CASE AUTH/3091/9/18

DIRECTOR v UCB

Clinical trial disclosure

A study published online in the British Medical Journal (12 September 2018) was entitled 'Compliance with requirement to report results on the EU Clinical Trials Register: cohort study and web resource' (Goldacre *et al* 2018).

The study objectives included assessing compliance rates with the European Commission's requirement that all trials on the EU Clinical Trials Register (EUCTR) posted results to the registry within 12 months of completion (final compliance date 21 December 2016). The study objectives also included identifying features associated with non-compliance, ranking sponsors by compliance and building a tool for live ongoing audit of compliance. The published paper listed the trial sponsors with the highest proportion of trials reported and the trial sponsors with the highest proportion of trials unreported. The results were that of 7,274 trials where results were due, 49.5% (95% confidence interval 48.4% to 50.7%) reported results.

Goldacre *et al* stated that the European Commission (EC) Guideline required the results of all trials to be reported in structured form on to the register itself. It was possible that some trials that did not report results to EUCTR reported results elsewhere eg in a conference presentation, an academic journal article, as part of a meta-analysis after data were requested by systematic reviewers, or in the grey literature. Such publications did not meet the reporting requirements of the EC Guideline and were therefore outside the scope of the study.

Goldacre *et al* listed sponsors with more than 50 trials on the EUCTR and did not mention products or specific clinical trials. Goldacre *et al* gave details of disclosure of clinical trial results for each sponsor.

The Director decided that the Goldacre *et al* article was such that she had received information from which it appeared that UCB 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 detailed response from UCB is given below.

General detailed comments from the Panel are given below.

The Panel noted the data in Goldacre *et al* in that results for five of UCB's due trials had not been reported on EUCTR; the disclosure percentage was 87.5%.

The Panel noted UCB Pharma's submission that although UK sites were planned in trial SP935 , the trial was cancelled on 26 March 2008 before any patients were enrolled and

so no data was collected. The Panel therefore ruled no breaches of the Code including no breach of Clause 2 in relation to trial SP935.

The Panel noted UCB Pharma's submission that trial RA0134 had no UK involvement, no UK sites, investigators or patients and UCB Pharma Ltd was not involved in the funding nor conduct of the clinical trial. The Panel considered that as there was no UK involvement, the matter did not come within the scope of the UK Code. No breach of the Code was ruled in relation to trial RA0134.

The Panel noted UCB's submission that trials RA0056, RA0057 and CD0001 related to a product which was out-licensed from UCB to R-Pharm in June 2013, upon completion of the Phase II programme (to which RA0056, RA0057 and CD0001 belong) and before the start of the Phase III programme (which would be the responsibility of R-Pharm).

The Panel noted that the sponsor for trials RA0056 and RA0057 was UCB Biosciences Inc, UCB's entity in the US. The Panel noted UCB Pharma's submission that the UK was not involved in funding or conducting these two trials but both had sites in the UK.

The Panel noted that trial RA0056 had 10 study sites in UK and completed on 29 June 2012. The Panel noted UCB's submission that study results were published in a peer-reviewed journal in 2014. However, the Panel noted that the results did not appear to be published on EUCTR within the required timeframe. The Panel therefore ruled a breach of the Code. The Panel noted from the evidence before it that there did not appear to have been any formal finding by any judicial authority or appropriate body charged with determining matters in relation to the Commission Guidelines that the company had not complied with the relevant laws and regulations. The Panel therefore ruled no breach of the Code in that regard. The Panel was unsure whether or not the results were now disclosed on EUCTR but noted that they were published elsewhere as stated above. The Panel therefore did not consider that in the circumstances a breach of Clause 2 was warranted and ruled accordingly.

The Panel noted that trial RA0057 had 19 sites in UK and completed on 5 August 2013. However, the Panel noted that the results did not appear to be published on EUCTR within the required timeframe. The Panel therefore ruled a breach of the Code. The Panel noted from the evidence before it that there did not appear to have been any formal finding by any judicial authority or appropriate body charged with determining matters in relation to the Commission Guidelines that the company had not complied with the relevant laws and regulations. The Panel therefore ruled no breach of the Code in that regard. The Panel was unsure whether or not the results were now disclosed on EUCTR or elsewhere. On balance, the Panel did not consider that in the circumstances a breach of Clause 2 was warranted and ruled accordingly.

