CASE AUTH/2620/7/13

NOVO NORDISK/DIRECTOR V SANOFI

Breach of undertaking

Novo Nordisk alleged that a claim for Lyxumia (lixisenatide) in a journal supplement about diabetes management, breached the undertaking given by Sanofi in Case AUTH/2604/5/13.

As the complaint was about an alleged breach of undertaking, it was taken up by the Authority in the name of the Director as the Authority was responsible for ensuring compliance with undertakings.

The detailed response from Sanofi is given below.

The Panel noted that an undertaking was an important document. Companies had to give an undertaking that the material in question and any similar material, if not already discontinued or no longer in use, would cease forthwith and give an assurance that all possible steps would be taken to avoid similar breaches of the Code in the future. It was very important for the reputation of the industry that companies complied with undertakings.

The Panel disagreed with Sanofi's submission that the supplement was entirely different from the advertisement previously at issue and the implication that it was thus not covered by the undertaking in Case AUTH/2604/5/13. The undertaking covered all closely similar materials.

The Panel noted that Case AUTH/2604/5/13, concerned an advertisement which, *inter alia*, claimed that 'Lyxumia is the only once-daily GLP-1 receptor agonist licensed for type 2 diabetes mellitus patients not optimally controlled on oral antidiabetic drugs and/or basal insulin'. The claim now at issue, 'Lyxumia is the *only once-daily* GLP-1RA that is licensed for use in combination with basal insulin and/or oral glucose lowering agents', was worded differently and 'only once-daily' was not emboldened.

Lyxumia and Novo Nordisk's product Victoza (liraglutide) were both licensed as adjunctive therapy – to be added to existing antidiabetic therapy to achieve improved glycaemic control. Both medicines could be added to existing oral antidiabetic (OAD) therapy but only Lyxumia was also indicated to be added to an existing treatment regimen which included basal insulin. The Panel considered that the use of 'and/or' in the claim did not make this distinction between the two medicines entirely clear. The claim meant that Lyxumia was the only once-daily GLP-1 RA that was licensed for use in combination with basal insulin alone, in combination with OADs and basal insulin and in combination with OADs. The Panel accepted that, in the round, this claim was true, but considered that the 'and/or' made it unclear as to what 'only' referred to. Whilst the earlier two treatment scenarios were correct in that only Lyxumia could be added to existing basal insulin therapy, the last was not; both Victoza and Lyxumia could given in combination with OAD therapy. The Panel considered that the claim was misleading and ambiguous and sufficiently similar to that at issue in Case AUTH/2604/5/13 to be covered by the previous undertaking. The Panel therefore ruled a breach of the undertaking. High standards had not been maintained and a breach was ruled. These rulings were appealed.

The Panel noted Sanofi's account of its review and withdrawal of material following resolution of matters during inter-company dialogue and prior to notification of the ruling and provision of the undertaking in Case AUTH/2604/5/13. It appeared that Sanofi had not validated the decisions made during its withdrawal process after providing its undertaking in Case AUTH/2604/5/13 dated 25 June 2013. The Panel was concerned that the supplement in question had appeared in the Nursing Times on 10 July 2013. The copy deadline for the journal to receive the supplement was after Sanofi had signed its undertaking in Case AUTH/2604/5/13 and as such Sanofi could have prevented the supplement from being published.

The Panel noted its comments above about the importance of compliance with undertakings. The Panel considered that the conduct of Sanofi in this regard had brought discredit upon, and reduced confidence in, the pharmaceutical industry. A breach of Clause 2 was ruled. This ruling was appealed.

The Panel noted that this was the second time that Sanofi had breached the undertaking given in Case AUTH/2604/5/13 (Case AUTH/2619/7/13). The Panel was very concerned as it appeared Sanofi had not paid sufficient attention to ensure that its materials were comprehensively reviewed. The Panel considered Sanofi's conduct warranted further consideration and reported the company to the Code of Practice Appeal Board under Paragraph 8.2 of the Constitution and Procedure for it to consider whether further sanctions were necessary.

The Appeal Board noted that the claim at issue in Case AUTH/2604/5/13, 'Lyxumia is the only once-daily GLP-1 receptor agonist licensed for type 2 diabetes mellitus patients not optimally controlled on oral antidiabetic drugs and/or basal insulin' appeared in an advertisement. The claim now at issue 'Lyxumia is the only once-daily GLP-1RA that is licensed for use in combination with basal insulin and/or oral glucose lowering agents' appeared in a promotional supplement in a non-specialist journal. The Appeal Board noted that although the claims were not identical they were very similar; both contained 'and/or' which made the meaning of

'only' unclear. The Appeal Board noted that whilst Lyxumia was the only GLP-1RA that could be added to basal insulin it was not the only GLP-1RA that could be added to existing oral antidiabetic (OAD) therapy and thus the claim was misleading in that regard.

