CASE AUTH/3005/12/17

DIRECTOR v BIOGEN

Clinical trial disclosure (Tecfidera)

A study published online in Current Medical Research & Opinion (CMRO) on 8 December 2017 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 2014'. The study authors were B R Deane, LiveWire Editorial Communications and Dr S Porkess, Interim Executive Director of Research Medical and Innovation at the Association of the British Pharmaceutical Industry (ABPI) and Director of Actaros Consultancy and the MedicoMarketing Partnership. Publication support for the study was funded by the ABPI.

The 2017 study surveyed various publicly available information sources for clinical trial registration and disclosure of results searched between 1 May and 31 July 2016. It covered 32 new medicines (except vaccines) from 22 companies that were approved by the European Medicines Agency (EMA) in 2014. It included all completed company-sponsored clinical trials conducted in patients and recorded on a clinical trial registry and/or included in an EMA European Public Assessment Report (EPAR). The CMRO study 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 Biogen 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 supplemental information gave details of disclosure of clinical trial results for each product irrespective of sponsor in the form of a table which gave details for the studies for Tecfidera (dimethyl fumarate).

The detailed response from Biogen is given below.

General detailed comments from the Panel are given below.

With regard to Tecfidera, the Panel noted the CMRO publication in that three evaluable trials 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 67%. The disclosure percentage at 31 July 2016 was 100%.

Tecfidera was first approved and available in March 2013.

The Panel considered that the Second 2012 Code and thus the Joint Position 2009 were relevant.

The Panel noted that the trials completed in October 2009, March 2012 and March 2010. The three trials should have been disclosed by March 2014. The Panel noted Biogen's submission that Biogen UK was sponsor of the three trials despite there being no UK investigators, sites or patients. The trials therefore fell within the scope of the UK Code. The results of the three trials had not been disclosed by March 2014. The Panel thus ruled a breach of the Code. The delay in disclosure meant that high standards had not been maintained and a breach of the Code was ruled.

As the data had now been publicly disclosed the Panel considered that there was no breach of Clause 2 and ruled accordingly.

A study published online in Current Medical Research & Opinion (CMRO) on 8 December 2017 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 2014'. The study authors were B R Deane, LiveWire Editorial Communications and Dr S Porkess, Interim Executive Director of Research Medical and Innovation at the Association of the British Pharmaceutical Industry (ABPI) and Director of Actaros Consultancy Ltd and the MedicoMarketing Partnership. Publication support for the study was funded by the ABPI.

The study referred to the three previously reported studies which covered medicines approved in Europe in 2009, 2010 and 2011 (Rawal and Deane 2014), in 2012 (Rawal and Deane 2015) and in 2014 (Deane and Sivarajah 2016).

The 2017 study surveyed various publicly available information sources for clinical trial registration and disclosure of results searched between 1 May and 31 July 2016. It covered 32 new medicines (except vaccines) from 22 companies that were approved by the European Medicines Agency (EMA) in 2014.

It included all completed company-sponsored clinical trials conducted in patients and recorded on a clinical trial registry and/or included in an EMA European Public Assessment Report (EPAR). The CMRO study 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 Biogen Idec Limited 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.

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 either by the EMA or by the US Food and Drug Administration (FDA) or trial completion, or by 31 July 2016 (end of survey). Of the completed trials associated with 32 new medicines licensed to 22 different companies in 2014, results of 93% (505/542) had been disclosed within 12 months and results of 96% (518/542) had been disclosed by 31 July 2016.