The Panel noted UCB Pharma's submission that trial CD0001 was sponsored by UCB Biosciences GmbH, Inc, UCB's entity in Germany. UCB in the UK was not involved in the funding nor conduct of the clinical trial which had no UK sites. The study was prematurely terminated in October 2013, with no patient enrolled. The Panel considered that as there was no UK involvement, the matter did not come within the scope of the UK Code. No breach of the Code was ruled in relation to trial CD0001.

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Following its completion of the consideration of four appeals in the clinical trial cases on 18 September 2019 (Cases AUTH/3079/9/18 (Pfizer), AUTH/3087/9/18 (GlaxoSmithKline), AUTH/3118/11/18 (Tesaro) and AUTH/3102/9/18 (Lilly), the Appeal Board noted that the respondent companies in Case AUTH/3084/9/18 (Boehringer Ingelheim), Case AUTH/3091/9/18 (UCB), Case AUTH/3097/9/18 (Teva), and Case AUTH/3099/9/18 (Allergan), accepted the Panel's rulings of breaches of the Code and had not appealed.

The Appeal Board noted that a series of cases had been taken up by the PMCPA as a result of the data published in Goldacre *et al*. Four cases (Cases AUTH/3079/9/18, AUTH/3087/9/18, AUTH/3118/11/18 and AUTH/3102/9/18) were the subject of an appeal by the respondent companies. Each was determined on its own merits but there were a number of common themes. (Full details can be found in the relevant case reports)

The Appeal Board noted that Article 57(2) of Regulation (EC) No 726/2004 and Article 41(2) of Regulation (EC) No 1901/2006 required that clinical trial data be published on EUCTR. European Commission (EC) Guideline 2012/c302/03 gave guidance as to when the clinical trial results data should be published. According to the guideline posting of results of clinical trials which ended one year or more prior to finalisation of the programming of the relevant database, should be done within 24 months of finalisation of that programming. According to the 'What's New' section of EudraCT public website (post-dated 13 January 2016) the deadline for submission of these results was 21 December 2016. This date was referred to in Goldacre *et al.* It appeared to the Appeal Board that whilst the regulation mandated disclosure of results on EUCTR, the EC Guideline and other material advised companies how to comply with the regulation including in relation to the timing of such disclosures. The Appeal Board considered that it was within the spirit of the Code and good practice to comply with the EC Guideline in question.

The Appeal Board noted that, where companies had merged or the rights to a particular product had been bought or sold, there appeared to be difference of opinion as to which company would be responsible for posting the retrospective results. There were also difficulties in correcting information once posted.

The Appeal Board also noted that, according to Goldacre *et al*, Phase 1 trial results that were not part of a paediatric plan did not need to be disclosed.

The Appeal Board considered that there would be a difference between action to deliberately hide clinical trial data or systematic failure resulting in non or late disclosure and late disclosure of results as part of a retrospective exercise contrary to non-mandatory timelines due to mitigating factors. The Appeal Board, nonetheless, noted its view above about good practice and disclosure in accordance with the EC Guideline.

The Appeal Board was concerned in each case about the failure to disclose the summary results on EUCTR within the timelines advised by the EC Guideline and other relevant advice. In the exceptional circumstances of each case, the Appeal Board did not consider that the late posting of the trial results on the EUCTR as part of a retrospective exercise warranted a breach of the Code particularly in two of the cases as in those the trial results had been publicly disclosed prior to receipt of the complaint. The appeals in the above four cases were successful.

