Executive Summary on Warning Letter Assessment

On August 21, 2002, the FDA announced its new initiative, "***Pharmaceutical CGMPs for the 21st Century: A Risk-Based Approach.***" In this announcement, the FDA indicated the importance that "regulation and manufacturing standards are applied consistently" and that "FDA resources are used most effectively and efficiently to address the most significant health risks." In an effort to help assure these goals, it was decided to have the appropriate Center "provide a scientific and technical review of all drug CGMP Warning Letters." In order to accomplish this, the Warning Letter Group was formed to effect the rescission of the field's Direct Reference Authority for issuance of cGMP Warning Letters for human and animal dosage form drugs and medicated feeds. The memorandum rescinding this authority is dated February 20, 2003. This rescission, which went into effect on March 1, 2003, required all recommendations for cGMP Warning Letters by the District to be submitted to CDER or CVM Headquarters Compliance Offices for review and clearance prior to issuance.

An assessment of the content, consistency, and outcome of the Warning Letter recommendation process related to cGMP deficiencies for human and animal dosage form drugs and medicated feeds was completed in March 2004. The intent of this assessment was to determine whether the rescission of Direct Reference Authority added value to the cGMP Warning Letter process.

The assessment was based on a review of Warning Letter recommendations received by Headquarters in the first 6-month period after the rescission of the Direct Reference Authority by the Office of Enforcement. A total of 44 Warning Letters were received (33 in CDER and 11 in CVM) and were assessed based on criteria obtained from the Centers' Compliance Offices as well as any documented processes, procedures or directives.

Overall, the assessment showed that the rescission of Direct Reference Authority added value to the CGMP Warning Letter process by identifying inconsistencies as well as the need to clarify and communicate policy to the field. The assessment revealed that there were areas in which the process could be enhanced to improve the consistency of recommendations between the field and Center Office(s) of Compliance. For example, in many instances the recommendations were changed because the Centers applied a risk-management strategy. When the risk-management strategy is completely developed, conveyed to the field, and implemented, it should help to more appropriately balance the Agency's enforcement resources between high risk and low risk products and processes.

In addition, the assessment noted that both Centers exceeded the 15-day timeframe guide for processing Warning Letters. The scope of the assessment did not include covering the timeliness of the entire regulatory procedure (from the last date of inspection to the final outcome).

Steps have been initiated to address the concerns noted in the assessment. The ORA Office of Enforcement is leading an agency-wide initiative to identify opportunities for the application of quality systems principles to enhance the overall Warning Letter process.