The Appeal Board considered that the claim in the supplement was so similar to that in the advertisement that it was covered by the undertaking given in Case AUTH/2604/5/13 and it upheld the Panel's ruling in that regard. In addition high standards had not been maintained and the Appeal Board upheld the Panel's ruling of a breach. The appeal on both points was unsuccessful.

In failing to comply with its undertaking the Appeal Board considered that Sanofi had brought discredit upon, and reduced confidence in, the pharmaceutical industry. The Appeal Board upheld the Panel's ruling of a breach of Clause 2. The appeal on this point was unsuccessful.

The Appeal Board noted that the journal supplement at issue had been certified the day after the undertaking in Case AUTH/2604/5/13 had been signed. Sanofi submitted that it had used the claim at issue in full knowledge of the undertaking and of the Panel's ruling in that case. In the Appeal Board's view, it should have been obvious to Sanofi that the claim in the supplement was so similar as to be almost the same as the claim at issue in Case AUTH/2604/5/13. That the claim was approved for use subsequent to the outcome of Case AUTH/2604/5/13, led the Appeal Board to query the rigour with which Sanofi had examined relevant materials to ensure compliance with its undertaking. After signing the undertaking, Sanofi had had time to cancel publication of the supplement. The Appeal Board noted that this was the second time that Sanofi had breached its undertaking given the Case AUTH/2604/5/13 (Case AUTH/2619/7/13) and so it decided, in accordance with Paragraph 11.3 of the Constitution and Procedure, to require an audit of the company's procedures in relation to the Code. The Appeal Board noted that Sanofi had already embarked on a programme of corrective measures and so it requested that the audit take place in March 2014 when the results of some of those measures should be obvious. In the meantime Sanofi should confirm in writing the measures it had implemented. On receipt of the audit report and Sanofi's comments upon it, the Appeal Board would consider if further sanctions were necessary.

Upon receipt of the March 2014 audit report, the Appeal Board noted a number of serious concerns regarding Sanofi's procedures and materials; the company had begun to address the issues including a change to the structure of company reporting, increasing compliance resource, training and updating its procedures and materials.

The Appeal Board decided that Sanofi should be re-audited in October 2014 at which point it expected to see changes implemented and significant progress made. Upon receipt of the report and Sanofi's comments upon it, the Appeal Board would decide whether further sanctions were necessary.

Upon receipt of the October 2014 audit report the Appeal Board noted that some progress had been made. However, the Appeal Board considered that there was still a lot of work to do and concerns to address. In addition the Appeal Board noted the recent issues raised concerning Sanofi's interaction with patient organisations (Case AUTH/2736/6/14). In relation to the re-audit in Case AUTH/2620/7/13, the Appeal Board decided to require a re-audit of Sanofi in March 2015 at the same time as the audit required in Case AUTH/2736/9/14; it would expect to see the recommendations of the October 2014 audit report implemented and significant progress made. On receipt of the re-audit report and Sanofi's comments upon it, the Appeal Board would consider whether further sanctions were necessary.

On receipt of the March audit report the Appeal Board noted that Sanofi had made progress since the audit in October 2014; a new, senior manager was fully involved and leading many of the company's compliance initiatives.

The Appeal Board however, noted its concern about some of the company's activities and considered that Sanofi should address the matters raised as a priority. On the basis that this work was completed, the progress otherwise shown in the March 2015 audit was continued and a company-wide focus and responsibility for compliance was maintained, the Appeal Board decided that no further action was required.

Novo Nordisk Limited alleged that, with regard to the promotion of Lyxumia (lixisenatide), Sanofi had breached its undertaking given in Case AUTH/2604/5/13. Lyxumia was a glucagon-like peptide-1 (GLP-1) receptor agonist (GLP-1RA) for the management of type 2 diabetes.

As the complaint was about an alleged breach of undertaking, it was taken up by the Authority in the name of the Director as the Authority was responsible for ensuring compliance with undertakings.

COMPLAINT

Novo Nordisk noted that in Case AUTH/2604/5/13, the claim 'Lyxumia is the only once-daily GLP-1 receptor agonist licensed for type 2 diabetes mellitus patients not optimally controlled on oral antidiabetic drugs and/or basal insulin' was found to be misleading and ambiguous in breach of Clause 7.2. Novo Nordisk was informed by the PMCPA that Sanofi had signed its undertaking in relation to this matter on 25 June 2013.

