CASE AUTH/2903/11/16 *NO BREACH OF THE CODE*

DIRECTOR v NOVO NORDISK

Clinical trial disclosure (Ryzodeg)

A study published online in Current Medical Research & Opinion (CMRO) on 25 November 2016 was entitled 'Clinical trial transparency update: an assessment of the disclosure of results of company-sponsored trials associated with new medicines approved in Europe in 2013'. The study authors were B R Deane, a freelance consultant in pharmaceutical marketing and research and Dr J Sivarajah, Head of Medical Affairs, ABPI. Publication support for the study was funded by the ABPI.

The study surveyed various publicly available information sources for clinical trial registration and disclosure of results searched between 1 May and 31 July 2015. It covered 34 new medicines (except vaccines) from 24 companies that were approved by the European Medicines Agency (EMA) in 2013. It included all completed company-sponsored clinical trials conducted in patients and recorded on a clinical trial registry and/or included in a European Public Assessment Report (EPAR). The CMRO publication did not include the specific data for each product. This was available in the supplemental information via a website link. Neither the study nor the supplemental information identified specific clinical trials. The study did not assess the content of disclosure against any specific requirements.

The Director decided that the study was such that she had received information from which it appeared that Novo Nordisk might have breached the Code and decided in accordance with Paragraph 5.1 of the Constitution and Procedure to take the matter up as a complaint.

The summary output for each medicine set out the sources for all trials found, irrespective of sponsor and an analysis of publication disclosure in the form of a table which gave details for the studies for Ryzodeg (insulin degludec/insulin aspart).

The detailed response from Novo Nordisk is given below.

General detailed comments from the Panel are given below.

The Panel noted the CMRO publication in that nine evaluable trials (two Phase I and II and seven Phase III) had not been disclosed within the timeframe. The disclosure percentage at 12 months measured from the later of the first date of regulatory approval or trial completion date was 61%. The disclosure percentage at 31 July 2015 was 70%.

Ryzodeg was first approved and commercially available in January 2013. The Second 2012 Code and thus the Joint Position 2009 were relevant.

The Panel noted Novo Nordisk's submission that the Phase I and II trials had no UK involvement including no UK patients, investigators or UK funding and neither of the studies were conducted on behalf of Novo Nordisk Ltd (the UK legal entity). The Panel considered that as there was no UK involvement in either of the Phase I or II trials that they did not come within the scope of the UK Code and no breach of the Code was ruled. The Panel noted Novo Nordisk's submission that full clinical trial reports were available from novonordisk-trials.com.

The Panel noted that according to the CMRO publication there were seven Phase III trials that had not been disclosed within the timeframe; six had still not been disclosed by 31 July 2015. The Panel noted Novo Nordisk's submission that only two Phase III trials had any UK involvement (UK sites and patients). Both studies completed on 2 December 2010 ie before Ryzodeg was launched 21 January 2013 and so results from these trials should have been published by 20 January 2014.

The Panel noted that although Novo Nordisk's submission and the table it provided differed slightly, the results for both trials with UK involvement had been disclosed by 20 January 2014. Thus the Panel ruled no breach of the Code including no breach of Clause 2.

The Panel noted that although, according to the CMRO publication, there were seven Phase III trials that had not been disclosed within the timeframe Novo Nordisk provided details of fifteen additional Phase III trials. Two of those are detailed above. The Panel noted Novo Nordisk's submission that the remaining thirteen trials had no UK involvement including no UK patients, investigators or UK funding and none of the studies were conducted on behalf of Novo Nordisk Ltd (the UK legal entity). The Panel considered that as there was no UK involvement in any of the remaining thirteen Phase III trials that they did not come within the scope of the UK Code and no breach of the Code was ruled.

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The study referred to the two previously reported studies which covered medicines approved in Europe in 2009, 2010 and 2011 (Rawal and Deane 2014) and in 2012 (Rawal and Deane 2015). The 2016 study surveyed various publicly available information sources for clinical trial registration and disclosure of results searched between 1 May and 31 July 2015.

It covered 34 new medicines (except vaccines) from 24 companies that were approved by the European Medicines Agency (EMA) in 2013. It included all completed company-sponsored clinical trials conducted in patients and recorded on a clinical trial registry and/or included in a European Public Assessment Report (EPAR). The CMRO publication did not include the specific data for each product. This was available in the supplemental information via a website link. Neither the study nor the supplemental information identified specific clinical trials. The CMRO study did not assess the content of disclosure against any specific requirements.

