complainant's comment under point 4 below in relation to Clause 2.

The Panel noted UCB's submission that the press releases were non-promotional and informed the intended audience of medical, trade and consumer journalists about the availability of Briviact (brivaracetam) in the NHS.

The Panel noted that Clause 26.3 covered material which related to a medicine and which was intended for patients taking that medicine and required, *inter alia*, that when the material related to a medicine which was subject to additional monitoring, an inverted black equilateral triangle must be included on it together with a statement about additional monitoring and reporting of side-effects. The Panel noted that contrary to the complainant's view, it was not only promotional material that required the inclusion of a black triangle.

The Panel considered that as the press releases were not specifically intended for patients taking the medicine Clause 26.3 did not apply and the Panel ruled no breach of that clause.

The Panel considered that although there was no requirement to include the black triangle within press releases, its inclusion and accompanying explanatory text was, nonetheless, a prudent approach given the intended audience of medical, trade and consumer journalists and that it was likely that the journalists would ultimately disseminate the information to health professionals and members of the public.

The Panel noted UCB's explanatory text:

> '▼ The black triangle symbol applies to all new medicines and means that it is subject to additional monitoring by the European Medicines Agency. This allows for quick identification of new safety information.'

The Panel noted UCB's submission that the black triangle was black when the press releases were examined but when published on the UCB UK website, the colour of the black triangle in the title changed to orange. The Panel also noted that, albeit somewhat belatedly and apparently on receipt of the complaint, UCB had identified the root cause of this technical issue.

The Panel noted that the inclusion of the inverted black triangle on press releases was not a Code requirement. Its use in promotional material reflected an agreement between the ABPI and the then Committee on Safety Medicines. In the Panel's view, it was a well-known and established symbol. Its appropriate use was an important part of medicines regulation. Thus, in the Panel's view, irrespective of the fact that its presence was not a Code requirement, the failure to publish the triangle in the correct colour across three press releases was, at the very least, inappropriate and might potentially cause confusion. The Panel also noted the complainant's comment that the company had not been meticulous or thorough enough to check whether the triangles were the required colour. High standards had not been maintained. A breach of Clause 9.1 was ruled.

During its consideration of this case the Panel noted that the final layout of the beginning of the version published on the website as provided by the complainant was different to that in the examined version. The published version had therefore never been examined in relation to the requirements of the Code. The Panel asked that UCB be advised of its concerns.

4 Summary

COMPLAINT

The complainant queried whether anyone at UCB checked and kept an eye on its website.

UCB was asked to respond to Clause 2.

RESPONSE

UCB recognised that the company should have maintained better oversight of the content of the website and therefore accepted a breach of Clause 9.1, as high standards had not been maintained.

UCB submitted that it took these findings very seriously and was committed to immediately rectifying the situation and had already:

- removed all the materials referenced in the complaint from the live website
- reviewing the full website and would correct any further inconsistency if identified
- UCB had identified potential root causes that led to this breach and was reviewing internal procedures.

In summary, UCB, while fully accepting this situation, submitted that it did not consider a breach of Clause 2 should be ruled, as the issues identified were not such to bring discredit upon, or reduce confidence, in the entire pharmaceutical industry and in no circumstances, was patient safety compromised. While the product list was inaccurate, those products no longer marketed by UCB were available through different manufacturers and UCB would have directed any enquiries to the appropriate source if contacted on the availability of such a product.

PANEL RULING

The Panel noted its rulings and comments above. The Panel noted the number of materials intended for patients which had not been correctly re-certified and the number of products that were incorrectly listed on its website. In the Panel's view, a robust certification procedure underpinned self-regulation. It was of concern that UCB only became aware of such matters on notification of the complaint rather than as a result of its own compliance oversight. The company's compliance failure in relation to these matters was compounded by the fact that they appeared to be longstanding; the earliest educational item was dated August 2012 and therefore ought to have been the subject of re-certification on two occasions. This was unacceptable, particularly in relation to materials directed at the general public including patients. No adequate explanation for the errors had been provided. The Panel considered that UCB's failure to review and re-certify materials aimed at the public or patients and the poor governance of its website which appeared to be longstanding meant that it had brought the industry into disrepute. A breach of Clause 2 was ruled.

Complaint received **21 August 2017**

Case completed **19 December 2017**

ANONYMOUS CLINICIAN v ViiV HEALTHCARE

Alleged promotion to the public

An anonymous non contactable clinician complained about the ViiV Healthcare International Aids Society (IAS) Webinar. The complainant appeared to be a pharmacist.

ViiV's product Tivicay (dolutegrivir) was indicated in combination with other anti retroviral medicines for the treatment of Human Immunodeficienty Virus (HIV).

The complainant stated that he/she took part in Viiv's live 'online' meeting which was mostly about dolutegrivir. The complainant was surprised to see an HIV patient on the stage with the ViiV doctors whilst they discussed their prescription products. The patient appeared to be giving a silent blessing for dolutegrivir. Further, the prescribing information for dolutegrivir was not easily available via a single click.

The complainant stated that ViiV did not appear to know the requirements of the Code which was not good for the industry profile, reputation or regulation. The complainant alleged that ViiV's standards were not high enough. Having the patient on stage looked like the thumbs up for ViiV's medicines which was not good for trust and the confidence in the industry. The complainant referred to Clause 2.

The detailed response from ViiV is given below.

The Panel noted that the meeting invitation clearly stated that two speakers from ViiV would present data on dolutegravir and a third speaker would present the results of a patient survey. The survey highlighted key global trends about the emotional support people living with HIV received.

According to the transcript the speaker did not mention ViiV's product or indeed any other product but he/she was presenting at a meeting where data on Tivicay was discussed in detail.

The Panel considered that in the particular circumstances of this case, contracting the expert to discuss his/her research into the impact of HIV on patients at a meeting where medicines were promoted, did not mean that a prescription only medicine had been promoted to the public. This speaker's expertise would be of interest and in this situation he/she was not a member of the public *per se*. In that regard, the Panel ruled no breach of the Code.

The Panel noted ViiV's submission that the prescribing information was included in the invitation, available on demand during the Webinar via four clicks as well as being shown on the slides for nearly four minutes during the Q&A session. The prescribing information was supplied and thus the Panel ruled no breach of the Code.

Given its rulings above the Panel did not consider that ViiV had failed to maintain high standards as alleged nor had it brought discredit upon or reduced confidence in the pharmaceutical industry. The Panel ruled no breach including of Clause 2.

An anonymous non contactable clinician complained about the ViiV Healthcare International Aids Society (IAS) Webinar filmed live in Paris on 27 July 2017. The complainant appeared to be a pharmacist.

ViiV's product Tivicay (dolutegrivir) was indicated in combination with other anti retroviral medicines for the treatment of Human Immunodeficienty Virus (HIV).

COMPLAINT

The complainant stated that he/she was an HIV positive clinician working with NHS patients who also had HIV. The complainant was also in a company doing research into medicines for very difficult infections.

The complainant stated that he/she took part in a meeting with colleagues at lunch time before busy clinics. The meeting was live 'online' by ViiV from the IAS conference in Paris. It was mostly about dolutegrivir [ViiV Healthcare's product Tivicay] to treat HIV/AIDS. The complainant was surprised to see an HIV patient on the stage with the ViiV doctors whilst they discussed their prescription products. The patient appeared to be giving a silent blessing for dolutegrivir. In the complainant's view the patient did not have to be there all the time and should have talked first and then left or come in at the end to discuss her patient project. It did not look right for him/her to sit there all the time. The complainant knew that companies were not to talk to patients about prescription medicines but it happened here. The complainant stated that he/she and his/her colleagues discussed the matter and many were unhappy that the patient had been continually present and in that regard he/she referred to Clause 26.1.

The complainant stated that in his/her company he/she was learning to give UK medicines information too, including digitally. In that regard the complainant noted that Clause 4.4 stated that prescribing information had to be accesible via a single click for easy access. Buttons onscreens for ViiV's medicines did not work in a click away so it was very difficult with colleagues getting annoyed when clicking continued. The prescribing information for dolutegrivir was not easily available. The complainant referred to Clause 4.1.

The complainant stated that ViiV did not appear to know the requirements of the Code which was not good for the industry profile, reputation or regulation. The complainant alleged that ViiV's standards were not high enough and referred to Clause 9.1 The patient on stage looked like the thumbs up for ViiV's medicines. This was not good for trust and the confidence in the industry. Companies needed the credit so that people, even the pharmacist with HIV could be sure of their safety in them. The complainant referred to Clause 2.

RESPONSE

ViiV stated that it took its responsibilities under the Code very seriously, and was concerned that a health professional considered that it might have breached the Code by promoting to the public and not providing prescribing information correctly. The company refuted the allegations.

In response to the individual being present during the webinar, ViiV provided copies of contractual documents outlining the panellist's professional role on the panel. The panel member was employed as an expert and author on the research he/she was presenting and did not discuss or endorse dolutegravir at any point; he/she also formed part of the panel to answer questions from the audience and ViiV panellists at the end of the webinar. The questions asked related to the presented paper in light of his/her specific experience and expertise and were contained to these parameters.

ViiV submitted that in this capacity, he/she was not a patient, or a member of the public, but was a *bona fide* panellist in his/her own right as an author and steering committee member of the study with significant expertise and experience. Details were provided. ViiV thus considered that this vast experience in HIV made him/her an expert in that area and an appropriate panel member.

As such, the panellist concerned was contracted as an expert and was at the presentation in that capacity rather than as a patient, or a member of the public.

With regard to Clause 4.1, ViiV submitted that the UK prescribing information was available via 3 routes, the first of which alone the company considered satisfied Clause 4.1:

1 The prescribing information was integral and included in the presentation, shown for 3 minutes and 53 seconds during the question and answer section at the conclusion of the webinar;
2 The prescribing information was embedded and included in email and print invitations, (copies provided);
3 On-demand prescribing information was available for the entire webinar via 4 clicks: one to scroll, one to select prescribing information, one to press the download button in Adobe and one to click the 'click to download' (screen shots were provided).

ViiV recognized 4-click-access might cause frustration and it was working to reduce the number of clicks.