The Appeal Board agreed that Boehringer Ingelheim, UCB, Teva and Allergan should be contacted and informed of the outcome of the appeals in Cases AUTH/3079/9/18, AUTH/3087/9/18, AUTH/3118/11/18 and AUTH/3102/9/18. The PMCPA Constitution and Procedure did not cover this unusual situation where more than one company was involved in a similar set of circumstances and the Appeal Board had taken a different view to the Panel. Boehringer Ingelheim, UCB, Teva and Allergan were offered the opportunity to appeal out of time and the appeal process would operate in the usual way. The Appeal Board noted that each cases' circumstances might differ, and the result of any appeal could not be guaranteed. After consideration of the appeals the Appeal Board agreed that Boehringer Ingelheim, UCB, Teva and Allergan should each be offered the opportunity to appeal out of time.' Allergan and UCB declined the opportunity to appeal and Boehringer Ingelheim. Teva successfully appealed the Panel's rulings of breaches of the Code.

A study published online in the British Medical Journal (12 September 2018) was entitled 'Compliance with requirement to report results on the EU Clinical Trials Register: cohort study and web resource' (Goldacre *et al* 2018).

The study objectives included assessing compliance rates with the European Commission's requirement that all trials on the EU Clinical Trials Register (EUCTR) posted results to the registry within 12 months of completion (final compliance date 21 December 2016). The study objectives also included identifying features associated with non-compliance, ranking sponsors by compliance and building a tool for live ongoing audit of compliance. The published paper listed the trial sponsors with the highest proportion of trials reported and the trial sponsors with the highest proportion of trials unreported. The results were that of 7,274 trials where results were due, 49.5% (95% confidence interval 48.4% to 50.7%) reported results. Results from trials with a commercial sponsor were substantially more likely to be posted than those from a non-commercial sponsor (68.1% v 11.0%, adjusted odds ratio 23.2, 95% confidence interval 19.2 to 28.2) as were trial results from a sponsor who conducted a large number of trials (77.9% v 18.4%, adjusted odds ratio 18.4, 15.3 to 22.1). More recent trials were more likely to report results (per year odds ratio 1.05, 95% confidence interval 1.03 to 1.07). Extensive evidence was found of errors, omissions, and contradictory entries in EUCTR data that prevented ascertainment of compliance for some trials.

The Director decided that the Goldacre *et al* article was such that she had received information from which it appeared that UCB 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 concluded that compliance with the European Commission requirement for all trials to post results on to the EUCTR within 12 months of completion had been poor, with half of all trials non-compliant. EU registry data commonly contained inconsistencies that might prevent even regulators assessing compliance. Accessible and timely information on the compliance status of each individual trial and sponsor might help to improve reporting rates.

Goldacre *et al* noted that any trial of any medicinal product conducted since 2004 in an EU country had already been required to register on the EUCTR, which was administered by the European Medicines Agency (EMA). Following the 2012 European Commission (EC) guideline 2012/c302/03, sponsors must ensure that they disclosed their results of all trials registered on EUCTR since 2004 to the EMA within 12 months of trial completion; Phase I trials were exempt

unless they were denoted as being part of a paediatric investigation plan. These trial reports were posted publicly on to the EUCTR within 15 working days of receipt by the EMA and were required to include salient features such as results for all pre-specified trial outcomes and statistical analyses, details of 'serious' and 'non-serious' adverse events, participants' baseline characteristics, and protocol deviations, as well as discussion of design limitations and caveats. Following various delays in the EMA's implementation of the software platform for results posting, the final date for sponsors' compliance was 21 December 2016.

Goldacre *et al* assessed compliance with the EU requirement to post results on to EUCTR for all trials on the registry, explored factors associated with non-compliance, identified the individual trial sponsors that were best at complying, and created a live online service, driven by regular updates of the EUCTR data, to give ongoing and regularly updated performance statistics for compliance.

The publication listed a number of variables.

Goldacre *et al* stated that the EUCTR data underlying this study were updated regularly. An interactive online website presenting the overall reporting rate for all due trials, the reporting rates for each sponsor, ranks for these reporting rates, and details of each sponsor's individual reported and unreported trials was developed. The data underlying this site was updated regularly following each new download of the EUCTR database: the results and ranks for each individual sponsor were therefore always current and changed as performance changed. All software underlying this service was shared as open source and available for open code review or for adaptation and re-use.