The Director decided that the study was such that she had received information from which it appeared that Novo Nordisk might have breached the Code and so she decided in accordance with Paragraph 5.1 of the Constitution and Procedure to take the matter up as a complaint.

COMPLAINT

The study assessed the proportion of trials for which results had been disclosed on a registry or in the scientific literature either within 12 months of the later of either first regulatory approval or trial completion, or by 31 July 2015 (end of survey). Of the completed trials associated with 34 new medicines licensed to 24 different companies in 2013, results of 90% (484/539) had been disclosed within 12 months and results of 93% (500/539) had been disclosed by 31 July 2015.

Ryzodeg

The supplemental information gave details of disclosure of clinical trial results for each product irrespective of sponsor. The data for Ryzodeg (insulin degludec/insulin aspart) were as follows:

Phase	Total	Un-evaluable	Evaluable	Disclosed in 12-month timeframe	Disclosure Percentage	Complete before 31 July 2015	Disclosed at 31 July 2015	Disclosure percentage at 31 July 2015
Phase I & II	9	0	9	7	78%	9	8	89%
Phase III	15	1	14	7	50%	14	8	57%
Phase IV	0	0	0	0		0	0	
Other	0	0	0	0		0	0	
Total	**24**	**1**	**23**	**14**	**61%**	**23**	**16**	**70%**

Footnote (company communication): Results of the seven remaining undisclosed trials (one phase I and six phase III) have since been posted on ClinicalTrials.gov and/or the company's own registry in October 2015, following the approval of the product in the US in September 2015, in compliance with the Food and Drug Administration Amendments Act (FDAAA) 801 (2007) requirements for results disclosure at ClinicalTrials.gov.

The explanation of terms given in the documentation was as follows:

Total	Total number of company sponsored trials identified which were completed by 31 July 2015
Unevaluable	Trials with completion date within the last 12 months or key dates missing – excluded from the analysis
Evaluable	Trials with all criteria present including dates, and hence the base number of trials which could be evaluated for the assessment
Results disclosed in 12 month timeframe	Evaluable trials which were disclosed within the target 12 months measured from the later of either first regulatory approval date in Europe or the US, or trial completion date
Disclosure percentage	Proportion of evaluable trials which were disclosed within 12 months measured from the later of either first regulatory approval date in Europe or the US, or trial completion date
Completed before 31 July 2015	Number of evaluable trials completed before 31 July 2015
Disclosed at 31 July 2015	Number of evaluable trials with results disclosed by 31 July 2015
Disclosure percentage at 31 July 2015	Proportion of evaluable trials which were disclosed by 31 July 2015

When writing to Novo Nordisk the Authority asked it to bear in mind the requirements of Clauses 2, 9.1 and 13.1 of the Code. The Authority noted that previous editions of the Code would be relevant and provided details.

RESPONSE

Novo Nordisk stated that it was committed to transparency of its clinical trials and took this matter very seriously. It submitted that it followed international and national laws on clinical trial disclosure.

Novo Nordisk provided result tables to clinicaltrials.gov following the US FDAAA legal requirements and to the EudraCT database for public disclosure at the EU Clinical Trials Register by EMA according to the EU Clinical Trials Directive, the Paediatric Regulation and other requirements governing the use of EudraCT. It adhered to the timelines below, as outlined in the company's policy 'Principles for the registration of clinical study information in external registries'.

The company submitted that a summary of results was provided to www.ClinicalTrials.gov at FDA product approval plus 30 days, or last patient last visit plus 12 months whichever came last. A summary of results for clinical trials, Phases I-IV in adults, was provided to EU Clinical Trials Register at the date of last patient last visit plus 12 months. Only results for Phases II-IV trials would be disclosed. It provided a summary of results for paediatric clinical trials, Phase I-IV, to EU Clinical Trials Register at last patient last visit plus 6 months.

Novo Nordisk stated that it posted a redacted clinical study report (CSR) for clinical trials, Phase I-IV, and non-interventional study (NIS) on www.novonordisk-trials.com 30 days after approval of product and indication in both EU and the US, or at last patient last visit plus 12 months whichever came last.