ViiV referred to Case AUTH/2931/1/17 in which the Panel noted that in relation to presentations delivered at a meeting:

> 'It was an established principle that prescribing information for a presentation should either be part of it or be otherwise available to each delegate, a leave piece provided to each delegate would suffice in this regards. If prescribing information formed part of the presentation in the absence of alternative formats, it should be displayed such that the audience had sufficient time to consider it ….'

With the above in mind, ViiV did not consider that it had breached Clauses 4.1 or 26.1 and therefore it was not in breach of Clauses 9.1 or 2 for failing to meet high standards or for reducing confidence in the industry.

ViiV stated that invitations to the meeting were sent by email and in print via the local ViiV representative and also hosted on the ViiV exchange website. One external UK health professionals watched the meeting online and no health professionals attended the meeting in person. Each attendee was verified as a health professional. The meeting was not available to view online after the event.

ViiV Healthcare UK was closely involved in the organization of the webinar and was aware of the speakers and the subject of the presentation from the initial meetings with its global colleagues. The UK attended calls every two weeks in the run up to the webinar, and provided the up-to-date prescribing information that was displayed on the slides and in the link during the webinar. The UK also certified the print and email invitations. The slides were certified by the global team who were ABPI signatories, but had been reviewed by a UK ABPI signatory via email before final certification.

ViiV submitted that the panellist in question was briefed twice before the webinar. Briefings were face-to-face with the medical team, and included a slide by slide run-through on what he/she would say and which questions would likely be directed to him/her at the end. These questions would be those related to his/her presented paper.

ViiV provided a video link to the webinar together with a transcript of what was said.

PANEL RULING

The Panel noted that the invitation clearly stated that two speakers from ViiV would present data on dolutegravir. A third speaker would present the results of a patient survey. The survey highlighted key global trends about the emotional support people living with HIV received.

The Panel considered that it was not necessarily unacceptable under the Code for pharmaceutical companies to include patients or members of the public as speakers at meetings where medicines were discussed. Much would depend on the circumstances.

The Panel noted that the speaker in question was presenting data from a patient survey and was a member of the study's steering committee. In addition the speaker had broad experience in HIV. According to the transcript this speaker did not mention ViiV's product or indeed any other product but he/she was presenting at a meeting where data on Tivicay was discussed in detail.

The Panel considered that in the particular circumstances of this case, contracting the expert to discuss his/her research into the impact of HIV on patients at a meeting where medicines were promoted, did not mean that a prescription only medicine had been promoted to the public. This speaker's expertise would be of interest and in this situation he/she was not a member of the public *per se*. In that regard, the Panel ruled no breach of Clause 26.1.

The Panel noted ViiV's submission that the prescribing information was included in the invitation, available on demand during the Webinar via four clicks as well as being shown on the slides for nearly four minutes during the Q&A session.

The Panel noted that the meeting was a Webinar and in that regard it queried whether the provision of prescribing information was covered by Clause 4.4 or Clause 4.5 of the Code. Neither clause specifically referred to Webinars. Clause 4.4 referred to advertisements in electronic journals, emails, electronic detail aids and such like whereas Clause 4.5 referred to audio visual materials such as films, DVDs, interactive data systems.

The Panel considered that it would be preferable if the prescribing information was supplied via a single click rather than four clicks. However given that the company had shown the prescribing information on the screen for nearly four minutes the Panel considered that ViiV had met the requirements of Clause 4.5. The invitation met the requirements of Clause 4.4. The prescribing information was supplied and thus the Panel ruled no breach of Clause 4.1 of the Code.

Given its rulings above the Panel did not consider that ViiV had failed to maintain high standards as alleged nor had it brought discredit upon or reduced confidence in the pharmaceutical industry. The Panel ruled no breach of Clauses 9.1 and 2.

Complaint received **7 September 2017**

Case completed **14 November 2017**

CASE AUTH/2975/9/17

VOLUNTARY ADMISSION BY A MENARINI

Late disclosure of research and development payments

A Menarini voluntarily admitted that following its initial timely disclosure in March 2017 of payments made in 2016, it subsequently received additional data from corporate colleagues about clinical trial payments made to a UK organisation. These payments were not uploaded into the UK disclosure portal until August 2017.

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

The detailed submission by A Menarini is given below.

The Panel noted that the payment at issue was not part of the company's initial disclosure in March 2017; it appeared that research and development (R&D) colleagues provided the data late and it was not uploaded until August 2017. The Code required transfers of value to be disclosed in the first six months after the end of the calendar year in which they were made. The deadline for disclosure had not been met. A breach of the Code was ruled.

A Menarini voluntarily admitted a breach of the Code as some research and development (R&D) payments were disclosed after the 6 month deadline.

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

VOLUNTARY ADMISSION

A Menarini noted that on 29 March 2017 it submitted its transfer of value data for 2016 for disclosure into the ABPI Transfer of Value Portal.

Subsequent to this full and timely submission, and following the receipt of internal information from colleagues in R&D, it submitted additional data on 21 August 2017 that it received from corporate colleagues about clinical trial payments made to a UK organisation during 2016. This R&D payment submission was beyond the deadline of disclosure of 30 June 2017.

A Menarini noted that Clause 24.4 stated that 'Disclosures must be made annually in respect of each calendar year. Disclosure must be in the first six months after the end of the calendar year in which the transfers of value were made', the use of the word 'must' twice led the company to interpret the clause in such a way that any submission of additional data after 30 June 2017 would be a breach of the Code. A Menarini therefore voluntarily admitted a breach of Clause 24.4.

A Menarini understood that the disclosure process was still at its early stages and that there might not be other similar cases reported. The company gave its assurance that it was developing new processes with its corporate colleagues to reduce the likelihood of late data submission in the future.

A Menarini was asked to respond to Clause 24.4 of the Code.

RESPONSE

A Menarini submitted that the R&D payment details at issue were uploaded into the UK disclosure portal on 21 August 2017 and confirmation was received on 6 September that the data was integrated on the portal.

PANEL RULING

The Panel noted that an R&D payment made in 2016 to a UK organisation did not form part of A Menarini's initial disclosure of transfers of value made in 2016 and submitted on 29 March 2017. It appeared that this was due to the data only being received late from colleagues in R&D. The relevant details were ultimately uploaded on to the disclosure portal on 21 August 2017, after the disclosure deadline of 30 June 2017. The Panel noted the requirements of Clause 24.4 and disagreed with A Menarini's statement that any submission of additional data after 30 June 2017 would be a breach of the Code. Clause 24.4 referred to disclosure which, in the Panel's view, meant that the data must be published in the first six months after the end of the calendar year in which the transfers of value were made. This deadline for disclosure had not been met and a breach of Clause 24.4 was ruled.

Voluntary admission received	**31 August 2017**
Case completed	**16 January 2018**

CASE AUTH/2976/9/17

HOSPITAL CONSULTANT v ASTRAZENECA

Email promotion of Qtern

A consultant in anaesthesia and intensive care medicine alleged that a promotional email for Qtern (saxagliptin and dapagliflozin) from AstraZeneca, via a third party, had been sent to him/her without prior permission. Qtern was indicated for use in adults with type 2 diabetes and the complainant submitted that such medicines were not relevant to his/her practice. Additionally the complainant alleged that the subject line indicated that the email contained important information about Qtern whereas it was just an advertisement.

The detailed response from AstraZeneca is given below.

The Panel noted that the Code required that, *inter alia*, promotional emails must not be sent except with the prior permission of the recipient. Pharmaceutical companies using third parties must be certain that their activities/materials complied with the Code.

The Panel noted AstraZeneca's submission that when the complainant registered on the third party website in 2002 the consent process for agreeing to receive promotional emails from pharmaceutical companies was to opt-in to receive 'external emails'.

The Panel considered that neither the consent process in 2002 nor the 2015 update amounted to the complainant consenting to the receipt of promotional emails from pharmaceutical companies. As AstraZeneca had not obtained prior permission to send the email at issue, the Panel ruled a breach of the Code as acknowledged by the company.

The Panel noted the complainant's concern regarding the relevance of the email which referred to the cost benefit of Qtern, a fixed dose combination, vs its individual components. The Panel noted that the Code required that material should be tailored to the audience. The basis for sending information about diabetes medicines to the complainant had not been made clear in the email; there was no mention that it had been sent to the complainant in relation to his role as a payer/ clinical lead. The Panel considered that although information about diabetes medicines might be of interest to the complainant, his/her need for, or interest in it could not reasonably be assumed. The Panel ruled a breach of the Code.

The Panel considered that given the subject of the email 'AstraZeneca Qtern information' and the sender's name which appeared to include a reference to a clinical alert, it was not unreasonable for the complainant to assume the email was some sort of a clinical alert or contained safety information. Only on opening the email was it obvious that the email was promotional. The Panel considered that, on balance, the nature of the email was misleading and was disguised. The Panel therefore ruled breaches of the Code.

The Panel noted its comments and rulings above and considered that AstraZeneca had failed to maintain high standards and a further breach of the Code was ruled.

A consultant in anaesthesia and intensive care medicine, complained about the email promotion of Qtern (saxagliptin and dapagliflozin) by AstraZeneca UK Ltd. Qtern was indicated for adults aged 18 years and over with type 2 diabetes.

The email referred to the fixed dose combination (saxagliptin/dapagliflozin) which was priced at a 27% discount compared with the individual components. Details of the indications and benefits to health professionals were provided and that a budget impact model was available to demonstrate potential savings.

COMPLAINT

The complainant alleged that the email had been sent without prior permission; he/she already received too much spam and this just added to the list. As an intensive care consultant the information was not relevant to his/her practice and so the consultant queried why he/she received it. The complainant noted that the same message went to all of his colleagues with email addresses with a particular professional network, and junior doctors, and was a waste of time. The complainant submitted that new tablets for diabetes were not relevant to intensive care, and companies should take more care as to whom such information was sent.

The complainant alleged that the subject line of the email [AstraZeneca Qtern information] looked as if the email would have some important information about Qtern – there were some known safety concerns that would have been helpful to detail – but on opening the email it was just an advertisement; that was misleading and very disappointing.

The complainant was appalled to think that the whole of the professional network membership might have received the email at issue, when it was not relevant to most of them.

When writing to AstraZeneca, the Authority asked it to consider the requirements of Clauses 7.2, 9.1, 9.9, 11.1 and 12.1 of the Code. The complainant gave permission for his/her email address to be provided to AstraZeneca.

