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U.S. Pharmacopeial Convention

May 1, 2017

**REF: USP Nystatin Reference Standard Catalog # 1477003**

**This final statement is being issued to summarize information for users regarding the USP Nystatin Reference Standard.**

**Status of Lot O2K402**

Lot O2K402 is no longer official as of October 18, 2016 and should no longer be used in testing. This lot was replaced because it was identified that the assigned value was not aligned with the current WHO International Standard for Nystatin. The current Lot R051D0 potency value assignment is aligned with the current WHO International Standard for Nystatin. To facilitate the value assignment transition for users, USP issued a correction factor (see below) in a statement to users on December 15, 2016. The shortened valid use date for Lot O2K402 was intended to limit instances where users would need to rely on the correction factor, especially in ongoing manufacturing situations. Results obtained using Lot O2K402 during its period of validity are considered valid and acceptable by USP.

**Correction factor for the transition of Lot O2K402 to Lot R051D0**

A thorough investigation and statistical analysis determined that the difference between Lot O2K402 and Lot R051D0 in the potency value assignment is 13.6%. Refer to the following example calculation for more details on how to adjust your results accordingly.

- **For example, if a sample (drug product or active pharmaceutical ingredient) previously assessed against Lot O2K402 has a microbial assay value per USP Chapter <81> of 5861 U/mg using Lot R051D0, that assay value would be adjusted to 6784 U/mg (5861/0.864) with the application of the correction factor.**

The use of the correction factor is only necessary if a batch/product previously tested against Lot O2K402 is now undergoing testing (e.g. stability, release testing) with Lot R051D0. If a batch/product has only been tested with Lot R051D0, then the correction factor should not be used. The provided correction factor acknowledges the value assignment difference between the two lots and will generate results equivalent to the potency assignment methodology used with Lot O2K402. The results will not be equivalent if the correction factor is not used as directed in the December 15, 2016 statement.

**Users should disregard statements issued prior to December 15, 2016 regarding the suitability for use and relative potency of Lot O2K402.**

For technical questions regarding the use of USP Nystatin Reference Standard in its associated USP compendial applications, please contact Reference Standard Technical Services at rstech@usp.org. As USP is not a regulatory authority, compliance matters cannot be addressed by USP.

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December 15, 2016

**REF: USP Nystatin Reference Standard (Catalog # 1477003, Lot O2K402)**

**USP Nystatin Reference Standard (RS) Catalog #1477003, Current Lot R051D0 will be released from quarantine and made available again with the guidance provided in the statement below. The following information is to support USP customers in the transition from the previous USP Nystatin RS Lot O2K402 to Lot R051D0. Previously issued statements from the USP with respect to the potency of Lot O2K402 will be superseded by this statement; users should disregard previously issued statements regarding the suitability for use and relative potency of Lot O2K402.**

**Difference in potency between Lot R051D0 and Lot O2K402**

The potency difference observed between Lot O2K402 and Lot R051D0 is due to a value assignment difference. The difference has been determined to be approximately 13.6%.

The Lot R051D0 potency value assignment is consistent with WHO International Standard units for Nystatin and with the European Pharmacopeia Standard CRS 7.1.

Historically and through Lot O2K402, each USP Nystatin RS lot was calibrated based on the preceding lot of the USP Nystatin RS. This assignment practice has been adhered to since USP acquired the FDA master standard.

USP very recently identified that the USP and WHO International Standard units fell out of alignment in or around 2007. Data analyzed by USP supports that the difference in these values has been consistent over time since this alignment change, and accounts for the difference in the potency values of Lots O2K402 and R051DO. Based upon historical data, there is no evidence indicating deterioration of Lot O2K402 over time.

**Practical implications for users in compendial testing**

For products that were previously assessed using Lot O2K402 and will now be assessed using Lot R051D0, the unit measurement results obtained using Lot R051D0 should be divided by a correction factor of 0.864. This correction factor acknowledges the value assignment difference and will generate results equivalent to the potency assignment methodology used with the Lot O2K402. Application of this correction factor would be appropriate in conditions including, but not limited to, finished products in ongoing stability assessment or pending release testing that were previously assessed against Lot O2K402, but will now have to be assessed against the current Lot R051D0.

- **For example, if a sample (drug product or active pharmaceutical ingredient) previously assessed against Lot O2K402 has a microbial assay value per USP Chapter <81> of 5861 U/mg using Lot R051D0, that assay value would be adjusted to 6784 U/mg (5861/0.864) with the application of the correction factor.**

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