Results for non-interventional studies classified as post-authorisation safety studies (NI PASS) in the EU PAS Register were posted preferably within two weeks after the finalisation of the study report in the format of a redacted study report.

Novo Nordisk posted a CSR for clinical trials, Phase I-IV on www.novonordisk-trials.com 12 months after public announcement of discontinuation of project, or at last patient last visit plus 12 months whichever came last.

The company posted references to scientific publications for clinical trials, Phase I-IV, and NIS on www.novonordisk-trials.com and/or www.ClinicalTrials.gov within one year from publication. Links were provided as they became available.

Novo Nordisk released clinical trial reports (CTRs) (redacted for private personal data and company confidential information) on its portal www.novonordisk-trials.com within 30 days after the latest of the EU and US approvals.

Novo Nordisk stated that Ryzodeg was first licensed on 21 January 2013 in the EU. It was also commercially available from this date in Denmark. It was not commercially available in the UK. It was first licensed in the US on 25 September 2015.

With regard to the evaluable trials highlighted in the CMRO study supplemental information, Novo Nordisk Ltd (the UK legal entity) had no involvement and there were no UK patients in the Phase I and Phase II trials; therefore these were not addressed below. However, it emphasised that all trials had full clinical trial reports available for download from novonordisk-trials.com. This also included the Phase I and II trials with no UK involvement.

There were two Phase III studies with UK involvement (UK sites and patients). These were NN5401-3594 and extension study NN5401-3645. Details were provided.

Relevant trials in scope for results disclosure via the EudraCT database were submitted by the deadlines specified by EMA for the EudraCT results disclosure implementation in the period July 2014 - July 2015. For older trials completed prior to implementation the first of these deadlines was 21 July 2015, to which Novo Nordisk adhered.

Unfortunately EMA faced information technology issues with the release of results from EudraCT to the public register and had to close down the access to the public site and for further entry into the EudraCT system for approximately half a year from July 2015 – January 2016. The results submitted to EudraCT were therefore not available to the ABPI during its audit. The EU Clinical Trials Register and the EudraCT results database was back in operation as of 13 Jan 2016 and EMA had defined new deadlines for the trials that were due during the period when the system was inaccessible. All trials in scope for EudraCT had been submitted by Novo Nordisk and old ones re-released after the EMA requested quality control according to EMA's specifications.

Trials in scope for ClinicalTrials.gov were submitted within the deadline of 30 days after approval by the FDA. The results would be made publicly available by the ClinicalTrials.gov staff once they had completed their review.

Novo Nordisk stated that the results for the two trials with UK involvement were made publicly available by August 2012 (NN5401-3594) and November 2013 (NN5401-3645), both within 12 months of the product being licensed in the EU. Therefore the company submitted that it had not breached Clauses 13.1, 9.1 or 2.

In response to a request for further information Novo Nordisk confirmed that Novo Nordisk Ltd (the UK legal entity) had no involvement in the Phase I and II trials and that there were no UK investigators involved in the studies, nor were any of the studies conducted on behalf of Novo Nordisk Ltd. There was no UK funding nor any other UK involvement.

Novo Nordisk confirmed that that was also the situation for 13 of the 15 trials listed in the table provided titled 'Overview of trials with UK involvement (Ryzodeg)'. There were no UK investigators involved in the trials and none of the trials were conducted on behalf of Novo Nordisk

Ltd. There was no UK funding or any other UK involvement. Novo Nordisk submitted that only the two trials highlighted (NN5401-3594 and NN5401-3645) had any UK involvement.

GENERAL COMMENTS FROM THE PANEL

The Panel noted that all the cases would be considered under the Constitution and Procedure in the 2016 Code as this was in operation when the CMRO study was published and the complaint proceedings commenced. The Panel noted that the study concluded that of the completed trials associated with 34 new medicines licensed to 24 different companies in 2013, results of 90% had been disclosed within 12 months and results of 93% had been disclosed by 31 July 2015.