RESPONSE

AstraZeneca explained that it engaged a third party professional network, to distribute the email campaign in question to a subset of health professionals who had registered on the network website and who had:

- consented to receive promotional material from pharmaceutical companies about prescription only medicines; and
- indicated that they were professionals that fell into the broad category of payer.

AstraZeneca submitted that reasonable steps were taken to ensure that there had not been a breach of the Code in relation to the intended audience or initial impression of the email. However, despite receiving assurances from the professional network that appropriate consent had been obtained from all health professionals registered with it, AstraZeneca discovered that the historical consent process the complainant opted into was not of a standard the company expected, and in this regard it accepted a breach of Clause 9.9. AstraZeneca apologised to the complainant and thanked her for bringing this to its attention. It was now imperative that the third party made appropriate amends so that all health professionals who received information via its services, were appropriately consented to receive that information on behalf of AstraZeneca and the other companies that contracted with the third party.

Prior consent to receive promotional emails

AstraZeneca noted that when the email in question was sent, the complainant was registered with the third party professional network. Following permission granted by the complainant to allow the third party to share details of her opt-ins, including specialities and areas of interest, AstraZeneca ascertained that:

- The current registration process clearly clarified to users that they were opting-in to receive promotional emails from pharmaceutical companies about prescription only medicines. However, AstraZeneca's investigation had highlighted an issue with consent for those, including the complainant, who historically signed up to the third party before the existing registration process was in place.

- It appeared that the complainant registered on the third party website in 2002, and self-declared the specialty of anaesthetics and intensive care (dual accreditation). The consent process then to receive promotional emails from pharmaceutical companies was that users opted-in to receive 'external emails'. Unfortunately, the exact wording that users would have seen at the time had not been retained by the third party. The complainant had provided consent to receive 'external emails'. AstraZeneca provided confirmation of the services the complainant opted-in to receive at the point of, and post-registration in 2002. Examples of the type of material the recipient would have received were not available nor was consent validated annually. However, every email provided an opt-out option and users could proactively update their profiles and alter permissions at any time.

- In 2015, the third party updated its terms and conditions to include, *inter alia*, wording about 'Information from third parties' which was sufficient to obtain consent to send promotional emails from a pharmaceutical company about prescription only medicines. All registered members including the complainant were notified of this change on their logged-in account page and invited to update their profiles and permissions. However, members were not required to take any action to indicate that they agreed to receive such information.

- All emails sent by the third party included information on how to unsubscribe from receiving further emails. Since 2013 the complainant received 4 promotional emails via the third party, although under a different brand name, from different organisations. The complainant had now unsubscribed.

AstraZeneca submitted that the company had engaged the third party in good faith, believing that its opt-in process complied with the Code. However, the third party had not satisfactorily addressed the issue of historical membership. AstraZeneca considered that explicit consent was not specifically provided by the complainant to receive promotional content on products from pharmaceutical companies and thus AstraZeneca accepted a breach of Clause 9.9.

Objective and intended audience

AstraZeneca stated that the Qtern email in question was developed to inform senior NHS payers of relevant Qtern information and details of how to contact AstraZeneca's regional account managers for additional information. The content included the product indication and the cost benefit of the fixed dose combination compared with the mono-components. This information was therefore relevant to payer customers due to their potential impact on budgets and prescribing decisions. The intended audience was 'Managed Markets/Payers'.

AstraZeneca submitted that as the email was intended for payers, it took professional advice as to which of the third party's member specialities would fall in to this definition. Advice was sought indirectly from a primary care doctor and from a secondary care doctor as to which specialties, seniorities, and additional professional roles and organisation types would be appropriate to target as payers. A payers' group was created and agreed by AstraZeneca.

Health professionals registering with the third party professional network self-declared their speciality during the registration process, or could update their profile to include this at any time. All members whose self-declared roles matched those in the agreed payers group were identified. The works agreement was included as a supporting document during the review and certification process for the email to enable the signatories to review and agree the target audience.

The third party membership list numbers were provided and the number of those who had self-declared that they fell into one or more of the specialties included in the works agreement. Individuals with multiple qualifying specialties were eliminated from the list and AstraZeneca was satisfied that the remaining professionals were within the intended target audience and the certified email was sent in September 2017 to around 3,000 health professionals.

In February, 2017 the complainant updated the section 'Additional Professional Roles' in her profile to include 'Clinical Lead'. As a result of this self-declaration, and based on the payer group identified, the complainant was included in the payer group eligible for the email at issue. This was the first and only email that the third party professional network had sent to the complainant on behalf of AstraZeneca.

As the email was tailored to a payer audience and the complainant had self-declared herself into a speciality that was within the defined payer category, AstraZeneca submitted that the email was appropriate for the audience to which it was directed. Payers were often represented across medical specialities and had significant input into budgetary decisions that affected local budgets beyond their primary speciality. The information contained within the email referred to cost savings of Qtern vs its mono-components, thus the content of the email was relevant to payers and AstraZeneca denied a breach of Clause 11.1.

Subject heading

AstraZeneca stated that in 2013, the third party professional network rebranded its service via which promotional emails were sent on behalf of pharmaceutical companies. This service also sent emails in relation to safety, however, since 2013 the complainant had received four emails from this email address, all of which had been promotional. This raised the question as to why the complainant assumed that the email in question was related to safety given that she had never received safety-related emails from the third party and the subject line did not refer to such.

AstraZeneca did not consider the subject of the email 'AstraZeneca Qtern information' or the sender of the email, which appeared to include reference to a clinical alert, were misleading with respect to whether the email included any safety or other important information; the email subject did not contain the words 'urgent', 'important', or 'safety'. In addition, the email title was clear that the information was from AstraZeneca; the company denied a breach of Clauses 7.2 and 12.1.

Whilst AstraZeneca acknowledged that there had been a breach of Clause 9.9 in relation to the historical process used by the third party to gain explicit consent from the complainant to receive promotional emails from a pharmaceutical company, it had engaged the services of the third party in the belief that the current consent process was used to gain the complainant's consent. Given this, and that the company did not consider that there had been a breach of any other clause, AstraZeneca submitted that it had maintained high standards and thus it denied a breach of Clause 9.1. Furthermore, AstraZeneca had reviewed all planned activity with the third party, taken steps to ensure that the third party had identified all individuals who had consented before enactment of the existing consent process and would obtain re-consent accordingly.

Finally AstraZeneca believed that third parties, working on behalf of pharmaceutical companies, should be independently accredited and held to account according to PMCPA standards.

PANEL RULING

The Panel noted that Clause 9.9 required that, *inter alia*, email communications must not be used for promotional purposes, except with the prior permission of the recipient. Pharmaceutical companies were responsible under the Code and they needed to be certain that when using third parties their activities/materials complied with the Code. It was not for the PMCPA to accredit third parties.

The Panel noted AstraZeneca's submission that when the complainant registered on the third party website in January 2002, the consent process for agreeing to receive promotional emails from pharmaceutical companies was that users opted-in to receive 'external emails'. The exact wording that users would have seen at the time was not provided by AstraZeneca as it had not been retained by the third party.

The Panel considered that neither the historical consent process in 2002 nor the 2015 update amounted to the complainant consenting to the receipt of promotional emails from pharmaceutical companies. As AstraZeneca had not obtained prior permission to send the promotional email, the Panel therefore ruled a breach of Clause 9.9 as acknowledged by the company.

The Panel noted the complainant's concern regarding the relevance of the email which referred to the cost benefit of Qtern, a fixed dose combination, vs its individual components. The Panel considered that the email would be relevant to those who worked in the diabetes area and other payers, due to the potential impact on budgets and prescribing decisions. The intended audience was 'Managed Markets/Payers'.

The Panel noted that the complainant updated her details in the 'Additional Professional Roles' profile to include 'Clinical Lead' in February 2017. The Panel queried whether as a clinical lead in anaesthesia and intensive care medicine the complainant would be interested in the cost etc of medicines for diabetes or have any broader role in that regard. In the Panel's view, the email would be more likely to interest clinical leads in other specialities.

The Panel noted the supplementary information to Clause 11.1 that material should be tailored to the audience. The basis for sending information about

diabetes medicines to the complainant had not been made clear in the email in question. There was no mention that it had been sent to the complainant in relation to her role as a payer/clinical lead. The Panel considered that although information about diabetes medicines might be of interest to the complainant, the content of the email did not meet the requirements of Clause 11.1 in that complainant's need for, or interest in it could not reasonably be assumed. The Panel ruled a breach of Clause 11.1.

The Panel considered that given the subject of the email 'AstraZeneca Qtern information' and the sender of the email, which appeared to include a reference to a clinical alert, it was not unreasonable for the complainant to assume the email was some sort of a clinical alert or contained safety information. Only on opening the email was it obvious that the email was not a clinical alert but was promotional. The Panel considered that, on balance, the nature of the email was misleading and was disguised. The Panel therefore ruled breaches of Clauses 12.1 and 7.2 of the Code.

The Panel noted its comments and rulings above and considered that AstraZeneca had failed to maintain high standards and a breach of Clause 9.1 was also ruled.

Complaint received **9 September 2017**

Case completed **20 November 2017**

MEMBER OF THE PUBLIC v ViiV HEALTHCARE

Use of an iPad in public

A member of the public complained that a representative's use of an iPad on a train was such that the outline sales strategy for, and clinical information about, Triumeq (dolutegravir/abacavir/lamivinidine) was clearly visible. The complainant was concerned that an HIV patient could take the information back to his/her nurse or doctor and argue his/her current regime without fully understanding the overall treatment regime he/she was on.

The detailed response from ViiV is given below.

The Panel noted that the complainant had seen promotional material for Triumeq which an employee from a third party was working on whilst travelling by train. As no representative as defined by the Code was involved, no breach of the relevant clause of the Code was ruled.

The Panel considered that it was unfortunate that the complainant had seen the material and that the third party employee had not been more discrete. ViiV submitted that the train was not overcrowded; there was an empty seat between the third party employee and the next passenger. The Panel considered that there was a difference between proactively showing material to the public or making material readily available for them and a member of the public reading material over someone's shoulder. The material at issue had not been directed at fellow travellers or other members of the public. On balance, the Panel did not consider that in the particular circumstances of this case a prescription only medicine had been promoted to the public and thus ruled no breach of Code.

