Delayed Implementation for General Chapter <467> Residual Solvents

Type of Posting: Revision Bulletin

Posting Date: 15–Jun–2007

To: Manufacturers of Drugs, Biologics, and Excipients
From: Roger L. Williams, M.D., Chair, USP Council of Experts
Re: Delayed Implementation for General Chapter <467> Residual Solvents

Residual solvents are one of the three main types of impurities in pharmaceutical articles, the other two being organic and inorganic impurities. The implementation of modern standards to control these types of impurities has occupied regulatory agencies, pharmaceutical manufacturers, and pharmacopeias for many years.

Substantial progress in the overall effort came with development of the ICH Q3C Guideline in 1997 (Impurities: Guideline for Residual Solvents) and subsequent adoption of this Guideline as a FDA guidance. Implementation of the ICH approach in the US primarily affected new medicines coming to market. The impact on products already legally marketed in the US was less pronounced.

To resolve this differential impact and ensure the uniform application of the ICH-FDA approaches, USP has worked diligently over the past several years to extend these approaches to official articles in *USP* and *NF* via a requirement in General Notices. This includes official drug substances and excipients as well as official drug products. The effort has created substantial demands on pharmaceutical manufacturers, given that it affects thousands of ingredients and drug products. Manufacturers generally have supported USP's approach and have worked to understand and, where possible, conform to it. Nonetheless, USP has become increasingly aware that the new approaches may require additional time to implement due to the complexity of the requirement.

For these reasons, USP announces that the *USP–NF* General Notices statement indicating an official requirement for all articles in *USP–NF* for residual solvents is delayed from July 1, 2007, to **July 1, 2008**. This delay will allow manufacturers additional opportunity to develop the needed

analytical capability or to obtain appropriate information from other manufacturers to conform to the standards described in General Chapter <467> Residual Solvents, which itself has been recently revised. USP announces this delay in a June 15, 2007, Revision Bulletin, posted on USP's website. Separate from the change in the General Notices implementation date, on-going changes to <467> will become official in the *USP 30–NF 25* Second Supplement as scheduled. More information on the changes appearing in the Second Supplement.

USP has no evidence to indicate that any existing product in the US market poses any special risk for residual solvents. All products affected by the delay remain subject to FDA control. USP approaches only affect drug products and ingredients with monographs in *USP–NF* (official articles).

USP believes that the general goal of consistency in quality approaches for residual solvents—and for any attribute of an official article—benefits the American public in general and practitioners and patients in particular. For this reason, USP encourages all manufacturers to conform to the standards delineated in the *USP-NF* General Notices and General Chapter <467> Residual Solvents to assure that the drug substances, excipients and products are subject to relevant control of residual solvents, and that the tests for residual solvents, the procedures for the test, the acceptance criteria, and, when needed, the reference materials for the test (official USP Reference Standards) are the same from one manufacturer to another. Alternative tests that are improvements to the USP procedures should be submitted in a Request for Revision so that they can be considered and, if appropriate, included in the compendia.