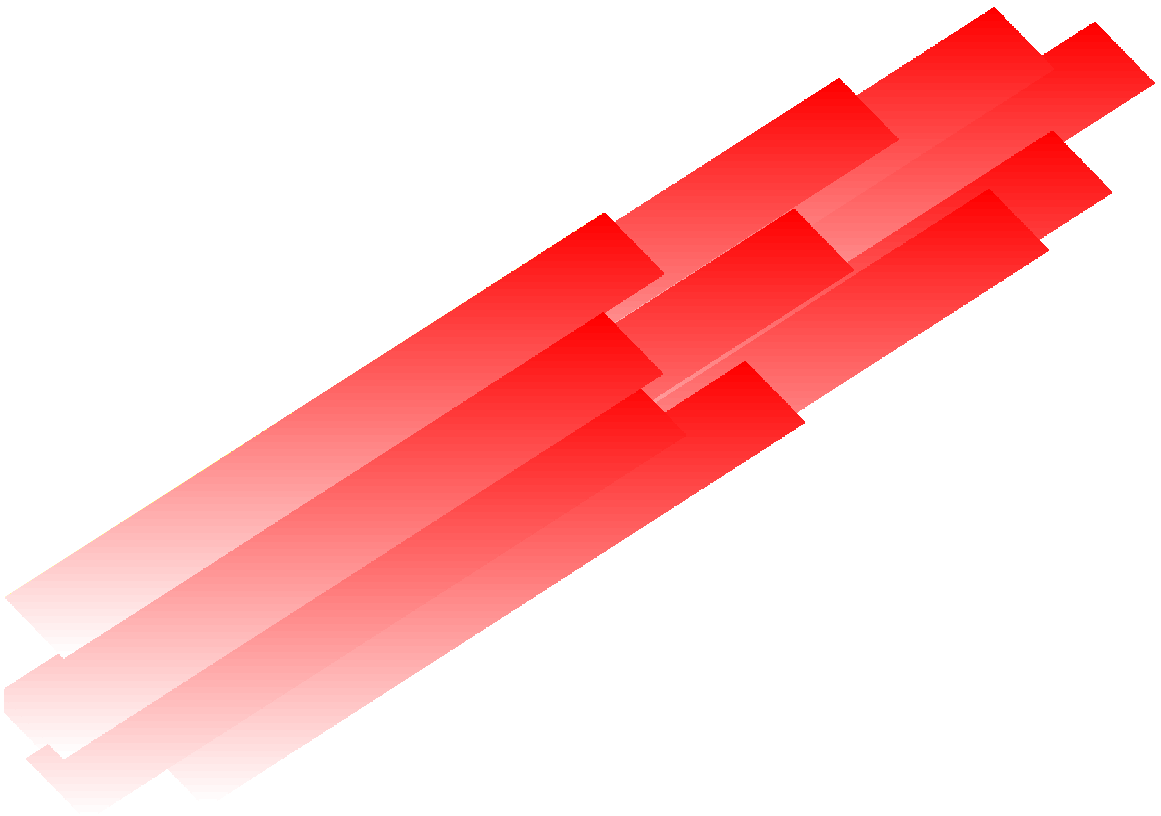
# Guidance for Industry

## PAC-ATLS: Postapproval Changes — Analytical Testing Laboratory Sites



**U.S. Department of Health and Human Services**
**Food and Drug Administration**
**Center for Drug Evaluation and Research (CDER)**
**April 1998**
**CMC 10**

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# GUIDANCE FOR INDUSTRY[1]

# PAC-ATLS: Postapproval Changes — Analytical Testing Laboratory Sites

## I. INTRODUCTION

This guidance provides recommendations to pharmaceutical sponsors of new drug applications (NDAs) and abbreviated new drug applications (ANDAs) who intend to change an analytical testing laboratory site for components, drug product containers, closures, packaging materials, in-process materials, or drug products during the postapproval period. Analytical testing laboratories include those performing physical, chemical, biological, and microbiological testing to monitor, accept, or reject materials as well as those performing stability testing.

Changes in an approved application to allow for the use of a different facility or establishment, including a different contract laboratory, normally require FDA approval before the change is made (21 CFR 314.70(b)). FDA regulations at 21 CFR 314.70(a) provide that applicants may make changes to an approved application in accordance with a guidance, notice, or regulation published in the *Federal Register* that provides for a less burdensome notification of the change (e.g., by notification at the time a supplement is submitted or in the next annual report). This document provides guidance on a less burdensome approach to providing notice (i.e., Changes Being Effected (CBE) supplement) of certain postapproval changes within the meaning of 314.70(a).

This guidance does not comment on or otherwise affect compliance/inspection documentation that has been defined by CDER's Office of Compliance or FDA's Office of Regulatory Affairs. This guidance does not affect any postapproval changes other than the ones specified. For changes filed in a Changes Being Effected (CBE) supplement (21 CFR 314.70(c)), the FDA may, after a review of the supplemental information, decide that the changes are not approvable.