The Panel noted that the CMRO publication in question was an extension of previously reported data from two studies, one related to new medicines approved in Europe in 2009, 2010 and 2011 (Rawal and Deane 2014) which found that over three-quarters of all these trials were disclosed within 12 months and almost 90% were disclosed by the end of the study. That study was the subject of an external complaint which gave rise to 27 cases in 2013 and 2014. The second study (Rawal and Deane 2015) was not the subject of external complaint but was taken up under Paragraph 5.1 of the Constitution and Procedure in 2015 leading to 15 cases. The second study found that the results of 90% had been disclosed within 12 months and results of 92% had been disclosed by 31 July 2014. Most of these cases were not in breach of the Code because they were not within the scope of the Code as there was no UK involvement and therefore only limited details were published on the PMCPA website. The present case was not the subject of external complaint. The study itself formed the basis of the complaint.

The Panel considered that the first issue to be determined was whether the matter was covered by the ABPI Code. If the research was conducted on behalf of a UK pharmaceutical company (whether directly or via a third party) then it would be covered by the ABPI Code. If a trial was run by a non UK company but had UK involvement such as centres, investigators, patients etc it was likely that the Code would apply. The Panel appreciated the global nature of much pharmaceutical company sponsored clinical research and a company located in the UK might not be involved in research that came within the ABPI Code. It was a well established principle that UK pharmaceutical companies were responsible for the activities of overseas affiliates if such activities came within the scope of the Code such as activities relating to UK health professionals or activities carried out in the UK.

Clause 13.1 of the 2016 and 2015 editions of the Code stated that companies must disclose details of clinical trials in accordance with the Joint Position on the Disclosure of Clinical Trial Information via Clinical Trial Registries and Databases and the Joint Position on the Publication of Clinical Trial Results in the Scientific Literature.

The relevant supplementary information stated that this clause required the provision of details about ongoing clinical trials (which must be registered within 21 days of initiation of patient enrolment) and the results of completed trials for medicines licensed for use and commercially available in at least one country. Further information was to be found in the current Joint Position on the Disclosure of Clinical Trial Information via Clinical Trial Registries and Databases and the current Joint Position on the Publication of Clinical Trial Results in the Scientific Literature, both at www.ifpma.org.en/ethics/clinical-trials-disclosure.html. Companies must include on the home page of their website, information as to where details of their clinical trials could be found.

The Panel noted that the first Joint Position on the Disclosure of Clinical Trial Information via Clinical Trial Registries and Databases was agreed in 2005 by the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA), the European Federation of Pharmaceutical Industries and Associations (EFPIA), the Japanese Pharmaceutical Manufacturers Association (JPMA) and the Pharmaceutical Research and Manufacturers of America (PhRMA). The announcement was dated 6 January 2005.

The Panel noted that Article 9, Clinical Research and Transparency, of the most recent update of the IFPMA Code of Practice (which came into operation on 1 September 2012) included a statement that companies disclose clinical trial information as set out in the Joint Position on the Disclosure of Clinical Trial Information via Clinical Trial Registries and Databases (2009) and the Joint Position on the Publication of Clinical Trial Results in the Scientific Literature (2010). As companies had, in effect, agreed the joint positions their inclusion in the IFPMA Code should not have made a difference in practice to IFPMA member companies but meant that IFPMA member associations had to amend their codes to reflect Article 9. Pharmaceutical companies that were members of national associations but not of IFPMA would have additional disclosure obligations once the national association amended its code to meet IFPMA requirements. The disclosures set out in the joint positions were not required by the EFPIA Codes.

The Panel noted that even if the UK Code did not apply many of the companies listed in the study were members of IFPMA and/or EFPIA.

The Panel considered that it was good practice for clinical trial results to be disclosed for medicines which were first approved and commercially available after 6 January 2005 (the date of the first joint position). This was not necessarily a requirement of the ABPI Codes from that date as set out below.

As far as the ABPI Code was concerned, the Panel noted that the first relevant mention of the Joint Position on the Disclosure of Clinical Trial Information via Clinical Trial Registries and Databases 2005 was in the supplementary information to Clause 7.5 of the 2006 Code:

'Clause 7.5 Data from Clinical Trials

Companies must provide substantiation following a request for it, as set out in Clause 7.5. In addition, when data from clinical trials is used companies must ensure that where necessary that data has been registered in accordance with the Joint Position on the Disclosure of Clinical Trial Information via Clinical Trial Registries and Databases 2005.'

Clause 7.5 of the 2006 Code required that substantiation be provided at the request of health professionals or appropriate administrative staff. Substantiation of the validity of indications approved in the marketing authorization was not required. The Panel considered this was not relevant to the complaint being considered which was about disclosure of clinical trial results. The Joint Position 2005 was mentioned in the supplementary information to Clause 21.5 but this did not relate to any Code requirement to disclose clinical trial results.

