CASE AUTH/3017/2/18

ANONYMOUS CONTACTABLE v CELGENE

Certification and approval of material for meetings

An anonymous, contactable complainant complained about a number of 'meetings in a box' materials produced by Celgene UK for use by its representatives. The material related to Otezla (apremilast) which was indicated for the treatment of adults with psoriatic arthritis or moderate to severe chronic plaque psoriasis.

The complainant alleged that the materials were not certified and were never approved for use by representatives. The immunology and inflammation (I&I) senior team knew this and sought to repress it rather than be transparent.

The detailed response from Celgene is given below.

The Panel noted that the complainant referred specifically to seven materials. The Panel noted that Celgene listed a further eighteen materials, the Panel noted that the only material that it considered from Celgene's list was the briefing document because although not specifically referred to by the complainant, it related to the training of the materials at issue which was a matter raised by the complainant.

The Panel noted Celgene's submission that all meetings in a box materials were withdrawn on 5 January 2018 because a final signatory did not consider that the wording on the job bag summary made it clear that the materials were intended for use by health professionals as well as for use by representatives.

In the Panel's view it was vital that signatories were given accurate information about the intended use and dissemination of materials. When materials were to be used both by representatives and by health professionals that should be made clear.

The Panel noted Celgene's submission that the wording on the job bag summaries could be construed to mean that the materials were for use only by the representatives to present and that was the information provided to the final signatories when certifying. Therefore in the Panel's view the materials and use by health professionals had not been certified and thus a breach of the Code was ruled. The Panel considered that Celgene had failed to maintain high standards on this point and a breach of the Code was ruled. Conversely and contrary to the complainant's allegation the use of the materials in question by representatives had been certified and no breach of the Code was ruled in that regard.

The Panel noted Celgene's submission that representatives were all extensively trained on the content of the meetings in a box materials as these data were also used in the then current promotional materials, such as detail aids Celgene had not provided a copy of the detail aids and other materials current at the relevant time and did not refer to or provide any relevant briefing on these materials. The Panel queried whether representatives had been properly trained on the specific content of the meetings in a box modules rather than merely being familiar with them. The Panel queried whether

familiarity was sufficient and was concerned, given that the meetings started in February 2017, that representatives only received further specific and detailed training on some of the meetings in a box materials in September 2017. Taking all of the circumstances into account the Panel decided on balance that detailed briefing on the clinical content of the meetings in a box modules had not been provided prior to their first use in February 2017 and a breach of the Code was ruled. The Panel considered that failure to brief representatives on the clinical content of the meetings in a box slide decks prior to their first use in February 2017 meant that Celgene had failed to maintain high standards and a breach of the Code was ruled.

The Panel noted that a briefing document for the meetings in question was certified on 6 March 2017, after the first meeting in a box meeting took place on 28 February. The Panel noted that the briefing material in question covered process and did not cover their clinical content. In the Panel's view the briefing material in question on the approval process should have been certified in advance of the first meeting being planned. The Panel noted Celgene's submission that this single briefing document was used prior to certification and a breach of the Code was ruled. The Panel considered that failing to certify the briefing document prior to its first use meant that Celgene had failed to maintain high standards and a breach of the Code was ruled.

The Panel noted that the complainant had provided no evidence in support of his/her allegation that the senior I&I team tried to repress the fact that the team was using uncertified materials and therefore ruled no breach of the Code.

The Panel noted its rulings and comments above. The Panel noted that Celgene had been the subject of PMCPA audits and had subsequently initiated a number of compliance initiatives. The Panel did not consider that this case warranted a ruling of a breach of Clause 2 which was a sign of particular censure and reserved for such. No breach of Clause 2 was ruled.

An anonymous, contactable complainant complained about a number of 'meetings in a box' materials (refs UK-I&I160318 (a-g)) produced by Celgene UK for use by its representatives. The material related to Otezla (apremilast) which was indicated for the treatment of adults with psoriatic arthritis or moderate to severe chronic plaque psoriasis.

COMPLAINT

The complainant alleged that the materials were trained to and used by the representative with customers without proper certification or approval. According to the complainant the materials were never approved for use by representatives. The immunology and inflammation (I&I) senior team knew this and sought to repress it rather than be transparent. The complainant stated that there was a big culture of not wanting to put anything in writing for fear of creating evidence for a later date and so the complainant was not convinced that the Authority would find written evidence. It was 'lucky' for Celgene that the prescribing information needed updating and as such it sought to repress the use of improper certified materials by the representatives with the prescribing information update.

When writing to Celgene, the Authority asked it to consider the requirements of Clauses 2, 9.1, 14.1 and 15.9 of the Code.