The Panel did not consider that there had been a failure to maintain high standards nor did the circumstances bring discredit upon, or reduced confidence in, the pharmaceutical industry. No breaches of the Code including Clause 2 were ruled.

A member of the public, complained about a representative using an iPad during a train journey such that information about Triumeq (dolutegravir/abacavir/lamivudine) was clearly visible. Triumeq was marketed by ViiV Healthcare and indicated for the treatment of Human Immunodeficiency Virus (HIV).

COMPLAINT

The complainant stated that he was saddened to see a representative using his iPad on a train such that he could clearly see the outline for Triumeq's sales strategy and the clinical data for flamingo/aria/step-2. The complainant stated that he actually enjoyed Chris's journey as detailed in the material and how he dealt with his HIV medicines.

The complainant stated that he did not think it right that this sort of information was visible on public transport and used in close quarters with the public like himself.

The complainant was concerned that an HIV patient could easily take the information back to his/her nurse or doctor and argue his/her current regime without full knowledge and understanding of the medicines and the overall treatment regime he/she was on.

The complainant briefly described the representative at issue and the journey details.

When writing to ViiV, the Authority asked it to consider the requirements of Clauses 2, 9.1, 15.2 and 26.1 of the Code.

RESPONSE

ViiV Healthcare stated that the individual in question was not a representative, he was employed by a third-party service supplier responsible for the technical development of promotional materials for use on iPads. This platform was used only by fully briefed and trained specialists to detail ViiV's medicines to health professionals treating HIV patients. Since no representative was involved the company denied a breach of Clause 15.2.

The third party employee confirmed that he opened the material on his company iPad for about 10 minutes while travelling on a train. He recalled that one or two passengers sat opposite him and one person next to him, with an empty seat between. The employee estimated to have swiped about 20 screens, to make a number of technical checks on interactive elements and functionality. The individual concerned believed that he was diligent and had made effective use of train-bound time. He did not engage the complainant or others in any communication (either verbally, by playing audio, making eye contact, or other); nor was he aware of anyone overlooking his work.

ViiV submitted that the material in question was written for hospital specialists, not in language likely to be readily understood by the public, with graphs of efficacy and tables listing side effects. The complainant had provided no detail of the promotional messages conveyed, and as the third party employee was not interested in reading the content, it was unlikely that any reader would have had the chance to digest much more than the name of the studies being displayed, as mentioned by the complainant. This information in itself was not promotional and was available to the public on the clinical trials register. As such, ViiV denied that it had

promoted a prescription only medicine to the public in breach of Clause 26.1.

In response to Clause 9.1, ViiV reviewed its internal governance processes relating to third party service providers, and submitted that appropriate agreements and training were in place. The written agreement between ViiV and the third party at issue stipulated that the third party must ensure compliance with the Code and decisions of the PMCPA and its staff must have the skill, expertise, and knowledge with respect to the products and services required of them, including for technical testing, which should be undertaken in a comprehensive, timely and professional manner. ViiV noted that the third party employee in question had been trained on the Code including a PMCPA familiarisation seminar in January 2015. The third party also regularly emailed the employee with updates about the Code, the latest email was sent in January 2017.

ViiV stated that although it acknowledged that the third party employee ought to have behaved with total discretion whilst on public transport, it considered that this was somewhat naïve and a wholly unintended error of judgement. As such, ViiV did not consider that it represented a failure to observe the standards set by the Code for the promotion of medicines and it thus denied a breach of Clause 9.1.

ViiV stated that it regretted the wholly unintended consequences arising from the conduct of the third party employee and had taken the following additional and immediate corrective actions to ensure that such incidents were not repeated:

- The third party had re-issued the Code and the ViiV Code of Practice to all staff and given them two days to acknowledge that they had read and understood the documentation
- Following the above, team meetings were scheduled over the coming weeks to ensure all third party staff fully understood the implications of their day-to-day activity in relation to the Code and were being reminded that they must not work on promotional materials for health professionals in public places
- The third party would provide refresher training on the Code to the individual involved in the incident and all other relevant staff working on the account within the coming month
- When there were updates to the Code, the third party would hold briefing sessions with all relevant team members in addition to continuing to circulate the changes over email
- As per its internal Third Party Oversight Process, ViiV had notified the Critical and Sensitive Information Risk team, which was currently undertaking a security assessment of the vendor
- ViiV had reminded all global ViiV suppliers that they must familiarise themselves with, and adhere to at all times, the laws and codes of practice in the country in which they were based

In response to Clause 2, although ViiV was sincerely disappointed by this isolated incident, it did not consider that the unintended actions of a technical third party provider brought discredit to, or reduced confidence in, the industry. Neither patient safety, nor public health, had been compromised or prejudiced.

PANEL RULING

The Panel noted that the complainant had seen material promoting Triumeq to hospital specialists which an employee from a third party was working on whilst travelling by train. The Panel accepted that no representative as defined by the Code was involved and thus ruled no breach of Clause 15.2.

The Panel considered that it was most unfortunate that the complainant had seen the material and that the third party employee had not been more discreet so that people sitting nearby could not see the material. The Panel noted that the part of the train where the third party employee was sitting did not appear to be overcrowded. There was an empty seat between the third party employee and the next passenger. The Panel considered that there was a difference between proactively showing material to the public or making material readily available for them and a member of the public reading material over someone's shoulder. The material at issue had not been directed at fellow travellers or other members of the public. On balance, the Panel did not consider that in the particular circumstances of this case a prescription only medicine had been promoted to the public and thus ruled no breach of Clause 26.1.

The Panel did not consider that there had been a failure to maintain high standards and no breach of Clause 9.1 was ruled. Clause 2 was a sign of particular censure and reserved for such use. The Panel did not consider the circumstances brought discredit upon, or reduced confidence in, the pharmaceutical industry and ruled no breach of Clause 2.

Complaint received **26 September 2017**

Case completed **23 November 2017**

CASE AUTH/2983/10/17

ANONYMOUS, NON-CONTACTABLE CLINICIAN v CELGENE

Promotion of Abraxane to the Public

An anonymous, non-contactable complainant, who appeared to be a clinician, complained that a booklet, 'Life We're working on it' produced by Celgene, promoted Abraxane (protein bound paclitaxel) to the public. Abraxane was indicated for the treatment of various cancers including in combination with gemcitabine for first line treatment of adult patients with metastatic adenocarinoma of the pancreas.

The 24 page booklet referred to Celgene's activities to discover and deliver innovative therapies for cancer and immune inflammatory diseases. The inside front cover and introduction referred to '... help many more people live longer, happier, healthier lives'. Rare disease therapy areas the company was working on and the company's clinical trial programme were outlined.

The complainant stated that he/she was compelled to complain following a very difficult consultation with a patient and a family member who had the booklet. The complainant noted the information about the availability of Celgene's medicine for pancreatic cancer and that it was the 'first therapy with clinical benefits for pancreatic cancer'. This was false. Abraxane was for advanced disease only. The references cited in support of the claim, 'the first therapy with clinical benefits for pancreatic cancer patients in almost 20 years', clearly referred to Abraxane and contained links to articles about the medicine.

The complainant submitted that it was wholly unacceptable for a pharmaceutical company to create such booklets with information about specific medicines so easily accessible to members of the public and those who were not medically qualified. The complainant stated that there were references to other medicines, as well as mentions of all other diseases in which Celgene had a vested interest. The complainant was dismayed that a pharmaceutical company found it acceptable to advertise in booklets that could be accessed by the public.

The complainant hoped that his/her complaint would help to ensure that pharmaceutical companies would begin to take their responsibility to the public more seriously; they needed to understand that compromising patients and their wellbeing was not acceptable.

The detailed response from Celgene is given below.

The Panel noted that Celgene described the booklet as a corporate brochure. The booklet discussed therapy areas where the company had a commercial interest. Whilst it did not name Abraxane, in the Panel's view, Abraxane was, contrary to Celgene's assertion and together with the first phosphodiesterase-4 inhibitor, indirectly identified. The Panel noted that the booklet discussed Celgene's interactions with clinicians and patients within the context of its clinical heritage and ongoing medical innovation. In the Panel's view, the booklet primarily sought to raise the company's corporate profile with a particular emphasis on cancer, inflammation and immunology and the company's ethos in relation to innovation, access, commitment and investment.

The Panel noted that, according to Celgene, the target audience was broad and included internal staff, external stakeholders, the public and parliamentarians. It was distributed to Celgene employees including copies to be shared with potential employees. In addition, copies were on display at an industry round table discussion which was not attended by members of the public. The complainant was concerned that the brochure had been obtained by his/her patient or carer. The Panel noted that it was not possible to contact the complainant to ascertain how and when the booklet had been received by his/her patient/carer. In this regard, the Panel noted that the date of the complaint was the same date the booklet was made available to the public for a limited time at a New Scientist Live event. In the particular circumstances of this case, and irrespective of the content of the booklet, there was insufficient evidence that Celgene had distributed the booklet to, or otherwise made it available to, the complainant's patient or carer as alleged on or before the date of the complaint and thus the Panel ruled no breach of the Code on this narrow point.

The Panel noted that the complainant also made a broader allegation about the principle of companies producing such booklets with information about specific medicines and stated that they should not be so easily accessible to members of the public and those who were not medically qualified. The complainant referred to advertising in the booklet. On this point, the Panel considered that the availability of the booklet at the New Scientist conference was relevant. Notwithstanding that the complainant was non-contactable, the Panel noted Celgene's submission that it accepted the booklet had ultimately been received by a patient and it was certified for such. In the Panel's view, the complaint was not about the provision of the booklet to employees, parliamentarians and such like (who might be considered members of the public) but rather to those individuals who would not normally interact professionally with a pharmaceutical

company and, solely for the purposes of this point of the complaint, it interpreted members of the public as referred to by the complainant accordingly. Whilst the job bag summary described the booklet as having undergone promotional certification, it was also described as a corporate brochure for both internal and external use. Whilst it was not unacceptable to have a broad audience, the company must ensure that such material was genuinely suitable for each component of the audience in relation to the requirements of the Code. For instance, material suitable for staff might not be suitable for the broader general public including individual patients. The Panel noted the references to pancreatic cancer patients, the first phosphodiesterase-4-inhibitor for the treatment of plaque psoriasis and rare disease areas that the company was working on, within the 'Passion for Discovery' section. The Panel considered that context was important and, in this regard, noted that page 9 began by referring to future proofing medical innovation and that the first therapy with clinical benefits for pancreatic cancer patients in 20 years was a result of Celgene's bold approach to innovation. The top of the page described Celgene as a leader in the field of rare diseases. In the Panel's view, there was an implication that Celgene's products were cutting edge and a significant advance on products currently available. The Panel noted its comments above about the target audience which included members of the public. On balance, within the overall context of the booklet, the Panel did not consider that page 9 promoted specific prescription only medicines to the public. No breach was ruled. In the Panel's view the material was such that patients might be encouraged to ask their doctors to prescribe specific medicines contrary to the requirements of the Code and a breach was ruled.