In the 2008 ABPI Code (which superceded the 2006 Code and came into operation on 1 July 2008 with a transition period until 31 October 2008 for newly introduced requirements), Clause 21 referred to scientific services and Clause 21.3 stated:

'Companies must disclose details of clinical trials.'

The relevant supplementary information stated:

'Clause 21.3 Details of Clinical Trials

This clause requires the provision of details about ongoing clinical trials (which must be registered within 21 days of initiation of patients enrolment) and completed trials for medicines licensed for use in at least one country. Further information can be found in the Joint Position on the Disclosure of Clinical Trial Information via Clinical Trial Registries and Databases 2005 (http://clinicaltrials.ifpma.org).

Details about clinical trials must be limited to factual and non-promotional information. Such information must not constitute promotion to health professionals, appropriate administrative staff or the public.'

In the 2011 Code (which superceded the 2008 Code and came into operation on 1 January 2011 with a transition period until 30 April 2011 for newly introduced requirements), the supplementary information to Clause 21.3 was updated to refer to the 2008 IFPMA Joint Position.

In the Second 2012 Edition (which came into operation on 1 July 2012 with a transition period until 31 October 2012 for newly introduced requirements), changes were made to update the references to the joint position and to include the Joint Position on the Publication of Clinical Trial Results in the Scientific Literature. Clause 21.3 now stated:

'Companies must disclose details of clinical trials in accordance with the Joint Position on the Disclosure of Clinical Trial Information via Clinical Trial Registries and Databases and the Joint Position on the Publication of Clinical Trial Results in the Scientific Literature.'

The relevant supplementary information stated:

'Clause 21.3 Details of Clinical Trials

This clause requires the provision of details about ongoing clinical trials (which must be registered within 21 days of initiation of patients enrolment) and completed trials for medicines licensed for use in at least one country. Further information can be found in the Joint Position on the Disclosure of Clinical Trial Information via Clinical Trial Registries and Databases 2009 and the Joint Position on the Publication of Clinical Trial Results in the Scientific Literature 2010, both at http://clinicaltrials.ifpma.org.

Details about clinical trials must be limited to factual and non-promotional information. Such information must not constitute promotion to health professionals, appropriate administrative staff or the public.'

The Panel noted that in the 2014 ABPI Code the disclosure requirements which had previously been stated in Clause 21 had been moved to Clause 13. In addition, the supplementary information stated that companies must include on their website information as to where details of their clinical trials could be found. The 2014 Code came into effect on 1 May 2014 for newly introduced requirements following a transition period from 1 January 2014 until 30 April 2014. These requirements were to be found in Clause 13.1 of the 2015 Code. The relevant supplementary information had been amended in the 2015 Code to replace the year of the relevant joint positions with the word 'current', to add a reference to the medicine being licensed and 'commercially available' and to update the website address. The 2015 Code came into effect on 1 May 2015 for newly introduced requirements following a transition period from 1 January 2015 until 30 April 2015. Similarly the 2016 Code came into effect on 1 May 2016 for newly introduced requirements following a transition from 1 January 2016 to 30 April 2016. The study at issue was posted online on 25 November 2016.

The Panel examined the Joint Position on the Disclosure of Clinical Trial Information which was updated on 10 November 2009 and superseded the Joint Position 2008. With regard to clinical trial registries the document stated that all trials involving human subjects for Phase I and beyond at a minimum should be listed. The details should be posted no later than 21 days after the initiation of enrolment. The details should be posted on a free, publicly accessible, internet-based registry. Examples were given. Each trial should be given a unique identifier to assist in tracking. The Joint Position 2009 provided a list of information that should be provided and referred to the minimum Trial Registration Data Set published by the World Health Organisation (WHO). The Joint Position 2009 referred to possible competitive sensitivity in relation

to certain data elements and that, in exceptional circumstances, this could delay disclosure at the latest until after the medicinal product was first approved in any country for the indication being studied. Examples were given.

The Panel noted that the matter for consideration related to the disclosure of clinical trial results.