RESPONSE

Celgene submitted that the meetings in a box consisted of a series of modular PowerPoint presentations which contained a standard set of slides, produced by the I&I department, to be approved for certification under the Code. The PowerPoint presentations were short and designed to cover specific topics; they were prepared based on the information contained in the Otezla detail aid and general information on psoriasis and psoriatic arthritis, which had been previously presented to the representatives. The slide decks were made available to the representatives for use by attendees at on-label, promotional, locally run (Type B) meetings. Type B meetings were representative-led Celgene speaker meetings, hosted by representatives, during which health professional speakers also presented. During some meetings, the health professional would be asked to present the meeting in a box slide decks, rather than the representatives.

The Otezla meeting in a box slide deck (refs UK-I&I 160318(a-g)) was made up of seven modules, referred to by the complainant:

1 Psoriasis- Disease Burden Module (ref UK-I&I160318a)
2 Psoriatic Arthritis- Disease Burden Module (ref UK-I&I160318b)
3 Psoriasis- Unmet Needs Module (ref UK-I&I160318c)
4 Ref UK-I&I160318d (withdrawn, not used)
5 Otezla Clinical Evidence in Psoriasis Module (ref UK-I&I160318e)
6 Otezla Clinical Evidence in Psoriatic Arthritis Module (ref UK-I&I160318f)
7 Otezla Clinical Practice in Psoriasis Module (ref UK-I&I160318g)

The original materials were certified and approved between February and March 2017. This was before the PMCPA re-audit in May 2017 and, following the re-audit, the implementation of 47 compliance-related CAPAs.

In addition to the original set of seven modules, 18 additional slide decks were produced details were provided.

All of the job bags for each module were approved and certified for use by representatives in the UK & Ireland, with the exception of one, which was cancelled, and never distributed or used.

The representatives had been trained on the content of the slide decks from previously approved materials, including the detail aid, and during their initial training course. The meetings in a box briefing document (ref UK-I&I160318y) and the briefing on template slide (ref UK-I&I160318z) were produced specifically to guide the representatives on how to use the materials in the field. Further training was provided during an internal meeting in September 2017 and this included the Psoriatic Arthritis Mode Of Action Slide Deck briefing document (ref UK-I&I160318ae) and the Psoriasis Mode Of Action briefing document (ref UK-I&I160318af).

All four of the briefing documents were certified. However, one of the briefing documents (UK-I&I160318y) was certified on 6 March 2017, which was after the first meeting in a box meeting took place on 28 February. This single use of a briefing document occurred before the PMCPA re-audit in May 2017 after which Celgene put in place 47 corrective and preventative actions, specifically to address a number of compliance issues and to prevent further occurrences. For example, all Zinc account holders had undergone full refresher training and Zinc Maps validation. In addition, a permanent healthcare compliance specialist role had been created and

filled, with responsibility for ongoing monitoring of Zinc job map quality and adherence to relevant standard operating procedures (SOPs) and working practices, including active job bag checking and quality and compliance checking of ongoing job bags. All final signatories had been validated following Celgene's established final signature training and validation process.

Celgene explained that the representatives had used the meetings in a box materials or materials modified from the initial slide decks in around 30 meetings between February and December 2017. Ten meetings used meetings in a box materials (UK-I&I160318a, b, c, e, f, g) and the others used other slide decks from the meetings in a box series or materials that were modified versions of the original meetings in a box materials (where, for example, a health professional wished to add slides detailing patient cases). All arrangements and all materials used for these promotional meetings were reviewed and approved by a final nominated medical signatory before each meeting took place.

Celgene noted that the complainant has suggested that the I&I senior team sought to repress the use of uncertified materials, stating that Celgene was 'lucky' that the prescribing information needed updating. Although the prescribing information was due to be updated, this was not the main reason why the materials were withdrawn. In December 2017, one of the final signatories reviewed the meetings in a box materials and noted that the statement contained in the job summary was not completely clear; the wording on the job bag summary stated: "This is the Meetings in a Box (MIB) Slide deck that will be used for by [representatives] in Local Type B meetings". The final signatory did not consider that this wording made it clear that the meetings in a box materials were intended for use by representatives, as well as for use by health professionals. The wording on the job bag summary could be construed to mean that the materials were for use only by the representatives to present, which was not the original intent of the activity. It was decided, therefore, to withdraw the materials and raise new job bags, so that the job bag summary information could be updated to state more clearly that health professionals in addition to representatives could present the meetings in a box material.

Based on the decision to clarify the job bag wording and the additional requirement to update materials following a prescribing information update, all materials pertaining to the meetings in a box were withdrawn on 5 January 2018.

Following receipt of this anonymous complaint, Celgene carried out a number of interviews with members of the Celgene I&I senior team, product team and representatives.

