



Implications of CT Directive for Investigational Medicinal Product Re-test Dates

The European Union (EU) Clinical Trials Directive became effective on 1 May 2001 and was due to have been implemented, via national laws, by 1 May 2004, although this did not happen in all member states. In addition to providing a legal basis for Good Clinical Practice (GCP) the Directive describes the regulatory and ethical review processes which now have to precede the initiation of clinical trials in the EU. The information which needs to be provided to Competent Authorities (CA) and Ethics Committees (EC) is more fully described in a series of guidelines to which the Directive refers. Although separate clinical trial applications need to be submitted in each member state in which a trial is to be performed the content and format for these is common, with some additional regional requirements, and there are maximum review times which apply across the EU. Information on the material to be tested in the trial is provided in an Investigational Medicinal Product Dossier (IMPD), the headings for which reflect the format of the Common Technical Dossier (CTD).

Once a trial has been approved, changes to the information in the IMPD have to be submitted as amendments. Substantive amendments, which are defined in the guidelines and seem to cover the majority of changes, need to have prior approval from both the CA and the EC. The EC has 35 days in which to review an amendment, the CA has no time limit but it is expected that review will be undertaken in 35 days. The requirement for prior approval has led to a need to consider the timing of certain quality changes that might previously have been implemented without regulatory or ethical review. One such example is a change to the retest date for a product which is undergoing real time stability testing. The product is usually analysed close to the retest date and then, assuming it continues to meet specification, a new retest date is assigned. The new retest date, and the data to support it, now has to be submitted to the CA and EC as a substantive amendment to the IMPD. It will therefore be necessary to analyse the product at least 40 days ahead of the retest date in order to prepare and submit the amendment and allow 35 days for CA and EC review of the data. If the timing of the analysis is not brought forward there is a danger that the approval for the new retest date will not be forthcoming before the current retest date has passed. In this circumstance dosing in the clinical study would need to be suspended as the product will technically be beyond its labelled shelf-life. Whilst some leeway may be given whilst everyone becomes familiar with the new requirements, the MHRA in the UK has said it expects data to be submitted in time for approval of a new retest date before the current expiry date has passed.

About This Article

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