The supplemental information gave details of disclosure of clinical trial results for each product irrespective of sponsor. The data for Tecfidera (dimethyl fumarate) were as follows:

Phase	Total Complete by July 2016	Un-evaluable	Evaluable	Disclosed in 12-month timeframe	Disclosed Percentage at 12 months	Complete by 31 July 2016	Disclosed at 31 July 2016	Disclosure percentage at 31 July 2016
Phase I & II	5	1	4	1	25%	4	4	100%
Phase III	6	3	3	3	100%	3	3	100%
Phase IV	5	4	1	1	100%	1	1	100%
Other	5	2	1	1	100%	1	1	100%
Total	**19**	**10**	**9**	**6**	**67%**	**9**	**9**	**100%**

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

Total complete by 31 July 2016	Total number of company sponsored trials identified which were completed by 31 July 2016
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
Disclosed in 12 month timeframe	Evaluable trials which were disclosed within the target 12 months [12 months measured from the later of: the first date of regulatory approval (in Europe or the US) or the trial completion date]
Disclosed percentage at 12 months	Proportion of evaluable trials which were disclosed within 12 months [12 months measured from the later of: the first date of regulatory approval (in Europe or the US) or the trial completion date]
Completed before 31 July 2016	Number of evaluable trials completed before 31 July 2016
Disclosed at 31 July 2016	Number of evaluable trials with results disclosed by 31 July 2016
Disclosure percentage at 31 July 2016	Proportion of evaluable trials which were disclosed by 31 July 2016

When writing to Biogen 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

Biogen stated that the complaint related to the product Tecfidera and was based on the study (sponsored by the ABPI) published online in the Current Medical Research and Opinion (CMRO) dated 8 December 2017 in which Biogen was listed as one of the companies with medicines approved in Europe in 2014. The complaint was that of the completed clinical trials of 32 new medicines licensed to 22 different companies in 2014, results of 93% had been disclosed within 12 months and results of 96% had been disclosed by 31 July 2016.

Biogen stated that there were 19 company sponsored clinical trials carried out in relation to Tecfidera ranging from Phase I to IV. Of these, all but 3 (Phase I and II) trials were disclosed by March 2014. These 3 remaining trials were disclosed by March 2015. In was Biogen's understanding that it was cited as being the responsible company as it was the European Market Authorisation Holder. Tecfidera received market authorisation by the EMA in January 2014.

Biogen submitted it was committed to sharing information and publishing clinical trials. To this end, by January 2014 it established and started to

implement policies and procedures to comply with the PhRMA/IFPMA/EFPIA Principles for Responsible Clinical Trial Data Share and to comply with national regulatory systems.

By 2015, Biogen had further advanced its procedures encompassing the PhRMA/EFPIA/IFPMA/JPMA Joint Position Statements and local industry bodies including the ABPI, to ensure registration and publication of clinical trial results in a timely manner. Biogen's corporate website was enhanced to provide additional details to the public regarding its policy and the results of completed clinical trials. It appreciated that in setting up and implementing the systems in the USA and its affiliates in Europe, there might have been some delay in the publishing of the clinical trial results. However, all disclosures were completed by March 2015 and since then disclosure of clinical trial results had been streamlined.

The three Phase I and II studies were disclosed as follows:

a) The CHMP summary for Tecfidera was published on 22 March 2013, the EPAR public assessment report was published on 26 February 2014. All three of the clinical trials complied with the requirements of the 2009 Joint Position Statement for registration of the clinical trial within 21 days after the initiation of patient enrolment.
b) All clinical trial results were disclosed in accordance with the EU Article 11 of the Clinical Trial Directive 2001/20/EC, Article 57 of Regulation (EC) No 726/2004 and Article 41 of the Paediatric Regulation (EC) No 1901/2006.
c) All three of the clinical trials were not in scope of US Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (PL110-85).
d) Study ID: 109MS101. The clinical trial results were published in March 2015;
   - The Clinical Study Report (CSR) Synopsis was shared via Biogen.com's website in March 2015
   - Results were submitted to the EudraCT database in March 2016 (prior to the required date); however, the EU did not make the results of Phase I studies publicly available.

   e) Study ID: 109MS201. The clinical trial results were published in March 2015;
   - The CSR Synopsis was shared via Biogen.com's website in March 2015
   - Results were not required to be submitted to the EudraCT database
   - Although results were not required per US on ClinicalTrials.gov; Biogen posted results in May 2015.

f) Study ID: 109RA201. The clinical trial results were published in March 2015
   - The CSR Synopsis was shared via Biogen.com's website in March 2015
   - Results were submitted to the EudraCT database in March 2016 (prior to the required date) and are publicly available
   - Results were not required per US on Clinical Trials.gov.