Novo Nordisk noted that on 10 July 2013 a supplement entitled 'Lantus (insulin glargine) and the evolution of diabetes management' was published in the Nursing Times. A sentence on the front page of the supplement stated: 'This promotional supplement has been produced by Sanofi'. Page 5 of the supplement included the claim 'Lyxumia is the only once-daily GLP-1RA that is licensed for use in combination with basal insulin and/or oral glucose lowering agents'. This claim was similar to that previously ruled in breach of the Code

(PMCPA letter of 17 June 2013); the Panel stated 'use of "and/or" in the claim did not make the distinction between the two medicines entirely clear'. The Panel also considered that 'use of "and/or" made it unclear as to what "only" referred to'.

Novo Nordisk stated that the Nursing Times had confirmed that the supplement was published 10 July 2013; the copy deadline for the journal to receive the supplement was 1 July 2013. Novo Nordisk submitted that as the copy deadline was nearly a week after the undertaking was signed by Sanofi, it appeared that Sanofi had continued to use the claim at issue despite the Panel's ruling. Novo Nordisk considered that there was sufficient time for Sanofi to have removed the claim from the supplement before the journal's copy deadline (1 July 2013), in light of its undertaking signed on 25 June 2013.

Novo Nordisk alleged that Sanofi had made available an item which featured a similar claim to that deemed misleading by the Panel, and after the signing of its undertaking. Novo Nordisk alleged a breach of Clause 25. Given the seriousness of such a matter, Novo Nordisk also alleged breaches of Clauses 2 and 9.1.

RESPONSE

Sanofi submitted that the Lyxumia advertisement (ref GBIE.LYX.13.02.11) at issue in Case AUTH/2604/5/13 was published in the Health Service Journal in March 2013. Before this complaint was made to the PMCPA, Sanofi and Novo Nordisk had participated in inter-company dialogue about the advertisement and Sanofi had agreed on 29 April 2013 to withdraw the item. This agreement was honoured in a timely fashion through the identification and withdrawal of the item, and all similar items. This was achieved through: a review of active Lyxumia materials within the validated approval system (Zinc), a review of active items on the iPad Catalogue system, and through instructions to the creative agency. The advertisement at issue was part of a campaign that ended by 29 April; however, the review identified additional materials which need to be withdrawn. The following detailed actions were undertaken as a result:

- The agency was advised verbally and in writing of the immediate withdrawal of two advertisements (Lyxumia Payor Advertisement ref GBIELYX.13.02.11 and Lyxumia Clinical Advertisement ref GBIE.LYX.13.02.12). The email notification sent on 29 April with the agency's response was provided. The agency was asked to identify the journals to which these items had been submitted as part of the advertising schedule and advised that no further submissions must be made with these items. A new brief was confirmed for a revised advertisement which did not have the claims concerned.
- A range of 'payor' materials were identified for withdrawal including 'awareness mailers'. These were all head office-led initiatives and the materials were withdrawn without need to involve the sales force. The items were withdrawn from Zinc.
- A leavepiece (ref GBIE.LYX.13.01.13), similar to the advertisement at issue was identified for withdrawal through the review of materials. Following discussion within Sanofi, it was agreed to withdraw within two weeks despite the fact that this piece was not the subject of the inter-company agreement. A revised leavepiece was produced (ref GBIE.LYX.13.04.14) which fully met the terms of the agreement with Novo Nordisk. Given that this involved material in circulation with a sales force, the following detailed actions were taken to ensure the complete withdrawal of the leavepiece and replacement with the revised item:

  – 29 April 2013: A brief for developing the revised leavepiece was provided to the agency.
  – 9 May: The sales force was notified that the leavepiece would be withdrawn from use on 13 May and briefed on the process for its return of the item and that each person should return signed declaration forms confirming his/her actions. Signed declarations were subsequently returned and logged.
  – The sales force was provided with a briefing document explaining the changes incorporated in the revised leavepiece (ref GBIELYX.13.04.14).
  – 9 May: Sanofi distribution centre was instructed to quarantine and destroy the original leavepiece (ref GBIE.LYX.13.01.14). It was also advised of the timeframe for the despatch of the revised leavepiece (ref GBIE.LYX.13.04.14) to the sales force;
  – 12 May: Distribution centre confirmed quarantine of the withdrawn items.
  – 23 May: Distribution centre confirmed that the withdrawn items (including returns from the field) were queued for destructions.

To manage these actions efficiently, a log of all the resulting unscheduled work was initiated and maintained.

In summary, as a result of the inter-company dialogue Sanofi had removed the advertisement and all similar material, before Case AUTH/2604/5/13 was referred to the Panel in the same manner and using the same process as if it had been the subject of an undertaking to the PMCPA.

The Panel notified Sanofi of the outcome of Case AUTH/2604/5/13 on 17 June 2013. The Panel found that the claims in the advertisement, 'Lyxumia is the only once-daily GLP-1 receptor agonist licensed for type 2 diabetes mellitus patients not optimally controlled on oral antidiabetic drugs and/or basal insulin' and 'Lyxumia leads to even greater cost savings of' and 'Turn to the GLP-1 that minimises costs' were in breach of the Code.