The internal understanding was that the meetings in a box materials were approved for use by representatives and by health professionals in promotional meetings. The materials were based on data in the current detail aids used by the representatives; this was why there was no extensive representative training provided at the start of 2017. However, training was given at the Cycle meeting in September 2017, which the representatives found to be highly valuable.

None of the individuals interviewed were aware of the concerns raised with regard to the meetings in a box material being used without approval, and all representatives understood how the meetings in a box materials were to be used. Meetings in a box materials were approved prior to use at promotional meetings.

Celgene submitted that the compliance environment within the company had improved significantly over the last 18 months. There were no remarks from the interviewees about leadership trying to repress or avoid putting things in writing. One of the outcomes of the May

2017 re-audit was to improve the speak-up culture within the company. Celgene had established a network of compliance champions throughout the affiliate who provided advice, signposting and additional checks within teams. Interviewees noted that these individuals were highly valued. In addition, 24 Speak Up meetings were held in September and October 2017, hosted by the Celgene Leadership Team, seeking feedback on compliance initiatives, to refine processes and approaches, and identify areas that required continuing focus.

With regard to Clause 9.1, Celgene noted that its compliance programme included policies, SOPs 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 throughout 2017 and early 2018. All of the 22 job bags for each module comprising the meetings in a box activity were approved and certified for use in the UK & Ireland. Three of the four briefing documents were compiled, approved and certified on time for the meetings in a box meetings with the exception of the first briefing document (ref UK-I&I160318y) which was certified on 6 March 2017, after the first meetings in a box meeting which was held on 28 February 2017.

All job bags for each module of the meetings in a box were approved and certified for use in the both the UK & Ireland before all of the promotional meetings held between February through December 2017 which involved the use of meetings in a box materials in their original or modified form. The representatives were previously trained on the data content of the meetings in a box decks as these same data were included in current promotional materials. Further training was provided in September 2017.

Celgene submitted that the PMCPA should take an overall view, and such an isolated incident should not trigger a breach. While Celgene regretted the failure of the final certification of the briefing document (ref UK-I&I160318y), the company has since been through a full audit procedure. Following the recommendations that came out of the May 2017 re-audit, the company had followed up on 47 compliance-related CAPAs. As a result, Celgene's procedures relating to compliance had been significantly strengthened and improved, which the PMCPA would have found during its re-audit of Celgene on 1 February 2018. Celgene, therefore, believed that high standards had been maintained and there had been no breach of Clause 9.1.

All the material pertaining to the meetings in a box meetings was duly approved and certified by at least one person on behalf of the company in the manner provided for by Clause 14.1, except for the final certification of the briefing document (ref UK-I&I160318y). The company regretted the failure but had put in place a number of measures to ensure that its certification processes followed internal SOPs and were in adherence with the Code.

With regard to Clause 15.9, the representatives were all extensively trained on the content of the meetings in a box materials, as these data were also used in current promotional materials, such as detail aids. The representatives were also extensively trained during their initial training courses. In addition, they received further training on the meetings in a box materials in September 2017, with the involvement of the medical department. All of the briefing materials and all of the meetings in a box materials were appropriately generated, reviewed and certified by at least one final nominated medical signatory. Three of the four briefing documents were compiled, approved and certified on time for the meetings in a box meetings with the exception of the briefing document (ref UK-I&I160318y) which was certified on 6 March, after the first meetings in a box meeting on 28 February 2017. However as stated above, the representatives

had already received extensive training on the content of the meetings in a box decks before the first meeting which used these materials. Celgene denied a breach of Clause 15.9.

Celgene noted that its I&I team had approved and certified all materials and all of the arrangements related to the promotional meetings that took place in 2017 that used either the original meetings in a box materials or modified meetings in a box materials. Briefing material to instruct the representatives on how to use the material had been appropriately compiled, reviewed and certified. The representatives had been extensively trained on the data content of the meetings in a box material. In addition, from the interviews that were conducted with members of the I&I senior team and six representatives, there was no evidence of the intention to suppress the use of improperly certified material used by the representatives. Celgene thus did not consider that the activities of its I&I team had brought discredit upon, or reduced the confidence in the industry; the company denied a breach of Clause 2.

In conclusion, Celgene hoped that the above addressed the PMCPA's questions about the development and use of the meetings in a box materials. The company would be happy to answer any additional questions or provide any further information if required. Celgene noted that the complaint referred to materials certified and approved in early 2017. Since then, the company had been through a full PMCPA audit procedure and had implemented a number of initiatives that had significantly strengthened and improved the company's compliance environment. The company had focused its efforts on further improving its SOPs; building up the Speak Up culture; improving the quality of its materials and undergone a full ZINC review process. This complaint therefore pre-dated a number of significant changes that had been made to Celgene's compliance environment, as the PMCPA would have observed during its recent re-audit in February 2018.

