EUROPEAN COMMISSION
ENTERPRISE DIRECTORATE-GENERAL

Single market : management & legislation for consumer goods
Pharmaceuticals : regulatory framework and market authorisations

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Ad Hoc GMP Inspections Services Group

Addition to Chapter 1 to the EU Guide to Good Manufacturing Practice

Title: Product Quality Review

Agreed by ad hoc GMP inspectors services group	July 2003
Released for public consultation	December 2003
Deadline for comments	June 2004
Final draft adopted by ad hoc GMP inspectors services group	
Adopted by Pharmaceutical Committee	
Date for coming into operation	

Note:

The proposal arises from the experience of Member States' inspectorates where quality problems with products on the market leading to recall could have been anticipated if the manufacturer/marketing authorisation holder had operated a system for formally reviewing process consistency and trends.

Product Quality Review (Proposed addition to Ch. 1 of EU GMP Guide)

Product Quality Review

1.5 Regular quality reviews of medicinal products should be conducted with the objective of verifying the consistency of the process and to highlight any trends. Such reviews should normally be conducted and documented annually and should include at least:

(i) A review of raw materials used in the product, especially those from new sources.
(ii) A review of critical in-process controls and finished product results.
(iii) A review of all batches that failed to meet established specification(s).
(iv) A review of all critical deviations or non-conformances and related investigations.
(v) A review of all changes carried out to the processes or analytical methods.
(vi) A review of Marketing Authorisation variations submitted/granted/refused, including those for third country dossiers.
(vii) A review of the results of the stability monitoring programme.
(viii) A review of all quality-related returns, complaints and recalls, including export only medicinal products.
(ix) A review of adequacy of previous corrective actions.
(x) For new marketing authorisations, a review of post-marketing commitments.
(xi) A list of validated procedures and their revalidation dates.
(xii) A list of qualified equipment and their requalification dates.

The manufacturer and marketing authorisation holder should evaluate the results of this review, where different, and an assessment made of whether corrective action or any revalidation should be undertaken. Reasons for such corrective actions should be documented. Agreed corrective actions should be completed in a timely and effective manner. Quality reviews may be grouped by product type, e.g. solid dosage forms, liquid dosage forms, sterile products, etc. where appropriate.

Where significant changes to the process have been identified and/or when revalidation of the process has been undertaken, then one or more batches should be entered onto the stability programme. In any case, one batch of each product should be included in the stability programme each year. If less than one batch per year is manufactured then samples of each batch should be entered onto the stability programme.

Where the marketing authorisation holder is not the manufacturer, there should be a technical agreement in place that defines their respective responsibilities in producing the quality review. The Qualified Person should ensure that the quality review is performed in a timely manner and is accurate.