Sanofi singed a written undertaking dated 25 June 2013 to accept the Panel's rulings and undertook that 'Use of the advertisement in question and any similar material, if not already discontinued or no longer in use, will cease forthwith'. When Sanofi signed the undertaking, the actions, as detailed above, had been completed. Furthermore, Sanofi had not issued any further advertisements

containing the claims at issue in that case. Sanofi noted that in the complaint now at issue (Case AUTH/2620/7/13) Novo Nordisk did not submit any evidence that Sanofi had issued or persisted to use any advertisement which contained the claims which were the subject of Case AUTH/2604/5/13.

Sanofi noted that Novo Nordisk had stated that Sanofi had breached its undertaking because 'Sanofi had made available an item which featured a similar claim to that deemed misleading by the Panel, and after the signing of its undertaking'.

The item referred to by Novo Nordisk (ref GBIE. DIA.13.05.03; 'Lantus (insulin glargine) and the Evolution of Diabetes Management') was a promotional 6 page supplement (including reference citations) published in the Nursing Times on 10 July 2013. Sanofi confirmed that the copy deadline for the supplement was 28 June 2013. As clearly indicated in its title, the supplement was about treatment with Lantus and most of the content was about Lantus monotherapy. However, the text also referred to other insulins and contained 1½ pages which introduced the paradigm of adding Lyxumia to treatment with Lantus. There was no consideration of Lyxumia, save in this context.

Lyxumia was first mentioned on page 4 of the supplement, which referred to the effects of GLP-1RAs and the benefits of combining 'prandial GLP-1RAs with a basal insulin'. The text stated that Lyxumia was one of 'four main GLP-1RAs available in the UK market'; all such products were listed. The opening paragraph of page 5 explained that 'Addition of Lyxumia to Lantus, the cornerstone of insulin therapy, is a new paradigm that will help your patients achieve glycaemic targets more sympathetically for years to come'. The second paragraph described the efficacy of the combination of Lantus and Lyxumia and stated that 'Lyxumia is also effective in combination with oral glucose lowering agents, or with both basal insulin and oral glucose lowering agents' before concluding 'Lyxumia is the only once-daily GLP-1RA that is licensed for use in combination with basal insulin and/or oral glucose lowering agents'. It was this final statement which Novo Nordisk alleged was similar to a claim considered in Case AUTH/2604/5/13.

Sanofi did not consider that Novo Nordisk's complaint was justified or that the claim at issue represented a breach of the undertaking provided by Sanofi. The wording of the claim now at issue which was not the same as that which was the subject of Case AUTH/2604/5/13 and the type of promotion and the context in which information was provided in the supplement was qualitatively different from the advertisement considered in Case AUTH/2604/5/13.

In Case AUTH/2604/5/13, the claim 'Lyxumia is the only once-daily GLP-1 receptor agonist licensed for type 2 diabetes mellitus patients not optimally controlled on oral antidiabetic drugs and/or basal insulin' was ruled in breach of the Code by the Panel. The reasons given in the case report were that (a) 'by emboldening "only once-daily" there was an implication that Lyxumia was the only once-daily GLP-1 receptor agonist which was not so …'; and (b) while 'the Panel accepted that, in the round, the quoted claim was true', it considered 'the "and/or" made it unclear what "only" referred to' and noted that 'both Victoza and Lyxumia could be given to patients not currently controlled on [oral antidiabetic] therapy'. The claim at issue in this case was 'Lyxumia is the only once-daily GLP-1RA that is licensed for use in combination with basal insulin and/or oral glucose lowering agents'. This claim was not similar to that in Case AUTH/2604/5/13 because:

- There were no emboldening and the clear construction of the text made clear that 'only' related to Lyxumia's authorization particulars, rather than its status as a GLP-1RA. Furthermore, the supplement expressly stated that Lyxumia was one of four main GLP-1RAs on the UK market.

- The use of 'and/or' appeared in a different context in the claim now at issue
  - In Case AUTH/2604/5/13, 'and/or' related to the types of diabetes patients who could receive Lyxumia and the ambiguity arose because some of these patients could also receive Victoza.
  - In this case use of 'and/or' related to the details of the licensed indication for Lyxumia. It was clearly the case that Lyxumia was the only once-daily GLP-1RA that was licensed for use 'in combination with basal insulin and/or oral glucose lowering agents' (the precise wording of the marketing authorization).