In the Panel's view, the material was misleading; it implied that the clinical benefits would potentially be seen in all patients and that was not so, Abraxane was only licensed for use in combination in patients with advanced disease. The Panel ruled a breach on this point.

Noting its rulings above, the Panel ruled a breach as high standards had not been maintained. Overall, the Panel did not consider that the circumstances warranted a ruling of a breach of Clause 2 and ruled no breach of that Clause.

An anonymous, non-contactable complainant, who appeared to be a clinician, complained that a booklet, 'Life We're working on it' (ref UK-CELG160202), produced by Celgene Limited, promoted Abraxane (protein bound paclitaxel) to the public. Abraxane was indicated for the treatment of various cancers including in combination with gemcitabine for first line treatment of adult patients with metastatic adenocarinoma of the pancreas.

The 24 page booklet referred to Celgene's activities to discover and deliver innovative therapies for cancer and immune inflammatory diseases. The inside front cover and introduction referred to '... help many more people live longer, happier, healthier lives'. Rare disease therapy areas the company was working on and the company's clinical trial programme were outlined. Page 9 referred to 'the first therapy with clinical benefits for pancreatic cancer patients in almost 20 years', referenced to the Abraxane summary of product characteristics (SPC) and a study by Al-Hajeli *et al* (2016).

COMPLAINT

The complainant stated that he/she was compelled to complain following a very difficult consultation with a patient. As a clinician, his/her duty of care was always to his/her patients.

The complaint stated that the booklet in question was brought in by one of his/her patients and a family member during a recent consultation. The complainant noted the pages entitled 'A passion for discovery' and in particular information about the availability of the Celgene's medicine for pancreatic cancer and that it was the 'first therapy with clinical benefits for pancreatic cancer'. This was false. The medicine at issue, Abraxane, was for advanced disease only, furthermore it was removed from the Cancer Drugs Fund some years ago. Cited in support of the claim, 'the first therapy with clinical benefits for pancreatic cancer patients in almost 20 years', references 6 and 7 were listed at the back of the book and clearly referred to Abraxane and contained links to articles about the medicine.

The complainant submitted that it was wholly unacceptable for a pharmaceutical company to create such booklets with information about specific medicines so easily accessible to members of the public and those who were not medically qualified. The complainant stated that he/she had gone through this booklet and had seen references to other medicines, as well as mentions of all other diseases in which Celgene had a vested interest. The complainant was dismayed that a pharmaceutical company found it acceptable to advertise in booklets that could be accessed by the public.

The complainant hoped that his/her complaint would help to ensure that pharmaceutical companies would begin to take their responsibility to the public more seriously; they needed to understand that compromising patients and their wellbeing was not acceptable.

Although no comment was made by the complainant, the copy of the booklet which he/she provided also underlined the following:

> 'We were also proud to contribute to the advancement of immune disorder therapies with the first phosphodiesterase-4 inhibitor approved for the treatment of plaque psoriasis.'

and:

> 'Rare disease therapy areas we are currently working with include Behçets disease, relapsed and refractory multiple myeloma and hepatocellular carcinoma.'

When writing to Celgene, the Authority asked it to consider the requirements of Clauses 2, 9.1 and 26.

RESPONSE

Celgene submitted that it was committed to operating according to the highest standards outlined in the Code in order to ensure that the healthcare industry fulfilled its commitment to patients and health professionals. Therefore, it was very concerned to receive this complaint and it immediately conducted an internal review and gathered information to address and respond to the allegations.

Celgene stated that corporate brochures were widely used by the industry. Celgene used its brochures as a vehicle to introduce the company, its culture, therapeutic focus, innovation and commitment to research and patients. The brochures were not designed or used to promote any medicines. The brochure at issue was prepared as part of the 10th anniversary of the company in the UK and Ireland; it was designed to enhance the reputation of the company and it described, in general terms, the mission and purpose of the company and its commitment to research.

Celgene stated that its 24 page brochure contained information about its activities in discovering and developing innovative therapies for cancer and immune inflammatory disease. The brochure, as a whole, had to be considered rather than one page of the text in order to objectively consider its apparent purpose. It included the following page headings:

- Putting patients first
- Improving the lives of patients worldwide
- A passion for discovery
- Cancer
- Inflammation & immunology
- Further innovation
- The virtuous cycle of innovation
- Corporate social responsibility
- References.

The brochure was produced and job bagged by the corporate affairs department to be approved for certification under the Code, with a target audience of internal staff, external stakeholders, the public and parliamentarians. The intended first use was 7 November 2016. Celgene provided a copy of the job bag summary.

Celgene reiterated that its brochure had no promotional intent. There was no reference to branded medicines in the body of the brochure, and there was no statement that could properly be viewed as encouraging members of the public to request treatment with a specific medicine because of the claim made about it. The brochure was not prepared with the intent to promote any products marketed by the company, but rather to describe the company's commitment to research and its focus on cancer, inflammation and immunology in general. While the brochure did not refer to medicines in the body of the text, in the references section (page 21 of the brochure) there was a reference to certain research in respect to products for which Celgene held the marketing authorization, including Abraxane. These were included to demonstrate that claims about Celgene's commitment to research were factual and balanced.

In line with the supplementary information to Clause 26.2, the brochure was intended to be used as 'non-promotional information about prescription only medicines to the public' which 'includes information provided by means of posters distributed for display in surgery waiting rooms etc and reference information made available by companies on their websites or otherwise as a resource for members of the public'.

Celgene understood that corporate brochures, as public relations tools, were therefore deemed acceptable under Clause 26.2. Clause 26 also stated that companies should consider including references to other credible sources of information about a medicine: 'Pharmaceutical companies are not obliged to provide reference information but it is considered good practice to provide as a minimum the regulatory information comprising the summary of product characteristics (SPC), the package leaflet (PIL) and the public assessment report (PAR) (UK or European) where such a document exists'.

The brochure at issue had no promotional intent and the only reference to Abraxane was in the reference section where the SPC was referenced in line with the guidance in Clause 26.2.

Celgene explained that Abraxane was indicated for the treatment of metastatic breast cancer in adults who had failed first-line treatment for metastatic disease and for whom standard, anthracycline containing therapy was not indicated. Abraxane, in combination with gemcitabine, was also indicated for the first-line treatment of adult patients with metastatic adenocarcinoma of the pancreas. Abraxane, in combination with carboplatin, was indicated for the first-line treatment of non-small cell lung cancer in adults who were not candidates for potentially curative surgery and/or radiation therapy.

The EU marketing authorization for Abraxane was first granted by the European Medicines Agency in January 2008 for metastatic breast cancer patients and thereafter, the additional indications were approved. A copy of the current SPC was provided.

Celgene noted, however, that it did not currently support promotional activities for Abraxane. In 2016, it disbanded its Abraxane sales team but continued to provide the required scientific support for the medicine. Celgene reiterated that there was no promotional intent in the brochure.

Celgene noted that the complainant alleged that the claim 'first therapy with clinical benefits for pancreatic cancer' was false. Celgene considered that the claim had been taken out of context. The statement in the brochure was presented in the context of highlighting Celgene's 'bold approach to innovation', which led to the development of 'the first therapy with clinical benefits for **pancreatic cancer patients** in almost 20 years' (emphasis added). When Abraxane was approved, data from Cancer Research UK demonstrated that, unlike the majority

of cancers, five and ten-year survival for pancreatic cancer had not shown much improvement since the early 1970s. In men and women, five-year age-standardised net survival for pancreatic cancer had not increased significantly between 1971-1972 and 2010-2011 in England and Wales.

Celgene submitted that there had only been two therapies licensed for the treatment of pancreatic cancer in the past 20 years. The first, Tarceva (erlotinib), showed a mean improvement in overall survival of 0.4 months (12 days).

Abraxane was the second therapy licensed in this 20 year period and was the first to provide a meaningful benefit – a 1.8 month increase in median overall survival. As such, Celgene submitted that the claim 'the first therapy with clinical benefits for **pancreatic cancer patients** in almost 20 years' (emphasis added) was fair and balanced and could be substantiated.

Celgene noted that nothing was stated in the brochure about the stage of disease that Abraxane treated or the types of patients for which the medicine was suitable. In fact, the product was only mentioned in the reference cited in support of the claim on page 8 to explain the context in which the claim was made.

Celgene noted the complainant's statement that Abraxane was removed from the Cancer Drug Fund (CDF) some years ago. The brochure did not mention the availability of Abraxane, whether within the CDF or otherwise within the NHS. Socio-economic variations across the UK were not addressed and could not be deduced from the current content of the brochure. Celgene should not be the addressee for a complaint about socio-economic variations in the UK. Abraxane was available across the UK since EMA approval. CDF fund was continuously supported in some parts of the UK, while in others access was temporarily limited. Since 7 August 2017 patients had been able to once again be treated with Abraxane through the CDF. Celgene considered that this reflected the importance that payors placed on treatments in this very difficult to treat area and Celgene was proud to strive to make medicines available for those conditions with very significant unmet need.

The complainant had also challenged the statement 'we are also proud to contribute to the advancement of immune disorder therapies with the first phosphodiesterase-4 inhibitor approved for the treatment of plaque psoriasis'. This was factually correct. Celgene believed that the claim was focused on science and on the innovative mode of action which was phosphodiesterase-4 inhibition. Similarly, it was correct that Celgene was currently working on Behçet's disease, relapsed and refractory multiple myeloma and hepatocellular carcinoma. Celgene submitted that this spoke to its innovative approach to drug development. There were no product claims made and the only mention of a product was in the reference section.