In conclusion, Biogen submitted that these were evaluable studies and were Phase I and II studies. The results of the studies were positive, therefore there was no incentive to not publish. As stated above, the policies, procedures and systems within Biogen were fully implemented, all studies were published and since then had been disclosed within time. Whilst it was unfortunate that the results were not disclosed within the required timeframes, all results were made publicly available as of March 2015. Most importantly, Biogen did not believe that the delay in disclosure impacted patient safety or public health.

In response to a request for further information, Biogen submitted that Tecfidera was first approved and available in the US on 27 March 2013. Biogen submitted that the completion dates (LPO dates) were October 2009 for trial 109MS101, March 2012 for trial 109MS201, and March 2010 for trial 109RA201. Biogen submitted that both Biogen USA and Biogen UK were listed on all trial documents as the trial sponsor even for the trial that only ran in the US. There were no trial sites or investigators in the UK. Trial 109MS101 had a site in Germany, trial 109MS201 had US sites and trial 109RA201 had sites in Australia, Canada, Czech, India, Poland and Slovakia. No UK patients were enrolled in these three trials.

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 32 new medicines licensed to 22 different companies in 2014, results of 93% had been disclosed within 12 months and results of 96% had been disclosed by 31 July 2016.

The Panel noted that the CMRO publication in question was an extension of previously reported data from three studies. One study 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 third study (Deane and Sivarajah 2016) was not the subject of external complaint but was taken up under Paragraph 5.1 of the Constitution and Procedure in 2016 leading to 17 cases. The third study found that the results of 90% had been disclosed within 12 months and results of 93% had been disclosed by 31 July 2015. 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 PMCPA had published an item in the May 2017 Code of Practice Review and the decision tree was 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 8 December 2017.

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.