Goldacre *et al* stated that the European Commission (EC) Guideline required the results of all trials to be reported in structured form on to the register itself. Ascertainment of the outcome – a results report on EUCTR – was therefore accurate and complete. It was possible that some trials that did not report results to EUCTR reported results elsewhere eg in a conference presentation, an academic journal article, as part of a meta-analysis after data were requested by systematic reviewers, or in the grey literature. Such publications did not meet the reporting requirements of the EC Guideline and were therefore outside the scope of the study. A manual search of academic journals and grey literature for a random sample of 100 trials unreported on EUCTR was conducted as requested as part of the peer review of the publication. Five were reported in the grey literature and 46 in a journal publication.

Goldacre *et al* listed sponsors with more than 50 trials on the EUCTR and did not mention products or specific clinical trials. The study publication listed the sponsors with the highest proportion of trials reported and those with the lowest proportion of trials reported.

Goldacre *et al* gave details of disclosure of clinical trial results for each sponsor. The data for UCB Pharma were as follows:

Sponsors with highest proportion of trials reported

Sponsor	Total trials on EUCTR	Due trials	Due trials with results	% reported
UCB	180	40	35	87.5

When writing to UCB Pharma the Authority asked it to bear in mind the requirements of Clauses 2, 9.1, 1.11 and 13.1 of the Code. The Authority noted that previous editions of the Code might be relevant and provided details.

RESPONSE

UCB noted that in the BMJ study it was stated that published results were due for 40 trials but only 35 were available; there was no reference to which studies the authors were referring.

UCB submitted that it had identified that the following were the 5 trials at issue:

Trial SP935

This trial was on rotigotine transdermal patch and was sponsored by Schwarz Biosciences GmbH (now known as UCB Biosciences GmbH) a UCB entity in Germany. UCB Pharma Ltd (UCB's UK entity) was not involved in the funding or conduct of this study. Although UK sites were planned and 14 April 2008 was the planned first patient first visit date, the trial was cancelled on 26 March 2008 before any patients were enrolled and so no data were collected. In the EU Clinical trials Register (EUCTR) the trial was recorded as 'prematurely ended' as the study was cancelled and never recruited patients.

From the decision tree developed by PMCPA and general comments provided by the Panel, the trigger for disclosure was the date the product was first approved and commercially available anywhere in the world. Rotigotine was first licensed globally in the EU on 15 February 2006. As the date of first approval was 2006 and the 2006 version of the Code did not require disclosure of clinical trial results, UCB considered that disclosure of trial SP935 results were not required even if available (which was not the case as the trial never enrolled patients).

In any respect and, (as noted above) the trial was cancelled; hence no results or relevant conclusion were available to be published.

Trial RA0134

This trial involved bimekizumab which was not yet licensed or commercialised. The trial was sponsored by UCB Biopharma Sprl, UCB's entity in Belgium. UCB Pharma Ltd was not involved in the funding nor conduct of the clinical trial and no sites, patients or investigators in the UK were involved. UCB submitted that the study, therefore, did not fall within the scope of the Code.

Furthermore, while the trial was recorded in the European Clinical Trials Database (EudraCT) registry as 'completed', in reality the study was cancelled before patients were enrolled and so no results were due for disclosure.

Trials RA0056, RA0057 and CD0001

All three trials related to a product which was out-licensed from UCB to R-Pharm in June 2013, upon completion of the Phase II programme (to which RA0056, RA0057 and CD0001 belong) and before start of the Phase III programme (which would be responsibility of R-Pharm). The product was not currently licensed anywhere in the world; hence with all three trials there was no current requirement to publish the study data under the Code.

The sponsor for trial RA0056 was also UCB Biosciences Inc, UCB's entity in the US. UCB in the UK was not involved in funding or conducting this clinical trial. The trial had 10 trial sites in UK, started on 25 February 2011 and completed on 29 June 2012. Study results were published in a peer-reviewed journal (Genovese, MC *et al* Ann Rheum Dis; 2014; 73; 9; 1607-1615;).