With regard to the disclosure of clinical trial results the Joint Position 2009 stated that the results for a medicine that had been approved for marketing and was commercially available in at least one country should be publicly disclosed. The results should be posted no later than one year after the medicine was first approved and commercially available. The results for trials completed after approval should be posted one year after trial completion – an adjustment to this schedule was possible to comply with national laws or regulations or to avoid compromising publication in a peer-reviewed medical journal.

The Joint Position 2009 included a section on implementation dates and the need for companies to establish a verification process.

The Joint Position 2005 stated that the results should be disclosed of all clinical trials other than exploratory trials conducted on a medicine that was approved for marketing and was commercially available in at least one country. The results generally should be posted within one year after the medicine was first approved and commercially available unless such posting would compromise publication in a peer-reviewed medical journal or contravene national laws or regulations. The Joint Position 2008 was dated 18 November 2008 and stated that it superseded the Joint Position 2005 (6 January and 5 September). The Joint Position 2008 stated that results should be posted no later than one year after the product was first approved and commercially available in any country. For trials completed after initial approval these results should be posted no later than one year after trial completion. These schedules would be subject to adjustment to comply with national laws or regulations or to avoid compromising publication in a peer reviewed medical journal.

The Joint Position on the Publication of Clinical Trial Results in the Scientific Literature was announced on 10 June 2010. It stated that all industry sponsored clinical trials should be considered for publication and at a minimum results from all Phase III clinical trials and any clinical trials results of significant medical importance should be submitted for publication. The results of completed trials should be submitted for publication wherever possible within 12 months and no later than 18 months of the completion of clinical trials for already marketed medicines and in the case of investigational medicines the regulatory approval of the new medicine or the decision to discontinue development.

Having examined the various codes and joint positions, the Panel noted that the Joint Position 2005 excluded any clinical trials completed before 6 January 2005. The position changed on 18 November 2008 as the Joint Position 2008 did not have any exclusion relating solely to the date the trial completed. The Joint Position 2009 was similar to the Joint Position 2008 in this regard.

The Panel noted that deciding which Code, and thus which joint position applied, was complicated. It noted that the 2011 Code which, taking account of the transition period, came into operation on 1 May 2011, was the first edition of the Code to refer to the Joint Position 2008.

The Panel concluded that from 1 November 2008, (allowing for the transition period) until 30 April 2011 under the 2008 Code companies were required to follow the Joint Position 2005. From 1 May 2011 until 30 April 2012 under the 2011 Code and 1 May 2012 until 31 October 2012 under the 2012 Code companies were required to follow the Joint Position 2008. Since 1 November 2012 companies were required to follow the Joint Position 2009. The Panel considered that since the 2008 Code companies were, in effect, required to comply with the joint position cited in the relevant supplementary information. The relevant supplementary information gave details of what was meant by Clause 21.3 (Clause 13.1 in the 2014, 2015 and 2016 Codes). The Panel accepted that the position was clearer in the Second 2012 Edition of the Code. The Panel noted that the 2011 Code should have been updated to refer to the Joint Position 2009.

For medicines first licensed and commercially available in any country from 1 November 2008 until 30 April 2011 the results of clinical trials completed before 6 January 2005 would not have to be posted.

From 1 May 2011 there was no exclusion of trials based solely on completion date and so for a product first licensed and commercially available anywhere in the world after 1 May 2011 the applicable joint positions required relevant clinical trial results to be posted within a year of the product being first approved and commercially available or within a year of trial completion for trials completed after the medicine was first available.