PANEL RULING

The Panel noted that the complainant was initially contactable but the email address given was now no longer in use. The Panel noted that the complainant bore the burden of proof on the balance of probabilities. A judgement had to be made based on the available evidence.

The Panel noted that the complainant referred specifically to materials (refs UK-I&I160318 (a-g)). The Panel noted that Celgene raised a further eighteen materials, the Panel noted that the only material that it considered from that list was the briefing document (ref UK-I&I160318y) because although not specifically referred to by the complainant, it related to the training of the materials at issue which was a matter raised by the complainant.

The Panel noted Celgene's submission that the Otezla meetings in a box modules (UK-I&I 160318 (a-g)) were certified between February and March 2017 for use by the key account managers (KAM) at KAM-led speaker meetings between February and December 2017 with the exception of UKI&I160318d, which was cancelled, and never distributed or used. The Panel noted Celgene's submission that all meetings in a box materials were withdrawn on 5 January 2018 because a final signatory did not consider that the wording on the job bag summary made it clear that the materials were intended for use by health professionals as well as for use by representatives. There was also an additional requirement to update the materials following a prescribing information update.

In the Panel's view it was vital that signatories were given accurate information about the intended use and dissemination of materials. When materials were to be used both by representatives and by health professionals that should be made clear.

The Panel noted Celgene's submission that the wording on the materials' job bag summaries could be construed to mean that the materials were for use only by the representatives to present and that was the information provided to the final signatories when certifying. This was inaccurate and was subsequently noted as such by a final signatory in December 2017. Therefore in the Panel's view the materials (UK-I&I 160318 (a-c) and (e-g)) use by health professionals had not been certified and thus a breach of Clause 14.1 was ruled. The Panel considered that Celgene had failed to maintain high standards on this point and a breach of Clause 9.1 was ruled. Conversely and contrary to the complainant's allegation the use of the materials in question by representatives had been certified and no breach of Clause 14.1 was ruled in that regard.

The Panel noted that Clause 15.9 required that companies must prepare detailed briefing material for medical representatives on the technical aspects of each medicine which they will promote. Briefing material must comply with the relevant requirements of the Code and was subject to the certification requirements of Clause 14. The Panel noted Celgene's submission that representatives were all extensively trained on the content of the meetings in a box materials as these data were also used in the then current promotional materials, such as detail aids and representatives were also extensively trained during their initial training courses. Celgene had not provided a copy of the detail aids and other materials current at the relevant time and did not refer to or provide any relevant briefing on these materials. The Panel queried whether representatives had been properly trained on the specific content of the meetings in a box modules rather than merely being familiar with them. The Panel queried whether familiarity was sufficient and was concerned, given that the meetings started in February 2017, that representatives only received further specific and detailed training on some of the meetings in a box materials in September 2017, which they found to be highly valuable. Taking all of the circumstances into account the Panel decided on balance that detailed briefing on the clinical content of the meetings in a box modules had not been provided prior to their first use in February 2017 and a breach of Clause 15.9 was ruled. The Panel considered that failure to brief representatives on the clinical content of the meetings in a box slide decks prior to their first use in February 2017 meant that Celgene had failed to maintain high standards and a breach of Clause 9.1 was ruled.

The Panel noted that a briefing document (UK-I&I160318y) for the meetings in question was certified on 6 March 2017, after the first meeting in a box meeting took place on 28 February. The Panel noted that the briefing material in question covered process: the roll-out of the pre-approved slide decks to the field force and the process for promotional slide approval. It did not cover their clinical content. In the Panel's view the briefing material in question on the approval process should have been certified in advance of the first meeting being planned. The Panel noted Celgene's submission that this single briefing document was used prior to certification and a breach of Clause 14.1 was ruled. The Panel considered that failing to certify the briefing document prior to its first use meant that Celgene had failed to maintain high standards and a breach of Clause 9.1 was ruled.

The Panel noted that the complainant had provided no evidence in support of his/her allegation that the senior I&I team tried to repress the fact that the team was using uncertified materials and therefore ruled no breach of Clause 9.1.

The Panel noted its rulings and comments above. The Panel noted that Celgene had been the subject of PMCPA audits and had subsequently initiated a number of compliance initiatives. The Panel did not consider that this case warranted a ruling of a breach of Clause 2 which was a sign of particular censure and reserved for such. No breach of Clause 2 was ruled.

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During the consideration of this case the Panel was concerned to note the number of items that were certified with an inaccurate method of dissemination information and that it took almost a year to identify the issue. The Panel noted that the Authority had previously audited Celgene and was aware that in March 2016 it was identified that Type B meeting slides were not certified and was disappointed that there were issues with the certification of said meeting materials discovered in January 2018. The Panel requested that Celgene be advised of its concerns.

Complaint received **31 January 2018**

Case completed **2 August 2018**