Celgene submitted that it was unclear as to how the content of the brochure, or the claims highlighted by the complainant, could compromise patient safety and wellbeing as alleged.

Celgene stated that 2016 represented a very important milestone for the company as it celebrated its 10th year of UK and Ireland operations. The Celgene brochure was electronically certified on 25 November 2016.

Celgene submitted that its investigation showed that the final hard copy of the brochure was not signed off.

Hard copies of the brochure were distributed internally to Celgene employees, including its field force, on 25 and 29 November 2016 as part of the 10-year anniversary celebration communication.

Celgene stated that it had looked closely into the distribution of the brochure externally before 28 September, the date of the letter from the complainant, and it found the following:

- 5 copies were provided to a human resources employee at Celgene who wanted them to share with potential candidates and recruiters for the purpose of introducing them to Celgene. As that employee had since left Celgene, the company did not know whether those copies were further distributed.
- On 22 September 2017, at an Institute of Public Policy Research event entitled 'Mind the Gap: The Health and Care Funding Crisis' which was a roundtable discussion about the gap in funding for social and health care in the UK, attended by UK policy makers and other health care, government and industry leaders. No members of the public attended that event. The general manager participated as a panel speaker at the event. Five copies of the corporate brochure were on display but all five copies were subsequently returned after the meeting.

The brochure had not been proactively distributed to patients or the public before 28 September 2017. Celgene could not explain how this patient received this brochure which, at this time, had only been distributed internally (bar a small number displayed, but not taken, at the IPPR event). It would welcome further information if that were available.

Celgene set out for the Authority's information, and in the interests of disclosure, additional information that it had been able to identify about the brochure. However, these events could not have influenced the complaint, given they occurred after the complaint was made. On 28 September, outside the scope of this complaint, at the New Scientist Live Exhibition event in London where Celgene sponsored a stand entitled 'This is Axiom', copies of the brochure were inadvertently made available to attendees between 10am and 12:30pm. Participants included members of the general public. On arriving at the stand, a final medical signatory who was responsible for review and approval for all materials used at the event, removed the brochure because it had not been specifically reviewed for use at the exhibition. On 9 October 2017, Celgene formally initiated a withdrawal

process to remove the brochure from use due to lack of final certification. Celgene noted that these events were initiated before the company was notified of this complaint. Celgene provided a copy of the withdrawal form which was sent electronically to all employees in the UK and Ireland.

Relevant provisions of the 2016 Code of Practice

Celgene did not prepare the brochure with the intent to promote specific products. The document was created to describe the company's mission, its culture, its therapeutic focus, its innovation and its commitment to research and to patients. The information was factually correct and accurate and Celgene understood that, under the Code, reference to the SPC was considered to be best practice. However, following the New Scientist Live Exhibition in London, the final signatory noticed the brochure had not been certified for use at the event and the withdrawal process was later initiated before Celgene was notified of this complaint. Celgene further noted that in response to a PMCPA audit in connection with a separate matter in October 2016, it had made significant updates to its internal processes, added compliance resources and trainings. While the company regretted the failure of the final certification, this did not affect the nature of the material itself, which was the focus of the complaint. Celgene submitted that the brochure did not bring discredit upon, or reduce confidence in, the industry.

Celgene stated that its compliance program included policies, standard operating procedures and electronic tools for the review and approval of materials. Celgene had reviewed and updated those policies, processes and systems and invested additional compliance resources in 2017. While certain aspects of the approval of this brochure were not in line with Celgene's procedures, the non-compliant brochure was identified and withdrawn quickly. Celgene thus submitted that high standards had been maintained and in fact Celgene's procedures were already being strengthened as a result of the recommendations from the audit.

The brochure contained information about Celgene's activities in discovering and developing innovative therapies for cancer and immune inflammatory disease for the wellbeing and benefit of patients. The brochure provided non-promotional information about prescription only medicines, disease areas and clinical trials. Celgene submitted that the information in the brochure was accurate and could be substantiated and that the content of the brochure did not compromise patient safety. Celgene did not actively distribute the brochure to patients, although it accepted that it was ultimately received by a patient without final certification. The only mention of the name of Abraxane, or any other prescription medicine in the brochure, was in the references section (page 21 of the brochure) in line with the guidance in the supplementary information in the Code and accurately cited the information about the company's research and development that was included in the body of the text. Based on these facts, Celgene submitted that the brochure did not advertise prescription only medicines to the public; it did not constitute direct to consumer advertising and the information in the brochure was factual and presented in a balanced way. Furthermore, Celgene did not believe, and certainly did not intend, that the information in the brochure would raise unfounded hopes of successful treatment or mislead with respect to the safety of the prescription only medicines and therefore the company denied a breach of Clauses 26.1 and 26.2. The brochure had now been withdrawn from use because of the lack of final certification, but a breach of Clause 26.1 and 26.2 was denied.

PANEL RULING

The Panel noted that the complainant was anonymous and non-contactable. The Constitution and Procedure for the Prescription Medicines Code of Practice Authority stated that anonymous complaints would be accepted but that, like all other complaints, the complainant had the burden of proving his/her complaint on the balance of probabilities. All complaints were judged on the evidence provided by the parties. The complainant could not be contacted for more information.

Clause 26.1 prohibited the promotion of prescription only medicines to the public and Clause 26.2 required that information about prescription only medicines, which is made available to the public directly or indirectly, must be factual and presented in a balanced way. It must not raise unfounded hopes of successful treatment or be misleading with respect to the safety of the product. The relevant supplementary information referred to the provision of non promotional information about prescription only medicines, *inter alia*, by dissemination of such information via public relation activities. The section headed 'Information to Current or Prospective Employees' stated that information about pharmaceutical companies, provided to current or prospective employees, might relate to both existing medicines or those not yet marketed. Such information should be presented in a balanced way.

The Panel noted that Celgene described the booklet as a corporate brochure. The Panel considered that corporate brochures were, of course, a legitimate activity. Such brochures that fell within the scope of the Code had to comply with it. The booklet discussed therapy areas where the company had a commercial interest. Whilst it did not name Abraxane, in the Panel's view, Abraxane was, contrary to Celgene's assertion and together with the first phosphodiesterase-4 inhibitor, indirectly identified. The Panel noted that the booklet discussed Celgene's interactions with clinicians and patients within the context of its clinical heritage and ongoing medical innovation. In the Panel's view, the booklet primarily sought to raise the company's corporate profile with a particular emphasis on cancer, inflammation and immunology and the company's ethos in relation to innovation, access, commitment and investment.

As noted above, the Panel considered that, in principle, corporate brochures were a legitimate

activity but considered that when assessing their acceptability under the Code, much would depend on, *inter alia*, the intended audience. The Panel noted that, according to Celgene, the target audience was broad and included internal staff, external stakeholders, the public and parliamentarians. In practice, and prior to the date of the complaint, the brochure was distributed internally to Celgene employees including 5 copies to a human resource employee to be shared with potential employees. In addition, 5 copies were on display at an industry round table discussion which was not attended by members of the public. The complainant was concerned that the brochure had been obtained by his/her patient or carer. The Panel noted the status of the complainant set out above. It was not possible to contact him/her to ascertain how and when the booklet had been received by his/her patient/carer. In this regard, the Panel noted that the complaint was dated 28 September, the same date the booklet was made available to the public for a limited time at the New Scientist Live event. In the particular circumstances of this case, and irrespective of the content of the booklet, there was insufficient evidence that Celgene had distributed the booklet to, or otherwise made it available to, the complainant's patient or carer as alleged on or before the date of the complaint and thus the Panel ruled no breach of Clauses 26.1 and 26.2 on this narrow point.

The Panel noted that the complainant also made a broader allegation about the principle of companies producing such booklets with information about specific medicines and stated that they should not be so easily accessible to members of the public and those who were not medically qualified. The complainant referred to advertising in the booklet. On this point, the Panel considered that the availability of the booklet at the New Scientist conference was relevant. Notwithstanding that the complainant was non-contactable, the Panel noted Celgene's submission that it accepted the booklet had ultimately been received by a patient and it was certified for such. The Panel noted the requirements of Clause 26 and the permissible activities described in the relevant supplementary information set out above and the booklet's broad intended audience. In the Panel's view, the complaint was not about the provision of the booklet to employees, parliamentarians and such like (who might be considered members of the public) but rather to those individuals who would not normally interact professionally with a pharmaceutical company and, solely for the purposes of this point of the complaint, it interpreted members of the public as referred to by the complainant accordingly. Whilst the Zinc job bag summary described the booklet as having undergone promotional certification, it was also described as a corporate brochure for both internal and external use. Whilst it was not unacceptable to have a broad audience for such material, the company must ensure that the material was genuinely suitable for each component of the audience in relation to the requirements of the Code. For instance, material suitable for internal staff might not be suitable for the broader general public including individual patients. The Panel noted the references to pancreatic cancer patients, the first phosphodiesterase-4-inhibitor for the treatment of plaque psoriasis and rare disease areas that the company was working on, on page 9 of the booklet within the 'Passion for Discovery' section. The Panel considered that context was important and, in this regard, noted that the page began by referring to future proofing medical innovation and that the first therapy with clinical benefits for pancreatic cancer patients in 20 years was a result of Celgene's bold approach to innovation. The top of the page described Celgene as a leader in the field of rare diseases. In the Panel's view, there was an implication that Celgene's products were cutting edge and a significant advance on products currently available. The Panel noted its comments above about the target audience which included members of the public. On balance, within the overall context of the booklet, the Panel did not consider that page 9 promoted specific prescription only medicines to the public. No breach of Clause 26.1 was ruled. In relation to members of the public as described above, and particularly individual patients, in the Panel's view the material was such that patients might be encouraged to ask their doctors to prescribe specific medicines contrary to the requirements of Clause 26.2. The Panel considered that sufficient information had been given for products to be identified. A breach of Clause 26.2 was ruled.

Clause 26.2 required relevant materials to be factual and presented in a balanced way and the relevant supplementary information stated that the requirements of, *inter alia*, Clause 7.2 also applied to information to the public. The Panel noted the complainant also alleged that Abraxane was for advanced disease only. In this regard, the Panel noted that it was licensed for use in combination with gemcitabine for first line treatment of adult patients with metastatic pancreatic cancer. The page in question referred to 'clinical benefits for pancreatic cancer patients'. In the Panel's view, the material was misleading; it implied that the clinical benefits would potentially be seen in all patients and that was not so, it was only licensed for use in combination in patients with advanced disease. The Panel ruled a breach of Clause 26.2 on this point.