- Applying the test suggested by Novo Nordisk in Case AUTH/2604/5/13 and removing the alternative 'and' or 'or', the text remained accurate:
  - Lyxumia was the only once-daily GLP-1RA that was licensed for use in combination with basal insulin or oral glucose lowering agents.
  - Lyxumia was the only once-daily GLP-1RA that was licensed for use in combination with basal insulin and oral glucose lowering agents.

Sanofi submitted that due to the nature, content, context, distribution and focus of the promotional supplement and the claims therein, it was entirely different from the advertisement at issue in Case AUTH/2604/5/13 and the subsequent undertaking not to use that advertisement or similar materials.

The claim now at issue should be considered in the context in which it appeared. The supplement clearly focussed on providing great detail on the use of Lantus, and Lyxumia was referred to in the context of an add-on to treatment with Lantus; the first 3 pages were devoted to information on Lantus and page 4 opened with an introduction to the concept of adding a GLP-1RA to Lantus. There was no suggestion that Lyxumia was the only GLP-1RA; the text stated explicitly that Lyxumia was one of four main products of this type available in the UK.

In summary, Sanofi considered that, taken as a whole, the supplement was not ambiguous or misleading and did not represent a breach of the undertaking provided pursuant to Case AUTH/2604/5/13.

Even if, contrary to Sanofi's position, the claim now at issue was considered in isolation, it was materially different from that which was the subject of Case AUTH/2604/5/13 and simply comprised a direct quotation from the Lyxumia marketing authorization. Sanofi considered that it was entirely appropriate to inform health professionals, quite correctly, that Lyxumia was the only GLP-1RA with that particular licensed indication.

PANEL RULING

The Panel noted that an undertaking was an important document. Companies had to give an undertaking that the material in question and any similar material, if not already discontinued or no longer in use, would cease forthwith and give an assurance that all possible steps would be taken to avoid similar breaches of the Code in the future. It was very important for the reputation of the industry that companies complied with undertakings.

The Panel disagreed with Sanofi's submission that due to the nature, content, context, distribution and focus of the promotional supplement and the claims therein, it was entirely different from the advertisement at issue in Case AUTH/2604/5/13 and the implication that it was therefore not covered by the subsequent undertaking in that case. The undertaking covered all closely similar materials.

The Panel noted that the previous case, Case AUTH/2604/5/13, concerned an advertisement which, *inter alia*, featured the claim 'Lyxumia is the **only once-daily** GLP-1 receptor agonist licensed for type 2 diabetes mellitus patients not optimally controlled on oral antidiabetic drugs and/or basal insulin'.

Turning to the claim at issue in this case, 'Lyxumia is the only once-daily GLP-1RA that is licensed for use in combination with basal insulin and/or oral glucose lowering agents' the Panel noted that the wording of the claim was different from that of the claim at issue in Case AUTH/2604/5/13 as 'only once-daily' was not emboldened in the claim now at issue.

The Panel noted Sanofi's submission that the claim was a direct quote from the marketing authorization. The Panel had not seen the marketing authorization but noted that the indication in the summary of product characteristics (SPC) was for the treatment of adults with type 2 diabetes mellitus to achieve glycaemic control in combination with oral glucose-lowering medicinal products and/or basal insulin when these, together with diet and exercise, did not provide adequate glycaemic control. The SPC indication did not state that Lyxumia was the 'only' medicine licensed as such.

The Panel noted that Lyxumia and Victoza were both licensed as adjunctive therapy – to be added to existing antidiabetic therapy to achieve improved glycaemic control. Both medicines could be added to existing oral antidiabetic (OAD) therapy but only Lyxumia was also indicated to be added to an existing treatment regimen which included basal insulin. The Panel considered that the use of 'and/or' in the claim did not make this distinction between the two medicines entirely clear. The claim meant that Lyxumia was the only once-daily GLP-1 RA that was licensed for use in combination with basal insulin alone, in combination with OADs and basal insulin and in combination with OADs. The Panel accepted that, in the round, this claim was true, but considered that the 'and/or' made it unclear as to what 'only' referred to. Whilst the earlier two treatment scenarios were correct in that only Lyxumia could be added to existing basal insulin therapy, the last was not; both Victoza and Lyxumia could given in combination with OAD therapy. The Panel considered that the claim was misleading and ambiguous and on the basis that the 'and/or' made it unclear as to what 'only' referred to and the claim did not make the distinction between the two medicines entirely clear, it was sufficiently similar to that at issue in Case AUTH/2604/5/13 to be covered by the undertaking in that case. The Panel therefore ruled the claim to be in breach of the undertaking previously given. A breach of Clause 25 was ruled. High standards had not been maintained; a breach of Clause 9.1 was ruled. These rulings were appealed.