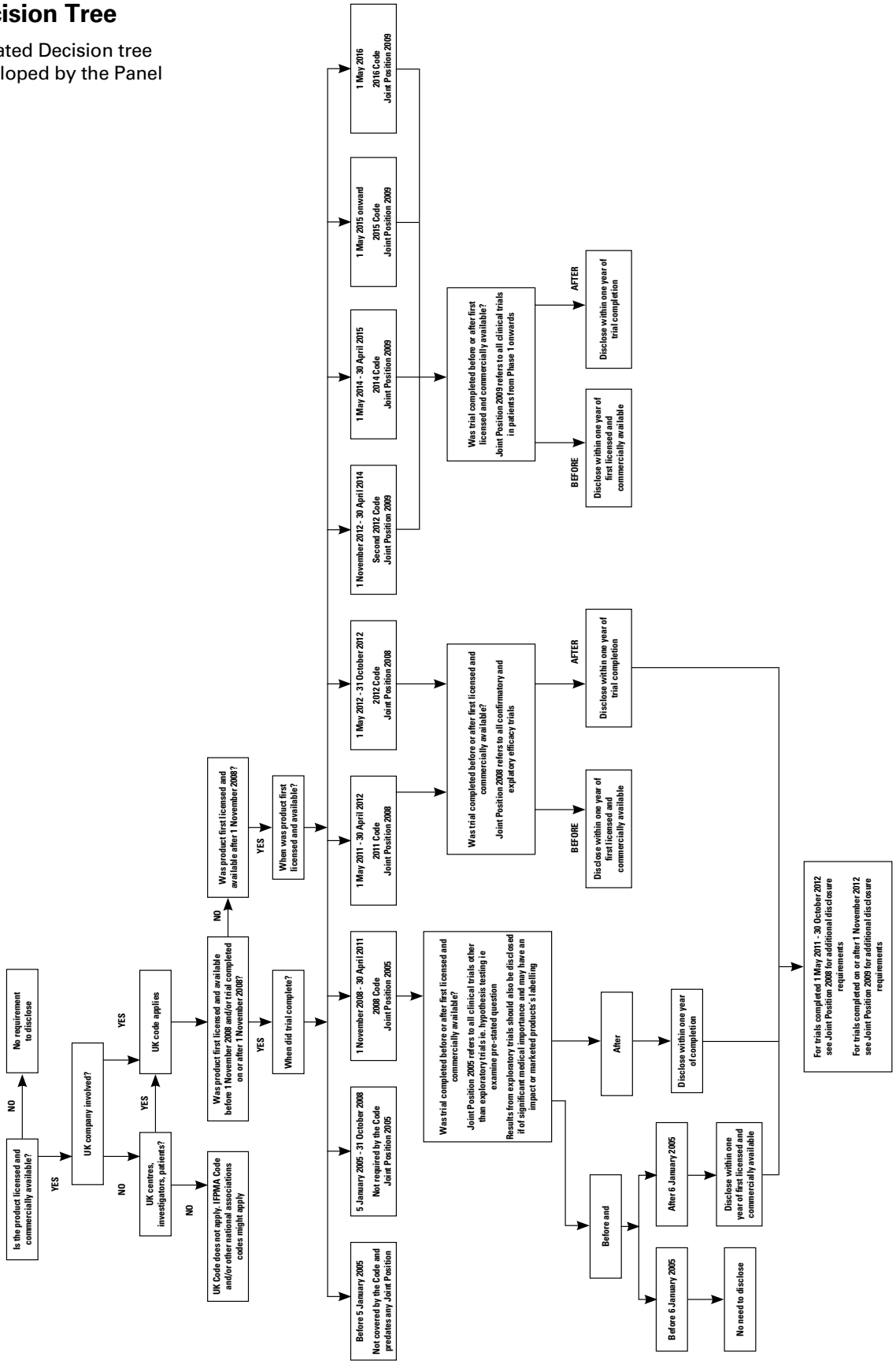
Noting that the CMRO study referred to licensed products the Panel considered that the trigger for disclosure was the date the product was first approved and commercially available anywhere in the world. This would determine which version of the Code (and joint position) applied for trials completed prior to first approval. The next consideration was whether the trial completed before or after this date. For trials completing after the date of first approval, the completion date of the trial would determine which Code applied. The Panel considered that the joint positions encouraged disclosure as soon as possible and by no later than one year after first availability or trial completion as explained above. The Panel thus considered that its approach was a fair one. In this regard, it noted that the matter for consideration was whether or not trial results had been disclosed, all the joint positions referred to disclosure within a one year timeframe and companies needed time to prepare

for disclosure of results. The Panel considered that the position concerning unlicensed indications or presentations of otherwise licensed medicines etc would have to be considered on a case by case basis bearing in mind the requirements of the relevant joint position and the legitimate need for companies to protect intellectual property rights.

The Panel referred to the decision tree in the previous cases (for example Case AUTH/2654/11/13 *et al*) which had been updated in 2015 and published in Case AUTH/2763/5/15. The Panel updated the 2015 decision tree to include the 2016 Code.