Noting its rulings above, the Panel considered that high standards had not been maintained. A breach of Clause 9.1 was ruled. Overall, the Panel did not consider that the circumstances warranted a ruling of a breach of Clause 2 and ruled no breach of that Clause.

Complaint received **6 October 2017**

Case completed **19 January 2017**

CASE AUTH/2986/10/17

ANONYMOUS, NON-CONTACTABLE v TEVA

Conduct of a representative

An anonymous, non-contactable complainant alleged that between July 2017 and October 2017, a named individual, employed by Teva as an account manager contacted/visited a named private hospital and falsely presented him/herself as an authorised adviser/specialist of another company with regard to that company's cell-based autologous product which was strictly regulated in the UK by the Medicines and Healthcare products Regulatory Agency (MHRA) and the Human Tissue Authority (HTA).

The complainant stated that the representative in question had no authority to represent the other company. He/she had never been engaged by that company nor trained as required on its product or any of the company's standard operating procedures etc. The complainant submitted that the last contact between the representative and the hospital was an email to the hospital in October.

The detailed response from Teva is given below.

The Panel noted that the complainant was anonymous and non-contactable. The Constitution and Procedure for the Prescription Medicines Code of Practice Authority stated that anonymous complaints would be accepted but that like all other complaints, the complainant had the burden of proving his/her complaint on the balance of probabilities. All complaints were judged on the evidence provided by the parties. The complainant had provided no evidence to support his/her allegations and could not be contacted for more information.

The Panel noted that the parties' accounts differed. Teva stated that its representative had never visited the hospital in question and had never presented him/herself as a representative from another company.

The Panel noted, however, that according to Teva the representative had in a personal capacity, on request of a health professional, emailed a management consultant at the private hospital about the possibility of that hospital obtaining a HTA licence. The representative had previously worked with the health professional whilst employed by another pharmaceutical company. The health professional had provided a letter stating that the representative in question had not attended the private hospital either on his/her behalf or on behalf of the other company and that the representative had offered to help with the HTA licence application as a friend and ex-colleague. The Panel queried whether this account was entirely consistent with Teva's submission that the email was sent at the request of the health professional.

The Panel had some concerns about the representative's activities. The complainant had alleged that the representative had 'contacted/ visited' the hospital. Whilst Teva had submitted evidence in support of its position that the representative had not attended the hospital it was, nonetheless, agreed that the representative had emailed the hospital. The Panel noted the email sent by the representative and Teva's submission that the representative had acted as a private individual and friend of a health professional at another hospital. The Panel did not consider that the matter was so straightforward. The representative had previously, whilst employed by another pharmaceutical company, worked professionally with the health professional employed at another hospital and according to that health professional had gained the specialist knowledge to do the HTA forms correctly. The email thus related to the representative's professional expertise albeit whilst employed by another pharmaceutical company. According to the complainant, the representative was now employed in a relevant area although Teva had not commented in this regard. The email was sent from the representative's personal email account and its content implied a degree of familiarity with the recipient. The email did not make it clear that the representative was not acting on behalf of Teva or any other pharmaceutical company; it was not sufficiently clear about the status of the representative. From the email, it would not be unreasonable to assume that the representative was acting on behalf of a company including a pharmaceutical company. In the Panel's view, companies should give representatives clear and unambiguous guidance to cover such personal interactions. Such interactions, especially when they involved healthcare matters, might potentially be covered by the Code. Companies should be mindful of the impression given. The Panel considered that the email was inextricably linked to the representative's professional status and related to healthcare; it was thus covered by the Code. Whilst there was no evidence that the representative had stated that he/she represented a company with commercial interests in human tissue as alleged, the representative had not been sufficiently clear about his/her status as set out above and was thereby misleading on this point. High ethical standards had not been maintained by the representative and a breach of the Code was ruled.

The Panel considered that there was no evidence that the representative had sought an appointment or had an interview and so no breach of the relevant clause was ruled. Similarly, there was no allegation that the representative had sought to employ any

inducement or subterfuge in relation to an interview and thus no breach of the Code was ruled.

With regard to high standards, the Panel considered that the matter was covered in relation to the conduct of the representative by its ruling of a breach of the Code above. There was no evidence that the company had encouraged such activity. No breach of the Code was ruled.

The Panel noted its rulings above and considered that the circumstances did not warrant a ruling of a breach of Clause 2 which was used as a sign of particular censure and was reserved for such use.

An anonymous, non-contactable complainant complained about the conduct of a named representative with Teva UK Limited when he/she contacted/visited a named private hospital.

COMPLAINT

The complainant alleged that between July 2017 and October 2017, the representative in question contacted/visited the named hospital and falsely presented him/herself to the health professionals as an authorised, trained and specialist representative of another company. The representative presented himself/herself as an adviser/specialist of the company in the area of Human Tissue Authority (HTA) licensing for procurement, storage, supply, distribution and testing (including specific blood testing) of the company's cell-based autologous product which was strictly regulated in the UK by the Medicines and Healthcare products Regulatory Agency (MHRA) and the HTA. The complainant alleged that the representative did this whilst solely engaged and employed by Teva in a relevant role. The last contact between the representative and the hospital was an email from the representative to the hospital.

The complainant stated that the representative in question had no authority to present him/herself as representing the other company nor its products in any capacity or manner. The representative had never been engaged by that company and had never had the compulsory training on its human tissue regenerative product as required by the regulatory authorities. Nor was the representative trained on the other company's quality assurance/ quality management system, standard operating procedures, processes and pathways which were also a compulsory training requirement for representing the product or company.

When writing to Teva, the Authority asked it to consider the requirements of Clauses 2, 9.1, 15.2, 15.3 and 15.5 of the Code.

RESPONSE

Teva submitted that the representative had never visited the private hospital named by the complainant and in that regard it provided a copy of his/her call reporting summary for 1 June to 31 October 2017. Further, the representative had never presented him/herself to any health professional as an authorised, trained and specialist representative from another company. The representative had never promoted any products for Teva or any other organisation to any health professional at the private hospital in question and he/she had never represented the other company or any other organisation while employed by Teva. Teva noted that the other company knew about the complaint and had proactively stated that the representative had never represented that company.

Teva noted that the representative had emailed a management consultant at the private hospital at the request of a trauma and orthopaedic health professional employed at another hospital. The health professional wanted to establish a service and had asked the representative if he/she could assist with the forms, as a private individual and a personal friend, not as a pharmaceutical company representative. The health professional had proactively emailed Teva, to confirm this and express concern.

Teva submitted that the representative had maintained high standards at all times and had not employed any subterfuge or inducement; he/she had never visited the private hospital in question or misled anyone as to his/her identity or that of the company he/she represented. The company denied breaches of Clauses 9.1, 15.2, 15.3 and 15.5. As there were no activities associated with promotion the company also denied a breach of Clause 2.

PANEL RULING

The Panel noted that the complainant was anonymous and non-contactable. The Constitution and Procedure for the Prescription Medicines Code of Practice Authority stated that anonymous complaints would be accepted but that like all other complaints, the complainant had the burden of proving his/ her complaint on the balance of probabilities. All complaints were judged on the evidence provided by the parties. The complainant had provided no evidence to support his/her allegations and could not be contacted for more information.

The Panel noted that the parties' accounts differed. The Panel noted that Teva denied the allegations. It stated that its representative had never visited the hospital in question and in support provided a copy of the representative's call reporting summary for 1 June to 31 October 2017. In addition, Teva submitted that the representative had never represented him/herself as a representative from any another company.

The Panel noted however that according to Teva the representative had in a personal capacity emailed a management consultant at the private hospital at the request of a trauma and orthopaedic health professional about the possibility of that hospital obtaining a HTA licence. The email stated that the representative was happy to support the application of a licence. The representative had previously worked with the health professional whilst employed by another pharmaceutical company. The health professional had provided a letter stating that

the representative in question had not attended the private hospital either on his/her behalf or on behalf of the other company and stated that the representative in question had offered to help him/her with the HTA licence application in his/her own time, as a friend and ex-colleague. The Panel queried whether this account was entirely consistent with Teva's submission that the email was sent at the request of the health professional.

The Panel had some concerns about the representative's activities. The Panel noted that the complainant alleged that the representative in question had 'contacted/visited' the hospital. The Panel noted that the complainant was anonymous and non-contactable. Whilst Teva had submitted evidence in support of its position that the representative had not attended the hospital it, nonetheless, agreed that the representative had emailed the hospital. The Panel noted the email sent by the representative and Teva's submission that the representative had acted as a private individual and friend. The Panel did not consider that the matter was so straightforward. The representative had previously, whilst employed by another pharmaceutical company, worked professionally with the health professional and according to him/her had gained the specialist knowledge to do the HTA forms correctly. The email thus related to the representative's professional expertise albeit whilst employed by another pharmaceutical company. According to the complainant, the representative was now employed in a relevant therapeutic area although Teva had not commented in this regard. The email was sent from the representative's personal email account and its content implied a degree of familiarity with the management consultant. The email did not make it clear that the representative was not acting on behalf of Teva or indeed any other pharmaceutical company. In the Panel's view the email was not sufficiently clear about the status of the representative. It would not be unreasonable for anyone reading the email to assume that the representative was acting on behalf of a company including a pharmaceutical company. In the Panel's view, companies should give representatives clear and unambiguous guidance to cover such personal interactions. Such interactions, especially when they involved healthcare matters, might potentially be covered by the Code. Companies should be mindful of the impression given by such activities. The Panel considered that the email was inextricably linked to the representative's professional status and related to healthcare; it was thus covered by the Code. Whilst there was no evidence before the Panel that the representative had stated that he/she represented the other company, a company with relevant commercial interests in human tissue as alleged, the representative had not been sufficiently clear about his/her status as set out above and was thereby misleading on this point. High ethical standards had not been maintained by the representative and a breach of Clause 15.2 was ruled.

The Panel considered that there was no evidence that the representative had sought an appointment or had an interview and thus considered that Clause 15.5 did not apply. No breach of that clause was ruled. Similarly, there was no allegation that the representative had sought to employ any inducement or subterfuge in relation to an interview and thus Clause 15.3 did not apply. No breach of Clause 15.3 was ruled.

