CASE AUTH/3099/9/18

DIRECTOR v ALLERGAN

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 Allergan 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 Allergan is given below.

General detailed comments from the Panel are given below.

The Panel noted the data in Goldacre *et al* in that the results of sixteen of Allergan's due trials had not been reported on EUCTR; the disclosure percentage was 65.2%.

The Panel noted Allergan's submission that 12 of the 16 trials identified did not involve UK sites or investigators or any involvement of the UK. 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 these 12 trials.

The Panel noted that one trial which did have UK sites or investigators (trial 2010-020691-28) was completed by Kythera Biopharmaceuticals Inc in January 2012. Allergan acquired Kythera Biopharmaceuticals Inc in June 2015. The Panel noted that Allergan was thus responsible as at 21 December 2016. The results were published in poster format at a World Congress in April 2017 and registered on EUCTR in March 2018. 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 in relation to this trial. 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 noted that the results were now disclosed on EUCTR and were previously 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 Allergan's submission that three trials included work from the UK Allergan entity, Allergan Limited. The first study (2013-002327), had no planned UK sites, and was withdrawn with no patients enrolled. There were no results to post. The CTA Global completion date was listed as 2 July 2014. The Panel therefore ruled no breaches of the Code including no breach of Clause 2 in relation to this trial.

The second trial (2005-006169-15), was coordinated by Allergan Limited and only recruited patients in Germany. The trial involving botulinum toxin A (Botox) was terminated in September 2007 after it had only recruited 21 of the target 66 patients. The Panel noted that the results were posted on EUCTR in June 2018.

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 in relation to this trial. 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 noted that the results were now disclosed on EUCTR as stated above. The Panel therefore did not consider that in the circumstances a breach of Clause 2 was warranted and ruled accordingly.

The third trial (009-012799-28), was coordinated by Allergan Limited and only recruited patients in sites in Spain and Portugal. The trial completed in February 2012. The Panel noted Allergan's submission that results were posted on clinicaltrials.gov in February 2013 and the primary manuscript was published in 2014. The Panel noted Allergan's submission that results were posted on EUCTR in March 2018.

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 in relation to this trial. 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 noted that the results were now disclosed on EUCTR and were previously 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.

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 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 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 Allergan 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 Allergan were as follows:

Sponsors with highest proportion of trials reported

Sponsor	Total trials on EUCTR	Due trials	Due trials with results	% reported
Allergan	115	46	30	65.2

When writing to Allergan 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

Allergan noted that the BMJ study reported that the company had 46 trials which required the posting of trial results within the time window of the analysis (2016). The authors suggested that for 16 of these trials the results were not present on the EU Clinical Trials Register (EUCTR) as required. Allergan identified the 16 trials at issue and provided tables of relevant data including sponsor's name, product, global completion date, first worldwide approval and any publications.

Allergan noted that 15 of the 16 trials identified did not involve UK sites or investigators. The one trial that had UK sites or investigators (study 2010-020691-28 (by EUCTR number)) was completed by Kythera Biopharmaceuticals Inc in January 2012. The product at issue was deoxycholic acid which was first approved in April 2015. Allergan acquired Kythera Biopharmaceuticals Inc in June 2015. The results were published in poster format at a World Congress in April 2017 and registered on EUCTR in March 2018.

In addition, there were 3 trials that included work from the UK Allergan entity, Allergan Limited. Allergan explained that the overarching global company was Allergan plc which was headquartered in Dublin. Allergan Limited was the UK affiliate of Allergan plc and included the UK sales and marketing company as well as study management for specific studies.

The first trial (2013-002327), had no planned UK sites, and was withdrawn with no patients enrolled. Thus, there was no requirement to post results on EUCTR.

The second trial (2005-006169-15), was coordinated by Allergan Limited and only recruited patients in Germany. The trial was terminated in September 2007 after it had only recruited 21 of the target 66 patients. Results were posted on EUCTR in June 2018. Following the Decision Tree from the Code of Practice Review, May 2007, as the trial completed before 31 October 2008, results posting was not required by the Code. For this reason, the trial did not fall within the Code.

The third trial (009-012799-28), was coordinated by Allergan Limited and only recruited patients in sites in Spain and Portugal. The study completed in February 2012. Results were posted on EUCTR in March 2018. Results were posted on clinicaltrials.gov in February 2013 and the primary manuscript was published in 2014.

Allergan considered that 2 of the above 4 trials (2009-012799-28, 2009-012799-28 [sic]) did fall within the Code and did not post results on the EU CTR within 12 months of trial completion. The company considered that the remaining 12 [sic] trials also [sic] did not come within scope of the Code.

With regards to clauses of the Code, Allergan acknowledged that Clauses 1.11, 9.1 and 13.1 were relevant to the reporting of clinical trial results on the EUCTR, and thus relevant to this case. All the trials that completed and remained the responsibility of Allergan now had results posted on the EUCTR, which demonstrated that Allergan was fully committed to the process and that it had made significant advances in addressing the situation. For this reason, Allergan did not consider that it had brought discredit to the industry and so it had not breached Clause 2.

In summary, Allergan acknowledged that in 2016 not all clinical trials had trial results posted on the EUCTR within 12 months of the trial ending. With the number of acquisitions and divestitures from 2007 to 2016, this was a complex environment for Allergan to operate within. There were, however, rigorous systems in place to support this area and that there had been significant progress, demonstrated how seriously this taken. Of the 16 trials highlighted in the BMJ study all of them that completed and remained the responsibility of Allergan had results postings on EUCTR.

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 the results of sixteen of Allergan's due trials had not been reported on EUCTR; the disclosure percentage was 65.2%.

The Panel noted Allergan's submission that 12 of the 16 trials identified did not involve UK sites or investigators or any involvement of the UK. 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 these 12 trials.

The Panel noted that one trial which did have UK sites or investigators (trial 2010-020691-28) was completed by Kythera Biopharmaceuticals Inc in January 2012. Allergan acquired Kythera Biopharmaceuticals Inc in June 2015. The Panel noted that Allergan was thus responsible as at 21 December 2016. The results were published in poster format at a World Congress in April 2017 and registered on EUCTR in March 2018. 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 in relation to this trial. 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 noted that the results were now disclosed on EUCTR and were previously 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 Allergan's submission that three trials included work from the UK Allergan entity, Allergan Limited. The first trial (2013-002327), had no planned UK sites, and was withdrawn with no patients enrolled. There were no results to post. The CTA Global completion date was listed as 2 July 2014. The Panel therefore ruled no breach of Clauses 1.11, 9.1 and 2 in relation to this trial.

The second trial (2005-006169-15), was coordinated by Allergan Limited and only recruited patients in Germany. The trial involving botulinum toxin A (Botox) was terminated in September 2007 after it had only recruited 21 of the target 66 patients. The Panel noted that the results were posted on EUCTR in June 2018.

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 in relation to this trial. 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 noted that the results were now disclosed on EUCTR as stated above. The Panel therefore did not consider that in the circumstances a breach of Clause 2 was warranted and ruled accordingly.

The third trial (009-012799-28), was coordinated by Allergan Limited and only recruited patients in sites in Spain and Portugal. The trial completed in February 2012. The Panel noted Allergan's submission that results were posted on clinicaltrials.gov in February 2013 and the primary manuscript was published in 2014. The Panel noted Allergan's submission that results were posted on EUCTR in March 2018.

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 in relation to this trial. 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 noted that the results were now disclosed on EUCTR and were previously 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.

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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 **18 July 2019**