The Panel noted Sanofi's detailed account of its review and withdrawal of material which it undertook and completed following resolution of matters during inter-company dialogue and prior to notification of the ruling and provision of the undertaking in Case AUTH/2604/5/13. It appeared that Sanofi had not validated the decisions made during its withdrawal process after providing its undertaking in Case AUTH/2604/5/13 dated 25 June 2013. The Panel was concerned that the supplement in question had been submitted to Nursing Times for publication on 10 July 2013. The Panel noted that Novo Nordisk had stated that the Nursing Times had confirmed that the copy deadline for the journal to receive the supplement was 1 July 2013 whereas Sanofi submitted that the copy deadline was 28 June 2013. Both of these dates were after the date on which Sanofi had signed its undertaking in Case AUTH/2604/5/13 and as such Sanofi could have prevented the supplement from being published.

The Panel noted its comments above about the importance of compliance with undertakings. The Panel considered that the conduct of Sanofi in this regard had brought discredit upon, and reduced confidence in, the pharmaceutical industry. A breach of Clause 2 was ruled. This ruling was appealed.

The Panel noted that this was the second time that Sanofi had breached the undertaking given in Case AUTH/2604/5/13 (Case AUTH/2619/7/13). The Panel was very concerned as it appeared Sanofi had not paid sufficient attention to ensure that its materials were comprehensively reviewed following the provision of an undertaking. The Panel considered Sanofi's conduct warranted consideration by the Code of Practice Appeal Board and decided to report the company to the Appeal Board under Paragraph 8.2 of the Constitution and Procedure for it to consider whether further sanctions were warranted.

APPEAL BY SANOFI

Sanofi submitted that the context and specific nature of the claim in the supplement was significantly different to the advertisement at issue in Case

AUTH/2604/5/13. The journal supplement was significantly different as demonstrated by the greater depth, comprehensive nature of the information and different method of distribution to the intended audience. As such Sanofi concluded that use of the supplement was not subject to the obligations set out in its undertaking which covered the use of 'similar materials'. In addition, Sanofi was confused by the additional clarification provided in the Panel ruling that the undertaking applied to '… closely similar materials'. Sanofi submitted that the undertaking which it signed on 25 June 2013 stated that 'Use of the advertisement in question and any similar material, if not already discontinued or no longer in use, will cease forthwith'. The undertaking did not refer to the claim which was considered in Case AUTH/2604/5/13.

Sanofi stated that it was a well-established principle in the application of the Code that the context and method of use of promotional material was of considerable relevance when deciding the acceptability of any activity, claim, or information provided; this was referred to in the context of certification in the supplementary information to Clause 14.1.

Sanofi submitted that the nature, content, context, distribution and focus of a piece were all important when determining what was and was not 'similar' or 'closely similar' material and that the Panel had not given sufficient consideration to how a company might determine what was and what was not 'similar material' when interpreting the nature of any undertaking it agreed to be bound by.

Sanofi stated that it had considered the Panel ruling and concluded that the six page supplement for a portfolio of diabetes products containing detailed information on the treatment of diabetes with both insulin and Lyxumia and whether it could be considered 'similar' or 'closely similar' to a simple, one page Lyxumia advertisement. Just as a mouse and an elephant were easy to identify they were difficult to define. In Sanofi's view, a one page advertisement and a six page journal supplement were clearly promotional items, just as a mouse and an elephant were mammals, but were equally quite dissimilar in many important ways, such as depth and breadth of content, overall context, delivery and the inherent understanding of the intended audience.

Sanofi submitted that the Panel had not given due consideration to how the wording of the undertaking agreed by Sanofi could be reasonably considered alongside the Panel's ruling concerning the claim at issue which stated that 'The Panel accepted that, in the round, this claim was true but that the "and/or" made it unclear as to what "only" referred to'.

Sanofi submitted that in the light of this clear position and the wording of the undertaking, it was reasonable to conclude that providing greater context about what 'and/or' referred to would satisfy the Panel's concern. Sanofi submitted that the undertaking did not prohibit a modified version of this claim being used in materials that were sufficiently dissimilar to the advertisement considered in Case AUTH/2604/5/13. Sanofi assured the Appeal Board that it would have acted differently had the undertaking stated that it must not use the claim, or if the Panel had not stated that 'The Panel accepted that, in the round, this claim was true but that the "and/or" made it unclear as to what "only" referred to'.

In summary, Sanofi did not believe that the meaning of what was, and importantly what was not considered 'similar material', as stated in the undertaking had been given due consideration in the Panel's ruling and therefore Sanofi appealed the ruling of a breach of Clause 25.

Sanofi noted the claim at issue 'Lyxumia is the only once-daily GLP1-RA that is licensed for use in combination with basal insulin and/or oral glucose-lowering agents' and that in its ruling the Panel re-iterated its findings concerning the claim from the previous case (Case AUTH/2604/5/13) and stated the use of a 'sufficiently similar claim' as rationale for ruling a breach of Clauses 9.1 and 25.

