

Title: Clean Process - External Vial Capping Operations					
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Introduction

This guidance addresses changes within the edition (Feb 2008) of European Commission Union EU Guidelines to Good Manufacturing Practice

Medicinal Products for Human and Veterinary Use -Annex 1: Manufacture of Sterile Medicinal Products (EU GMP Annex 1) effective on March 1, 2009 with a notable exception for the capping of freeze-dried vials effective on March 1, 2010 for those sites that market and/or manufacture for locations subject to EU GMP Annex 1.

This guidance applies to capping operations performed as an aseptic process using sterilized caps or as a clean process that is performed outside the aseptic core using clean non-sterilized caps. It is important to note that there may be other additional regional/local area requirements or expectations for capping operations that supersedes the information specified within EU GMP Annex 1 that must be considered (e.g. Irish Medicines Board (IMB) or the Medicines and Healthcare Products Regulatory Agency (MHRA)).

Summary & Recommendations: “Clean Process” Capping Operations

This guidance may be considered for GMP sites where aseptic processing operations as part of sterile medicinal product manufacture occur. The EU GMP Annex 1 includes the following statements:

“The container closure system for aseptically filled vials is not fully integral until the aluminium cap has been crimped into place on the stoppered vial. Crimping of the cap should therefore be performed as soon as possible after stopper insertion”.

(Paragraph 118)

“Vial capping can be undertaken as an aseptic process using sterilised caps or as a clean process outside the aseptic core. Where this latter approach is adopted, vials should be protected by Grade A conditions up to the point of leaving the aseptic processing area, and thereafter stoppered vials should be protected with a Grade A air supply until the cap has been crimped.”

(Paragraph 120).

These texts are additions to the previous version of the document that was published in May 2003. There are no requirements that the adjacent background area to the clean process area have any defined classification as long as the conditions of this area do not negatively impact the capping operation. What constitutes an acceptable operational environment or clean process for capping operations outside of an aseptic processing environment?