The sponsor for trial RA0057 was also UCB Biosciences Inc and again UCB in the UK was not involved in the funding or conduct of this trial. The trial had 19 sites in UK; it started on 27 April 2011 and completed on 5 August 2013.

The sponsor for trial CD0001 was UCB Biosciences GmbH, Inc, UCB's entity in Germany. UCB in the UK was not involved in the funding nor conduct of the clinical trial which had no UK sites. The trial started on 20 June 2012 and was prematurely terminated in October 2013, with no patient enrolled.

Summary

Based on the explanations provided above for all the 5 trials identified as the subject of this complaint, UCB believed that there was a clear explanation, in line with the Code, as to why the results were not published. In this context, UCB considered that Clause 13.1 did not apply to any of the identified studies. UCB had a robust governance framework in place for disclosing clinical trial results to which it was fully committed, hence it rejected a breach of Clause 1.11.

In conclusion, UCB considered that there had been no breach of the Code and therefore no breach of Clauses 9.1 and 2.

GENERAL COMMENTS FROM THE PANEL

The Panel noted that Goldacre *et al* was not the subject of external complaint but was taken up under Paragraph 5.1 of the Constitution and Procedure.

The Panel noted that Goldacre *et al* was the basis of the complaint in relation to the allegation that sponsors with less than 100% reported trials were not meeting the requirements of the EC Guideline.

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 Goldacre *et al* was published and the complaint proceedings commenced.

The Panel noted that there had been three previous studies looking at the disclosure of clinical trial data all published in Current Medical Research and Opinion (CMRO). The first 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 and led to 15 cases. The third study (Deane and Sivarajah 2016) was not the subject of external complaint but was also taken up under Paragraph 5.1 in 2016 and led to 17 cases. 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 previous studies surveyed various publicly available information sources for clinical trial registration and disclosure of results searched between specific dates covering medicines

(except vaccines) that were approved by the European Medicines Agency (EMA) in a particular year or years. The Panel noted that the previous cases had established a number of principles including deciding which Code applied.

Goldacre *et al* was different to the previous three studies which assessed compliance with the Joint Positions; it only assessed compliance with the EU requirement to post results on to the European Union Clinical Trial Register (EUCTR) for all trials listed on the registry. In that regard, trials involving investigational products that were not licensed for use anywhere in the world might be included. Companies had not made a detailed submission on this point.

The Panel noted that the European Clinical Trials Database (EudraCT) was a database hosted by the EMA in which clinical trial sponsors would upload summary results. These results would then be published on the EUCTR.

The Panel considered that in these circumstances the trial completion date would be the trigger for results disclosure on EUCTR. The Panel noted that the publicly available EudraCT and EUCTR Q&A document stated in response to the question 'if the trial is prematurely ended/early terminated due to lack of subjects or lack of data to analyse, do I have to provide results?', that in the case that no subjects were recruited, it was not appropriate to complete the full dataset. However, there was currently no functionality for sponsors to inform that recruitment never started or that the trial was prematurely ended in the results data model. In this specific case sponsors had to liaise directly with the National Competent Authority confirming that no results would be available for a specific trial due to 'lack of subjects' or that the trial was 'prematurely ended' so a statistical analysis could not be provided. The Panel noted that according to the Commission Guideline 'Guidance on posting and publication of result-related information on clinical trials in relation to the implementation of Article 57(2) and Regulation No 726/2001 and Article 41(2) of Regulation No 1901/2006', if the clinical trial ends prematurely, that date should be considered the end of trial date.

The Panel noted that according to Goldacre *et al* any trial of any medicinal product conducted since 2004 in an EU country had already been required to register on the EUCTR, which was administered by the European Medicines Agency (EMA). Following the 2012 European Commission (EC) guideline 2012/c302/03, sponsors must ensure that they disclosed the results of all trials registered on EUCTR since 2004 to the EMA within 12 months of trial completion; Phase I trials were exempt unless they were denoted as being part of a paediatric investigation plan. These trial reports were posted publicly on to the EUCTR within 15 working days of receipt by the EMA and were required to include salient features. Goldacre *et al* noted that following delays in the EMA's implementation of the software platform for results posting, the final date for sponsors' compliance was 21 December 2016.

