
[General Chapter Prospectus: <1099> Limit on Number of Large Deviations when Assessing Content Uniformity in Large Samples](#)

Type of Posting: General Announcement

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Expert Committee: General Chapters—Statistics

Input Deadline: March 24, 2017

Suggested audience: Pharmaceutical manufacturers, statisticians, regulatory professionals

Estimated proposal PF: *Pharmacopeial Forum* 43(4) [Jul.–Aug. 2017]

Background and objective(s): Product variability is inevitable and general chapter <905> Uniformity of Dosage Requirement is a long-accepted compendial requirement for measuring this variability. General chapter <905> has an explicit range of 75% to 125% of label claim for acceptable results when 30 units are tested. This approach is known as a zero tolerance criterion (ZTC). Finding the content of any of the 30 units tested according to <905> outside of the ZTC is cause for failure of the sample to comply. For various reasons, uniformity testing may be applied to samples beyond the maximum 30 units as tested in <905>. For small samples as tested in <905>, the probability of finding a unit with content outside the ZTC is vanishingly small; however, the ZTC has been interpreted to apply regardless of the sample size taken. This misapprehension has a chilling effect on those who would apply manufacturing controls to the large sample sizes made accessible by modern methods often classified as process analytical technology. The proposed new general information chapter <1099> would provide limits for the number of unit results falling outside of the ZTC when large samples are tested.

Description of scope and application: The General Chapters—Statistics Expert Committee intends to propose a new general information chapter that will provide calculated limits for values outside of the ZTC when samples larger than 30 are tested for dose uniformity. Testing samples greater

than 30 units for dose uniformity is outside of the scope of general chapter <905>.

Anticipated proposed design phase activities: The concepts in this new general information chapter were discussed in the *Stimuli to the Revision Process* article, “Applying the USP <905> Content Uniformity Zero Tolerance Criterion to Large Sample Sizes,” which was published in *PF* 42(5) [Sept.–Oct. 2016]. This article will be reprinted in *PF* 43(3) [May–Jun. 2017] to correct errors in the original article. The proposed new chapter will be presented in *PF* 43(4) [Jul.–Aug. 2017] for public comment.

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