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Beyond-use dating in the newly proposed USP General Chapter <795> underwent significant changes, particularly to the recommended maximum beyond-use dates allowed for different types of formulations. One of the biggest changes is a new focus on microbial growth and preservative efficacy. The guidelines define aqueous preparations as those having a water activity (aw) greater than or equal to 0.6, and only preparations with an aw less than 0.6 are considered anhydrous dosage forms.1

What is water activity?

Water activity is a measurement of the ratio of vapor pressure of the substance in question when at equilibrium with the surrounding air to the vapor pressure of distilled water under identical conditions.2 So, for example, an aw of 0.6 means that the vapor pressure of the substance in question is 60% that of pure water.

Water activity should not be mistaken for water content. Water content is a measure of how much water is in a particular substance by weight or volume, whereas aw is a measure of water that is available for reaction or accessible to microbes. Even items with relatively low water content can still have relatively high aw.

Why does water activity matter?

Water activity is a reliable measure of a microbe's ability to grow in a particular substance. Generally, bacteria can grow at aw greater than 0.85, and fungi such as yeasts and molds at aw greater than 0.6.3,4 Newly

proposed USP <795> guidelines consider anything with an aw less than 0.6 to be anhydrous, and therefore can be given longer recommended maximum beyond-use dates without necessarily having a preservative.1

Water activity is also a useful reference parameter when considering how much water is available in a substance to act in chemical reactions, potentially resulting in degradation of active ingredients in that substance.5

What does this mean for my practice?

This new focus on aw not only means a potential change in beyond-use dating guidelines, but also a new focus on preservatives and how to select one for a particular compounded preparation. Notably, USP clarifies that these new guidelines do not require compounders to measure aw for particular compounds, but can use table 3, Water Activity (a) of Common Compounded Nonsterile Dosage Forms, presented in USP <795> to infer whether their preparation is aqueous or non-aqueous.6 General Chapter <1112> (Application of Water Activity Determination to Nonsterile Pharmaceutical Products) provides further information on the water activity of pharmaceutical products.6,7 If aw is not tested for a preparation known to contain water, such as a cream or aqueous suspension, the aw should be assumed to be equal to or greater than 0.6 and, in the absence of an appropriate study, the beyond-use date should be consistent with the maximum beyond-use date listed in table 4 of new proposed USP <795> guidelines.1 In the absence of explicit data on a particular compound, General Chapter <1112> and table 3 from the proposed revision to USP <795> provide good resources for justifying an assigned beyond-use date.

Sources:

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2. Food and Drug Administration. 2014 Aug 27th. Water Activity (aw) in Foods. https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/inspection-technical-guides/water-activity-aw-foods. Accessed 03/04/22
3. Sperber W. Influence of water activity on foodborne bacteria – a review. Journal of Food Production. 1983; 46(2): 142-150.
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5. Maltini E, Venir E. Relevance of physical properties in the stability of plant-based food products. Indian Journal of Experimental Biology. 2013; 51: 895-904.
6. United States Pharmacopeia and National Formulary (USP 1112). GCM2015 General Chapters-Microbiology; 2015. https://online.uspnf.com/uspnf/document/GUID-088FEEB1-8BD8-4120-AC2A-106AAE5E8E4E_1_en-US. Accessed 03/04/22

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