The Panel considered that the subject matter of the complaint was failure to publish results on EUCTR. It appeared to the Panel that under EUCTR for non-paediatric trials, at least one investigator site of the clinical trial should be located in Europe or in a contracting state of the European Economic Area (EEA). The Panel noted that it could only consider the matter with regard to the Code. In the Panel's view, only those with a UK nexus would be considered to be within the scope of the Code.

The Panel noted that the Code did not explicitly refer to publication on the EUCTR. Clause 13.1 referred, *inter alia*, to disclosure of clinical trials in accordance with the Joint Positions on the Disclosure of Clinical Trial Information via Clinical Trial Registries and Databases and the Publication of Clinical Trial Results in the Scientific Literature. According to the 2009 Joint

Position, publication of clinical trial results in any free, publicly accessible internet-based clinical trials database should achieve the intended objectives.

The Panel noted the differences between the Joint Positions and the requirement to publish clinical trial results on the EUCTR; it was possible that results might not need to be published under the Joint Positions (for instance because the medicine was not licensed for use or commercially available) but might nonetheless be required to be published on the EUCTR. The Panel considered that companies would be well advised to ensure that all the clinical trial results were disclosed as required by the law, codes and Joint Positions. The Panel noted that Goldacre *et al* had not commented on whether the results disclosed met the requirements of the Joint Positions so this was not considered; in the Panel's view the only matter for consideration was whether or not trial results had been disclosed within the required timeframe as required by the Commission Guideline 2012/C302/03 which came into operation in 2012, and by 21 December 2016 which was referred to by Goldacre *et al* as the final data for sponsor's compliance. The Panel considered, therefore, that in this particular case it would make its rulings under the Code in operation on 21 December 2016, the 2016 Code. The Panel considered that its approach was a fair one.

The Panel noted that the companies had been asked to respond, *inter alia*, to Clause 13.1. Given that Goldacre *et al* did not refer to the Joint Positions and noting the differences between the requirements to disclose under the Joint Positions and under the Commission Guidelines the Panel considered, taking a pragmatic approach, that the matters raised by Goldacre *et al* would be considered under Clause 9.1, rather than Clause 13.1. The companies had been asked to respond to, *inter alia*, Clauses 9.1 and 1.11 at the outset and had been provided with a copy of Goldacre *et al*. The Panel noted that the publicly available EudraCT and EUCTR Q&A document referred to sponsors who were not fulfilling the legal requirements in providing results in EudraCT.

The Panel considered that the first issue to be determined was whether the matter was covered by the ABPI Code. If the clinical trial 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 those activities came within the scope of the Code such as those related to UK health professionals or carried out in the UK.

The Panel noted that the Authority was not an investigative body as such and its consideration of these cases relied upon the information provided by the parties. The quantitative data published by Goldacre *et al* formed the basis of the complaint. The Panel noted that in that regard the case preparation manager had not used the live data web resource to identify the trials at issue.

PANEL RULING

The Panel noted its general comments above about the subject matter of the complaint as set out in Goldacre *et al.* The Panel had decided that the alleged failure to publish results in accordance with the Commission Guidelines was more appropriately covered by Clause 9.1 and potentially Clause 1.11. The Panel made no ruling in relation to Clause 13.1.

The Panel noted the data in Goldacre *et al* in that results for five of UCB's due trials had not been reported on EUCTR; the disclosure percentage was 87.5%.

The Panel noted UCB Pharma's submission that trial SP935 involved rotigotine, for which the date of first approval was 15 February 2006 and it was subsequently commercialised across EU countries. The Panel noted that although UK sites were planned (14 April 2008 was the planned first patient first visit date), the trial was cancelled on 26 March 2008 before any patients were enrolled and so no data was collected. The Panel therefore ruled no breach of Clauses 1.11, 9.1 and 2 in relation to trial SP935.