Decision Tree

Updated Decision tree developed by the Panel



The Panel considered that companies would be well advised to ensure that all the clinical trial results were disclosed as required by the codes and joint positions. The Panel considered that there was no complaint about whether the results disclosed met the requirements of the joint positions so this was not considered. In the Panel's view the CMRO publication at issue and thus the matter for consideration was only about whether or not trial results had been disclosed and the timeframe for such disclosure. The CMRO publication focussed on the disclosure of evaluable trial results and the Panel only considered those evaluable trials.

The Panel noted that its consideration of these cases relied upon the information provided by the respondent companies. The CMRO publication did not identify the studies evaluated; it only provided quantitative data. The Panel noted that the study related to products approved for marketing by the EMA in 2013 and searched for the data between 1 May and 31 July 2015. The study was published online on 25 November 2016. It appeared that the authors of the CMRO publication had contacted various companies for additional information.

The Panel noted that the date the product was first licensed and commercially available anywhere in the world might pre-date EMA approval.

PANEL RULING

The Panel noted the CMRO publication in that nine evaluable trials (two Phase I and II and seven Phase III) had not been disclosed within the timeframe. The disclosure percentage at 12 months measured from the later of the first date of regulatory approval or trial completion date was 61%. The disclosure percentage at 31 July 2015 was 70%.

The Panel noted Novo Nordisk's submission that Ryzodeg was first approved and commercially available in Denmark on 21 January 2013. The Second 2012 Code and thus the Joint Position 2009 were relevant.

The Panel noted Novo Nordisk's submission that the Phase I and II trials had no UK involvement including no UK patients, investigators or UK funding and neither of the studies were conducted on behalf of Novo Nordisk Ltd (the UK legal entity). The Panel considered that as there was no UK involvement in either of the Phase I or II trials that they did not come within the scope of the UK Code and no breach of the Code was ruled. The Panel noted Novo Nordisk's submission that full clinical trial reports were available from novonordisk-trials.com.

The Panel noted that according to the CMRO publication there were seven Phase III trials that had not been disclosed within the timeframe; six had still not been disclosed by 31 July 2015. The Panel noted Novo Nordisk's submission that relevant trials in scope for results disclosure via the EudraCT database were submitted by the deadlines specified by EMA for the EudraCT results disclosure implementation in the period July 2014-July 2015. For older trials completed prior to implementation the first of these deadlines was 21 July 2015, to which Novo Nordisk adhered.

The Panel noted Novo Nordisk's submission regarding EudraCT submission deadlines and IT issues but considered that the applicable joint position required relevant clinical trial results to be posted within a year of the product being first approved and commercially available or within a year of trial completion for trials completed after the medicine was first available. Publication in any free, publicly accessible internet-based clinical trials database would achieve the intended objectives.

The Panel noted Novo Nordisk's submission that only two Phase III trials (NN5401-3594 and extension study NN5401-3645) had any UK involvement (UK sites and patients).

Studies NN5401-3594 and NN5401-3645 both completed on 2 December 2010 ie before Ryzodeg was launched 21 January 2013 and so results from these trials should have been published by 20 January 2014.

The Panel noted Novo Nordisk's submission that according to the table which it provided, the results for the two trials with UK involvement were made publicly available by August 2012 (NN5401-3594) and November 2013 (NN5401-3645). The Panel noted that the table actually stated that first results for both studies were available on Novonordisk-trials.com on 28 November 2013 with first full publication on 28 August 2012 (NN5401-3594) and February 2016 (NN5401-3645) respectively. The Panel noted that although Novo Nordisk's submission and the table it provided differed slightly, in both cases the results for both trials had been disclosed by 20 January 2014. Thus the Panel ruled no breach of Clause 13.1 of the Code and consequently no breach of Clauses 9.1 and 2.

The Panel noted that although, according to the CMRO publication, there were seven Phase III trials that had not been disclosed within the timeframe Novo Nordisk provided details of fifteen additional Phase III trials. Two of those were referred to above. The Panel noted Novo Nordisk's submission that the remaining thirteen trials had no UK involvement including no UK patients, investigators or UK funding and none of the studies were conducted on behalf of Novo Nordisk Ltd (the UK legal entity). The Panel considered that as there was no UK involvement in any of the remaining thirteen Phase III trials that they did not come within the scope of the UK Code and no breach of the Code was ruled.

Complaint received **29 November 2016**

Cases completed **23 February 2017**