Sanofi submitted that its understanding of the undertaking was that it referred to the use of the claim in 'similar materials' and not to the claim itself. Notwithstanding this, Sanofi understood why the Panel has revisited this issue and welcomed the Appeal Board's deliberation on whether this case centred on a 'similar claim' or use in 'similar materials'.

Sanofi submitted that it appeared from Case AUTH/2604/5/13, that the claim *per se* was accepted but that the concern was its context 'The Panel accepted that, in the round, this claim was true, but considered that the "and/or" made it unclear as to what "only" referred to'.

Sanofi noted out that in the preceding sentence of the paragraph of the promotional supplement at issue, Lyxumia was described as being '…effective in combination with oral … glucose lowering agents or with both basal insulin and oral glucose lowering agents'. This sentence was followed by 'Lyxumia is the only once-daily GLP-1RA that is licenced for use in combination with basal insulin and/or oral glucose lowering agents'. Sanofi submitted that the Panel had given insufficient consideration to the context which the preceding sentence gave the claim. Whilst Sanofi understood that the use of 'and/or' as a conjunction that was contained in the relevant section of the SPC, might produce debate as a point of grammar, the sentence immediately preceding the claim provided absolute clarity as to the inclusivity of the 'and/or' conjunction. As such it was clear that 'only' in the claim referred to the whole inclusive list of presented scenarios as one entity.

Sanofi submitted that insufficient consideration had been given to the fact that '…in combination with basal insulin and/or oral glucose lowering agents…' was the exact wording taken from the therapeutic indications section of the SPC. No other once-daily GLP-1RA had a marketing authorization for once-daily use in all of the indications linked by the conjunction 'and/or' in the claim.

Sanofi submitted that it always sought to act within the spirit as well as the letter of the Code. In particular it understood that the context in which a claim was made and the way in which it was presented was key to determining its acceptability. For example, although an SPC was not considered a promotional item *per se*, as stated in Clause 1.2 of the Code, it could be considered a promotional item if given to inappropriate recipients in a promotional manner.

Sanofi appealed the ruling that the claim at issue was a 'sufficiently similar claim', given the context to the claim that was provided, as per the advice of the Panel and that this therefore constituted a breach of Clauses 9.1 and 25.

Sanofi noted the Panel's rationale for ruling a breach of Clauses 25 and 2 and as evidence that its conduct warranted consideration by the Appeal Board. Namely that it appeared that Sanofi: had not validated the decisions made in its withdrawal process after providing its undertaking; could have prevented the supplement from being published after the undertaking was signed, and had paid insufficient attention to ensuring that materials were comprehensively reviewed following the provision of an undertaking. Given the detailed account of Sanofi's approach to the withdrawal of its materials provided above, Sanofi submitted that these assertions were not valid.

Sanofi submitted that it decided to use the claim in the journal supplement in the full knowledge of the undertaking and the information contained in the Panel's ruling. Indeed it was the specifics of the wording of the ruling and the undertaking that guided Sanofi to modify the claim and allow its use in a clearly dis-similar piece from that which it undertook not to use.

Sanofi submitted that the supplement was comprehensively reviewed by its scientific service and then by both signatories of the promotional certificate.

Sanofi denied breaches of Clauses 2, 9.1 and 25.

COMMENTS FROM NOVO NORDISK

Novo Nordisk noted that in Case AUTH/2604/5/13 the Panel had ruled that the claim 'Lyxumia is the only once-daily GLP-1 receptor agonist licensed for type 2 diabetes mellitus patients not optimally controlled on oral antidiabetic drugs and/or basal insulin', which appeared in an advertisement, was misleading and ambiguous in breach of Clause 7.2. Sanofi had accepted this ruling and signed an undertaking. To use a similar claim again in another form of promotional material such as a supplement should not negate the Panel's original decision about this claim.

Novo Nordisk did not accept Sanofi's submission that the supplement was 'significantly different' to the advertisement. Both items were promotional and the supplement (which featured a misleading claim) was made available after Sanofi had signed its undertaking. Referring to Paragraph 7 of the Constitution and Procedure, Novo Nordisk failed to see how this supplement could not be covered by Sanofi's undertaking given in Case AUTH/2604/5/13.