The Panel noted UCB Pharma's submission that trial RA0134 had no UK involvement, no UK sites, investigators or patients and UCB Pharma Ltd was not involved in the funding nor conduct of the clinical trial. The Panel considered that as there was no UK involvement, the matter did not come within the scope of the UK Code. No breach of the Code was ruled in relation to trial RA0134.

The Panel noted UCB's submission that trials RA0056, RA0057 and CD0001 related to a product which was out-licensed from UCB to R-Pharm in June 2013, upon completion of the Phase II programme (to which RA0056, RA0057 and CD0001 belong) and before the start of the Phase III programme (which would be the responsibility of R-Pharm).

The Panel noted that the sponsor for trials RA0056 and RA0057 was UCB Biosciences Inc, UCB's entity in the US. The Panel noted UCB Pharma's submission that the UK was not involved in funding or conducting these two trials but both had sites in the UK.

The Panel noted that trial RA0056 had 10 study sites in UK, started on 25 February 2011 and completed on 29 June 2012. The Panel noted UCB's submission that study results were published in a peer-reviewed journal in 2014. However, the Panel noted that the results did not appear to be published on EUCTR within the required timeframe. The Panel therefore ruled a breach of Clause 9.1. The Panel noted from the evidence before it that there did not appear to have been any formal finding by any judicial authority or appropriate body charged with determining matters in relation to the Commission Guidelines that the company had not complied with the relevant laws and regulations. The Panel therefore ruled no breach of Clause 1.11 in relation to this trial. The Panel was unsure whether or not the results were now disclosed on EUCTR but noted that they were published elsewhere as stated above. The Panel therefore did not consider that in the circumstances a breach of Clause 2 was warranted and ruled accordingly.

The Panel noted that trial RA0057 had 19 sites in UK; it started on 27 April 2011 and completed on 5 August 2013. However, the Panel noted that the results did not appear to be published on EUCTR within the required timeframe. The Panel therefore ruled a breach of Clause 9.1. The Panel noted from the evidence before it that there did not appear to have been any formal finding by any judicial authority or appropriate body charged with determining matters in relation to the Commission Guidelines that the company had not complied with the relevant laws and regulations. The Panel therefore ruled no breach of Clause 1.11 in relation to this trial. The Panel was unsure whether or not the results were now disclosed on EUCTR or elsewhere. On balance, the Panel did not consider that in the circumstances a breach of Clause 2 was warranted and ruled accordingly.

The Panel noted UCB Pharma's submission that trial CD0001 was sponsored by UCB Biosciences GmbH, Inc, UCB's entity in Germany. UCB in the UK was not involved in the funding nor conduct of the clinical trial which had no UK sites. The study started on 20 June 2012 and was prematurely terminated in October 2013, with no patient enrolled. The Panel considered that as there was no UK involvement, the matter did not come within the scope of the UK Code. No breach of the Code was ruled in relation to trial CD0001.

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Following its completion of the consideration of four appeals in the clinical trial cases on 18 September 2019 (Cases AUTH/3079/9/18 (Pfizer), AUTH/3087/9/18 (GlaxoSmithKline), AUTH/3118/11/18 (Tesaro) and AUTH/3102/9/18 (Lilly), the Appeal Board noted that the respondent companies in Case AUTH/3084/9/18 (Boehringer Ingelheim), Case AUTH/3091/9/18 (UCB), Case AUTH/3097/9/18 (Teva), and Case AUTH/3099/9/18 (Allergan), accepted the Panel's rulings of breaches of the Code and had not appealed.