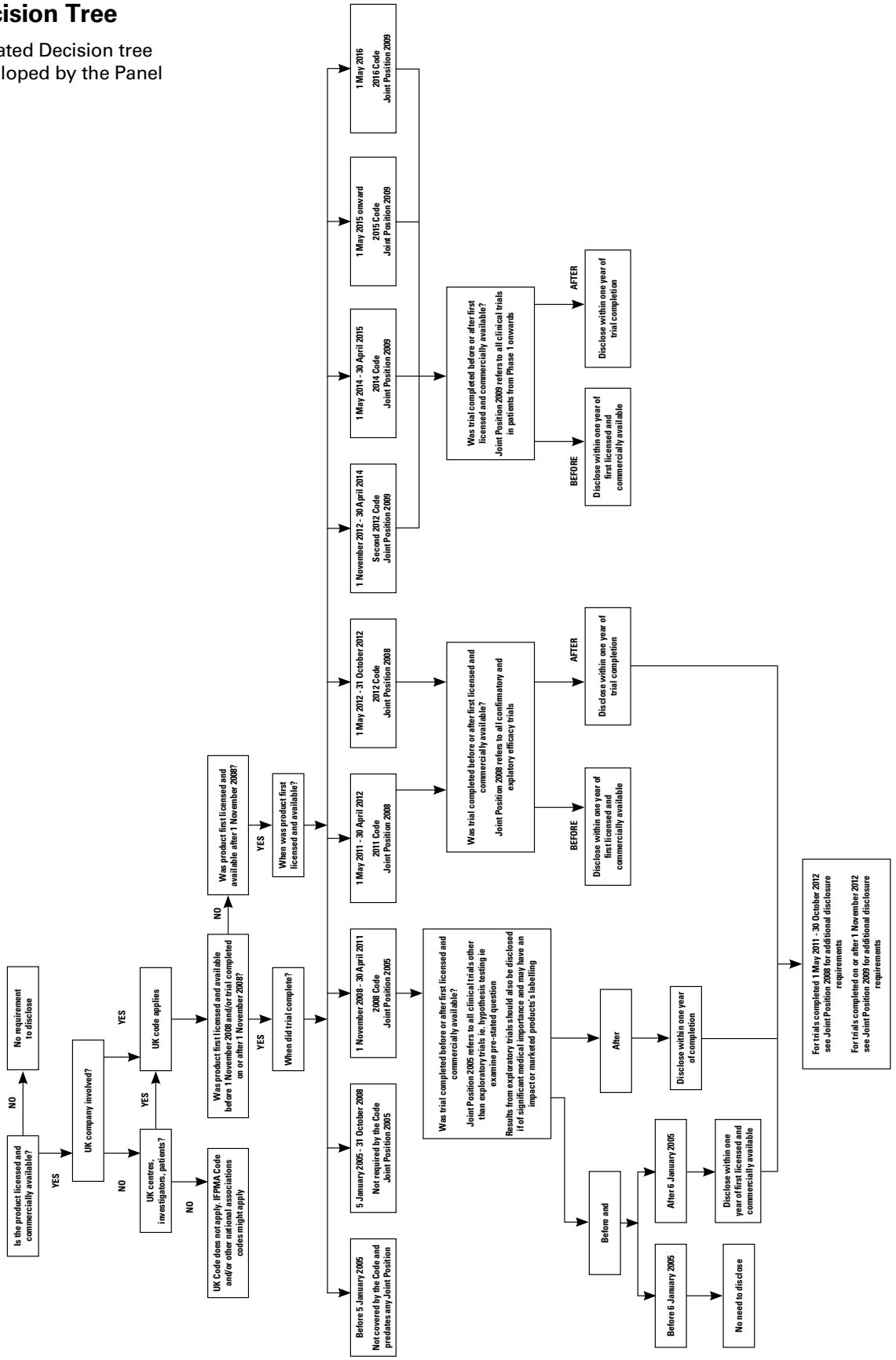
Noting that the CMRO study referred to licensed products the Panel considered that the trigger for disclosure was the date the product was first approved and commercially available anywhere in the world. This would determine which version of the Code (and joint position) applied for trials completed 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 which had been updated in 2016 and published in case reports and on the PMCPA website in May 2017. An update (to the information about the 2015 and 2016 Codes) appears on the next page.

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.

Decision Tree

Updated Decision tree developed by the Panel



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 2014 and searched for the data between 1 May and 31 July 2016. The study was published online on 8 December 2017. 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 and/or the US approval.

PANEL RULING IN CASE AUTH/3005/12/17

The Panel noted the CMRO publication in that three evaluable trials 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 67%. The disclosure percentage at 31 July 2016 was 100%.

The Panel noted Biogen's submission that Tecfidera was first approved and available in the US on 27 March 2013. The Second 2012 Code and thus the Joint Position 2009 were relevant.

The Panel noted that one of the trials (109MS101) completed in October 2009, one (109MS201) in March 2012 and the other (109RA201) in March 2010. The Panel noted that on the information before it all three trials should have been disclosed by 27 March 2014. The Panel noted Biogen's submission that Biogen UK was sponsor of the three trials despite there being no UK investigators, sites or patients. The trials therefore fell within the scope of the UK Code. The Panel noted that the results of the three trials had not been disclosed by 27 March 2014. The Panel thus ruled a breach of Clause 13.1. The Panel noted Biogen's submission with regards to when the results of each trial were disclosed. The delay in disclosure meant that high standards had not been maintained and a breach of Clause 9.1 was ruled.

As the results had now been publicly disclosed the Panel considered that there was no breach of Clause 2 and ruled accordingly.

Complaint received **20 December 2017**

Case completed **13 March 2018**