With regard to Clause 9.1, the Panel considered that the matter was covered in relation to the conduct of the representative by its ruling of a breach of Clause 15.2. There was no evidence before the Panel that the company had, in any way, encouraged such activity. No breach of Clause 9.1 was ruled.

The Panel noted Teva's submission that as there were no activities associated with promotion there could be no breach of Clause 2. The Panel considered that it was important to note that Clause 2 was broadly interpreted as evidenced by published cases and the relevant supplementary information which included breaches of undertaking and other non-promotional activities and materials. Nonetheless, the Panel noted its rulings above and considered that the circumstances did not warrant a ruling of a breach of Clause 2 which was used as a sign of particular censure and was reserved for such use.

Complaint received **24 October 2017**

Case completed **11 January 2018**

CASE AUTH/2990/11/17

VOLUNTARY ADMISSION BY ABBVIE

Failure to comply with examination requirements

AbbVie voluntarily admitted that one of its representatives had not taken an appropriate examination within one year of starting such employment and nor had he/she passed it within the first two years of being so employed.

In accordance with Paragraph 5.6 of the Constitution and Procedure, the Director treated the matter as a complaint.

The detailed submission by AbbVie is given below.

The Panel noted that the Code required that representatives must take an appropriate examination within their first year of employment and pass it within two years of starting such employment. The representative in question had commenced such employment in October 2015. The representative first sat some of the examination modules in November 2016 and passed one; a further two modules were sat and passed July 2017. Four other modules were each taken on at least two occasions and had not been passed. As acknowledged by AbbVie the requirements of the Code had not been met; an appropriate examination had not been taken within the first year of employment and had not been passed within two years. A breach of the Code was ruled.

AbbVie Ltd voluntarily admitted a breach of the Code in that one of its representatives failed to pass an appropriate examination within two years of starting such employment.

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

VOLUNTARY ADMISSION

AbbVie noted that Clause 16.3 provided that first time pharmaceutical representatives must take an 'appropriate examination' within the first year of employment 'and pass it within two years of starting such employment'. AbbVie had recently noted that a representative who joined the company in October 2015 did not take all of the ABPI examination units within the first year of employment. This individual's role at AbbVie was the first time he/she was employed in the pharmaceutical industry. Once this breach of Clause 16.3 was known, the employee was promptly withdrawn from working in the field pending the outcome of a disciplinary process.

AbbVie had reviewed the representative's conduct against the company's standard operating procedure (SOP) and declaration/training requirements.

AbbVie noted that its 'ABPI Code of Practice Training' SOP specifically required representatives to take the ABPI Examination, and it also set out roles and responsibilities for line managers and human resources ('HR') to ensure representatives had the qualifications required for their role. In particular:

- adherence to the Code was a condition of employment and failure to adhere to it was a disciplinary offence and could result in the termination of employment; and
- it was an express requirement of the SOP that representatives must take an appropriate examination within their first year of employment as a representative and must pass it within two years of starting such employment.

The representative and his/her line manager completed training on this SOP. The representative's current line manager raised the representative's failure to take the appropriate examination and pass it with human resources (HR) in October 2017.

On joining AbbVie, all representatives had to certify that they had read and understood the meaning and the applicability of the Code to their role. The representative in question signed this declaration before starting employment with AbbVie.

All representatives had to complete in-house annual Code training. The training was supplementary to the Code and all applicable AbbVie policies and procedures. All documents had to be read and understood, which was confirmed in writing. This training covered topics such as:

- scope of Code and how it was regulated
- promotion and non-promotional activities – considerations and approval requirements
- items for patients, promotional aids, the provision for medical and educational goods and services, agreements to patients such as joint working, outcome agreements and patient access schemes
- meetings, hospitality and sponsorship
- use of consultants and transfers of values
- principles of communicating with the public, media and digital communications.

Although the representative in question completed this training in accordance with AbbVie's requirements, he/she did not comply with the requirement to take the requisite examinations.

AbbVie explained that the representative's contract of employment included a clause that his/her role was subject to obtaining the ABPI Examination qualification and abiding with the Code. AbbVie stated that as a result of the representative in

question's conduct, the company was currently following an appropriate disciplinary process.

AbbVie submitted that in the first quarter of 2017, in order to ensure timely communication between HR, a line manager and AbbVie's learning and development team, it had implemented a new process for recording and monitoring the education of representatives.

AbbVie stated that, out of an abundance of caution, it would review the examination status of all of its representatives.

AbbVie was asked to provide the Authority with any further comments in relation to the requirements of Clause 16.3.

RESPONSE

AbbVie provided full details of the representative's examination history.

As the representative started employment in October 2015, he/she failed to take the initial unit(s) within the first year of employment and pass all ten units by October 2017. AbbVie stated that when it was notified of this by the representative's current line manager, the representative was withdrawn from the field and told that he/she should not communicate with any customers either directly or indirectly. This remained the case until the outcome of the disciplinary process was known.

PANEL RULING

The Panel noted that Clause 16.3 required that representatives must take an appropriate examination within their first year of employment and pass it within two years of starting such employment. The representative had commenced employment as a representative in October 2015. One module was sat and passed in November 2016 and a further two modules were sat and passed July 2017. Four other modules were each taken on at least two occasions and had not been passed. As acknowledged by AbbVie the requirements of Clause 16.3 had not been met; an appropriate examination had not been taken within the first year of employment and had not been passed within two years, a breach of that clause was ruled.

Voluntary admission received	**2 November 2017**
Case completed	**12 January 2018**

CODE OF PRACTICE REVIEW – February 2018

Cases in which a breach of the Code was ruled are indexed in **bold type.**

AUTH/2951/4/17	**Consultant physician v Sanofi**	**Promotion of Toujeo**	**Breaches Clauses 7.2, 7.4, 9.1 and 15.9**	**No appeal**	**Page 3**
AUTH/2968/8/17	Director/Media v Bausch & Lomb	Promotion of Emerade	No breach	No appeal	Page 9
AUTH/2972/8/17	**Anonymous, non-contactable v UCB**	**UCB website**	**Breaches Clauses 2, 7.2** **Three breaches Clause 9.1** **Breach Clauses 14.5 and 26.2**	**No appeal**	**Page 13**
AUTH/2974/9/17	Anonymous, non-contactable clinician v ViiV Healthcare	Alleged promotion to the public	No breach	No appeal	Page 18
AUTH/2975/9/17	**Voluntary admission by A Menarini**	**Late disclosure of research and development transfer of value**	**Breach Clause 24.2**	**No appeal**	**Page 21**
AUTH/2976/9/17	**Hospital consultant v AstraZeneca**	**Email promotion of Qtern**	**Breaches Clauses 7.2, 9.1, 9.9, 11.1 and 12.1**	**No appeal**	**Page 22**
AUTH/2981/9/17	Member of the public v ViiV Healthcare	Use of an iPad in public	No breach	No appeal	Page 26
AUTH/2983/10/17	**Anonymous, non-contactable clinician v Celgene**	**Promotion of Abraxane to the public**	**Breach Clause 9.1** **Two breaches Clause 26.2**	**No appeal**	**Page 28**
AUTH/2986/10/17	**Anonymous, non-contactable v Teva**	**Conduct of a representative**	**Breach Clause 15.2**	**No appeal**	**Page 34**
AUTH/2990/10/17	**Voluntary admission by AbbVie**	**Failure to comply with examination requirements**	**Breach Clause 16.3**	**No appeal**	**Page 37**

PMCPA | Prescription Medicines Code of Practice Authority

The Prescription Medicines Code of Practice Authority was established by the Association of the British Pharmaceutical Industry (ABPI) in 1993 to operate the Code of Practice for the Pharmaceutical Industry at arm's length from the ABPI itself. Compliance with the Code is obligatory for ABPI member companies and, in addition, over sixty non member companies have voluntarily agreed to comply with the Code and to accept the jurisdiction of the Authority.

The Code covers the advertising of medicines to health professionals and other relevant decision makers and also covers information about prescription only medicines made available to the public.

It covers:

- journal and direct mail advertising
- the activities of representatives, including any printed or electronic material used by them
- the supply of samples
- the provision of inducements in connection with the promotion of medicines and inducements to prescribe, supply, administer, recommend, buy or sell medicines by the gift, offer or promise of any benefit or bonus, whether in money or in kind
- the provision of hospitality
- the organisation of promotional meetings
- the sponsorship of scientific and other meetings, including payment of travelling and accommodation expenses
- the sponsorship of attendance at meetings organised by third parties
- all other sales promotion in whatever form, such as participation in exhibitions, the use of audio or video-recordings in any format, broadcast media, non-print media, the Internet, interactive data systems, social media and the like.

It also covers:

- the provision of information on prescription only medicines to the public either directly or indirectly, including by means of the Internet
- relationships with patient organisations
- disclosure of tranfers of value to health professionals and organisations
- joint working between the NHS and pharmaceutical companies
- the use of consultants
- non-interventional studies of marketed medicines
- the provision of items for patients
- the provision of medical and educational goods and services
- grants, donations and benefits in kind to institutions.

Complaints submitted under the Code are considered by the Code of Practice Panel which consists of three of the four members of the Code of Practice Authority acting with the assistance of independent expert advisers where appropriate. One member of the Panel acts as case preparation manager for a particular case and that member does not participate and is not present when the Panel considers it.

Both complainants and respondents may appeal to the Code of Practice Appeal Board against rulings made by the Panel. The Code of Practice Appeal Board is chaired by an independent legally qualified Chairman, Mr William Harbage QC, and includes independent members from outside the industry. Independent members, including the Chairman, must be in a majority when matters are considered by the Appeal Board.

In each case where a breach of the Code is ruled, the company concerned must give an undertaking that the practice in question has ceased forthwith and that all possible steps have been taken to avoid a similar breach in the future. An undertaking must be accompanied by details of the action taken to implement the ruling. Additional sanctions are imposed in serious cases.

Further information about the Authority and the Code can be found at www.pmcpa.org.uk

Complaints under the Code should be sent to the Director of the Prescription Medicines Code of Practice Authority, 7th Floor, Southside, 105 Victoria St, London SW1E 6QT

telephone 020 7747 8880
facsimile 020 7747 8881
by email to: complaints@pmcpa.org.uk.