The Appeal Board noted that a series of cases had been taken up by the PMCPA as a result of the data published in Goldacre *et al*. Four cases (Cases AUTH/3079/9/18, AUTH/3087/9/18, AUTH/3118/11/18 and AUTH/3102/9/18) were the subject of an appeal by the respondent companies. Each was determined on its own merits but there were a number of common themes. (Full details can be found in the relevant case reports)

The Appeal Board noted that Goldacre *et al* formed the basis of the complaint. Goldacre *et al* did not refer to disclosure of clinical trial results and the Joint Position which was covered by Clause 13.1 of the Code. The article assessed companies' compliance with EC Guideline 2012/c302/03. The Appeal Board noted that disclosure of clinical trial results on EUCTR was not mentioned in Clause 13 and its supplementary information, or indeed elsewhere in the Code. The Appeal Board noted that the Code was not exhaustive and in such circumstances the Appeal Board did not consider it unreasonable to consider the subject matter of the complaint in relation to Clause 9.1. In this regard the Appeal Board noted the long-established broad application of Clause 9.1 to promotional and non-promotional materials and activities including matters within the scope of the Code but not expressly referred to. The Appeal Board did not consider that a ruling of a separate clause was required as a condition precedent to ruling under Clause 9.1; in the Appeal Board's view, Clause 9.1 could be ruled upon in isolation.

The Appeal Board noted that Article 57(2) of Regulation (EC) No 726/2004 and Article 41(2) of Regulation (EC) No 1901/2006 required that clinical trial data be published on EUCTR. European Commission (EC) Guideline 2012/c302/03 gave guidance as to when the clinical trial results data should be published. According to the guideline posting of results of clinical trials which ended one year or more prior to finalisation of the programming of the relevant database, should be done within 24 months of finalisation of that programming. According to the 'What's New' section of EudraCT public website (post-dated 13 January 2016) the deadline for submission of these results was 21 December 2016. This date was referred to in Goldacre *et al.* It appeared to the Appeal Board that whilst the regulation mandated disclosure of results on EUCTR, the EC Guideline and other material advised companies how to comply with the regulation including in relation to the timing of such disclosures. The Appeal Board considered that it was within the spirit of the Code and good practice to comply with the EC Guideline in question.

The Appeal Board noted that, where companies had merged or the rights to a particular product had been bought or sold, there appeared to be difference of opinion as to which company would

be responsible for posting the retrospective results. There were also difficulties in correcting information once posted.

The Appeal Board also noted that, according to Goldacre *et al*, Phase 1 trial results that were not part of a paediatric plan did not need to be disclosed.

The Appeal Board considered that there would be a difference between action to deliberately hide clinical trial data or systematic failure resulting in non or late disclosure and late disclosure of results as part of a retrospective exercise contrary to non-mandatory timelines due to mitigating factors. The Appeal Board, nonetheless, noted its view above about good practice and disclosure in accordance with the EC Guideline.

The Appeal Board was concerned in each case about the failure to disclose the summary results on EUCTR within the timelines advised by the EC Guideline and other relevant advice. In the exceptional circumstances of each case, the Appeal Board did not consider that the late posting of the trial results on the EUCTR as part of a retrospective exercise warranted a breach of Clause 9.1 particularly in two of the cases as in those the trial results had been publicly disclosed prior to receipt of the complaint. The appeals in the above four cases were successful.

The Appeal Board agreed that Boehringer Ingelheim, UCB, Teva and Allergan should be contacted and informed of the outcome of the appeals in Cases AUTH/3079/9/18, AUTH/3087/9/18, AUTH/3118/11/18 and AUTH/3102/9/18. The PMCPA Constitution and Procedure did not cover this unusual situation where more than one company was involved in a similar set of circumstances and the Appeal Board had taken a different view to the Panel. Boehringer Ingelheim, UCB, Teva and Allergan were offered the opportunity to appeal out of time and the appeal process would operate in the usual way. The Appeal Board noted that each cases' circumstances might differ, and the result of any appeal could not be guaranteed. After consideration of the appeals the Appeal Board agreed that Boehringer Ingelheim, UCB, Teva and Allergan should each be offered the opportunity to appeal out of time'. Allergan and UCB declined the opportunity to appeal. Boehringer Ingelheim and Teva successfully appealed the Panel's rulings of breaches of Clause 9.1.

Complaint received **12 September 2018**

Case completed **22 July 2019**