## II. DISCUSSION

An analytical testing laboratory site change can be submitted as a Changes Being Effected (CBE) supplement[2] if (1) the test method(s) approved in the application or methods that have been

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[1] This guidance has been prepared under the direction of the Chemistry Manufacturing Controls Coordinating Committee, Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration (FDA). This guidance represents the Agency's current thinking on postapproval changes in analytical testing laboratory sites. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.

[2] Under certain sections of 21 CFR 314.70 (e.g., 314.70(b)(2)(vi)), a change in analytical testing site is currently designated as a prior approval supplement. However, under 21 CFR 314.70(g)(2)(ii)(A), this type of change is a "Supplement-Changes Being Effected in 30 Days," absent extraordinary circumstances. This guidance is intended to

implemented under 21 CFR 314.70(d) are used, (2) all postapproval commitments made by the applicant relating to the test method(s) have been fulfilled (e.g., providing methods validation samples), (3) the new testing facility has the capability to perform the intended testing, and (4) the new testing facility has had a satisfactory current good manufacturing practice (CGMP) inspection within the past 2 years.

Prior to submitting analytical testing laboratory site change supplements, an applicant should determine that the laboratory has the capability to perform the intended testing. Information to support the capability of a laboratory to perform the intended testing (e.g., comparative data, CGMP history of performing the test, appropriate standard operating principles (SOPs), equipment and personnel in place) should be available for FDA investigator review. Data demonstrating that the new testing facility can perform the analytical test(s) being transferred need not be included in the supplement, except for biological tests. In the case of biological tests, comparative data from an approved analytical testing laboratory site and the new testing facility should be included in the supplement with the exception that this information need not be submitted for the pyrogen and bacterial endotoxin tests.

Information about the cGMP status of a firm may be obtained by requesting a copy of the Quality Assurance Profile (QAP) from the FDA's Freedom of Information (FOI) Office. The QAP reports information on the cGMP compliance status of firms which manufacture, package, assemble, repack, relabel or test human drugs, devices, biologics and veterinary drugs. All FOI requests must be in writing and should follow the instructions found in the reference entitled *A Handbook for Requesting Information and Records from FDA*. An electronic version of this reference is on the Internet at http://www.fda.gov/opacom/backgrounders/foiahand.html.

When submitting a supplement for a change in an analytical testing laboratory site, the applicant should confirm in a written statement why a PAC-ATLS CBE supplement is appropriate (i.e., the four circumstances listed above exist). The supplement should also contain the name and address of the new analytical testing laboratory site and a full description of the testing to be performed by the new facility. The supplement should be clearly identified in the heading and text as being filed under PAC-ATLS. If the proposed change in the analytical testing laboratory site does not fall within the scope of PAC-ATLS, it is recommended that the change be filed in a prior approval supplement.

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provide for a less burdensome notification of change, under certain circumstances, for analytical testing laboratory site changes currently requiring prior approval supplements under 21 CFR 314.70. It is not intended to eliminate the need to delay distribution for 30 days of those products subject to 21 CFR 314.70(g)(2)(ii)(A).

## GLOSSARY OF TERMS

The following terms are being provided to assist the reader in using this guidance document.

**Active Ingredient:** This term is used interchangeably with active pharmaceutical ingredient (API) and drug substance. Any component that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of a disease, or to affect the structure of any function of the human body, but does not include intermediates used in the synthesis of such ingredient. The term includes those components that may undergo chemical change in the manufacture of the drug product and are present in the drug product in a modified form intended to furnish the specified activity or effect (21 CFR 210.3(b)(7) and 314.3(b)).

**Biological Tests:** Biological tests include animal, cell culture or biochemical based testing that measures a biological, biochemical or physiological response.

**Component**: Any ingredient intended for use in the manufacture of a drug product, including those that may not appear in such drug product (21 CFR 210.3(b)(3)).

**Drug Product**: A finished dosage form, for example, tablet, capsule or solution, that contains an active ingredient, generally, but not necessarily, in association with inactive ingredients (21 CFR 210.3(b)(4)).

**Inactive Ingredients**: Any component other than an active ingredient (21 CFR 210.3(b)(8)).

**In-process Material:** Any material fabricated, compounded, blended, or derived by chemical reaction that is produced for, and used in, the preparation of the drug product (21 CFR 210.3(b)(9)).

**Satisfactory Current Good Manufacturing Practice (cGMP) Inspection:** A satisfactory cGMP inspection is one during which (1) no objectionable conditions or practices were found during an inspection (No Action Indicated (NAI)) or (2) objectionable conditions were found, but corrective action is left to the firm to take voluntarily and the objectionable conditions do not justify further administrative or regulatory actions (Voluntary Action Indicated (VAI)).