APPEAL BOARD RULING

The Appeal Board noted that the claim at issue in Case AUTH/2604/5/13, 'Lyxumia is the only once-daily GLP-1 receptor agonist licensed for type 2 diabetes mellitus patients not optimally controlled on oral antidiabetic drugs and/or basal insulin' appeared in an advertisement. The claim at issue in the current case 'Lyxumia is the only once-daily GLP-1RA that is licensed for use in combination with basal insulin and/or oral glucose lowering agents' appeared in a promotional supplement in a non-specialist journal. The Appeal Board noted that although the claims were not identical they were very similar; both contained 'and/or' which made the meaning of 'only' unclear. The Appeal Board noted that whilst Lyxumia was the only GLP-1RA that could be added to basal insulin it was not the only GLP-1RA that could be added to existing oral antidiabetic (OAD) therapy and thus the claim was misleading in that regard.

The Appeal Board considered that the claim at issue in the supplement was so similar to that in the advertisement that it was covered by the undertaking given in Case AUTH/2604/5/13 and it upheld the Panel's ruling of a breach of Clause 25. The Appeal Board considered that high standards had not been maintained and it upheld the Panel's ruling of a breach of Clause 9.1. The appeal on both points was unsuccessful.

The Appeal Board noted that an undertaking was an important document. In failing to comply with its undertaking the Appeal Board considered that Sanofi had brought discredit upon, and reduced confidence in, the pharmaceutical industry. The Appeal Board upheld the Panel's ruling of a breach of Clause 2. The appeal on this point was unsuccessful.

COMMENTS FROM SANOFI ON THE REPORT

At the consideration of the report, Sanofi submitted that in response to the issues in these cases, it had compiled a file of disallowed claims, reviewed its compliance procedures, introduced a monitoring process and investigated the procurement of external compliance expertise.

APPEAL BOARD CONSIDERATION OF THE REPORT FROM THE PANEL

The Appeal Board noted that the journal supplement at issue had been certified the day after the undertaking in Case AUTH/2604/5/13 had been signed. Sanofi had submitted that it had decided to use the claim at issue in full knowledge of the undertaking and of the Panel's ruling in that case. In the Appeal Board's view, it should have been obvious to Sanofi that the claim in the supplement was so similar as to be almost the same as the claim at issue in Case AUTH/2604/5/13. That the claim was approved for use subsequent to the outcome of Case AUTH/2604/5/13, led the Appeal Board to query the rigour with which Sanofi had examined relevant

materials to ensure compliance with its undertaking. After signing the undertaking, Sanofi had had time to cancel publication of the supplement. The Appeal Board noted that this was the second time that Sanofi had breached its undertaking given the Case AUTH/2604/5/13 (Case AUTH/2619/7/13) and so it decided, in accordance with Paragraph 11.3 of the Constitution and Procedure, to require an audit of the company's procedures in relation to the Code. The Appeal Board noted that Sanofi had already embarked on a programme of corrective measures and so it requested that the audit take place in March 2014 when the results of some of those measures should be obvious. In the meantime it requested the Authority to ask Sanofi to confirm in writing the measures it had implemented. On receipt of the audit report and Sanofi's comments upon it, the Appeal Board would consider if further sanctions were necessary.

APPEAL BOARD FURTHER CONSIDERATION

Sanofi was audited in March 2014 and on receipt of the audit report, the Appeal Board noted a number of serious concerns regarding Sanofi's procedures and materials; the company had begun to address the issues including a change to the structure of company reporting, increasing compliance resource, training and updating its procedures and materials.

The Appeal Board decided that Sanofi should be re-audited in October 2014 at which point it expected to see changes implemented and significant progress made. Upon receipt of the report for the re-audit and Sanofi's comments upon it, the Appeal Board would decide whether further sanctions were necessary.

Sanofi was audited in October 2014 and on receipt of the audit report, the Appeal Board noted that some progress had been made; the company had a new general manger and there had been an increased focus on compliance. However, the Appeal Board considered that there was still a lot of work to do and concerns to address. In addition the Appeal Board noted the recent issues raised concerning Sanofi's interaction with patient organisations (Case AUTH/2736/6/14. In relation to the re-audit in Case AUTH/2620/7/13, the Appeal Board decided to require a re-audit of Sanofi in March 2015 at the same time as the audit required in Case AUTH/2736/9/14; it would expect to see the recommendations of the October 2014 audit report implemented and significant progress made. On receipt of the re-audit report and Sanofi's comments upon it, the Appeal Board would consider whether further sanctions were necessary.

Sanofi was audited in March 2015, and on receipt of the audit report the Appeal Board noted that Sanofi had made progress since the audit in October 2014; a new, senior manager was fully involved and leading many of the company's compliance initiatives.

The Appeal Board however, noted its concern about some of the company's activities and considered that Sanofi should address the matters raised as a priority. On the basis that this work was completed, the progress otherwise shown in the March 2015 audit was continued and a company-wide focus and responsibility for compliance was maintained, the Appeal Board decided that no further action was required.

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Appeal Board Consideration	**27 November 2013, 9 April and 10 December 2014, 16 April 2015**
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