**Water Soluble-Resin Storage Stability**

**Introduction**

POLYOX™ WSR consists of a family of high molecular weight polyethers with molecular weights ranging from 100,000 to 7,000,000. These materials have many uses in the pharmaceutical industry. For instance: as dispersants, binders, viscosifiers, mucoadhesives, and hydrophilic matrix tablets. In many of these applications, the properties that POLYOX WSR imparts are dependent upon its molecular weight. Therefore, maintaining the proper molecular weight is important for prolonging the utility of the polymer.

Polyethers, as a class, can undergo chain cleavage via autooxidation. Therefore, storage stability is an important consideration when formulating with POLYOX WSR polymers. The rate of autooxidation can be minimized through the addition of antioxidants and by controlling storage conditions.

**Key Points**

- BHT and Vitamin E efficiently stabilize POLYOX WSR under storage and use conditions.
- Product stability is greatly improved by minimizing long term exposure of the polymer to high temperature and oxygen.
- Tablets can be effectively stabilized by controlling the antioxidant concentration in the final formulation.

**Antioxidants**

Antioxidants can effectively terminate the free radicals generated during autooxidation and thereby reduce the rate of molecular weight loss. All POLYOX WSR NF grades are supplied with a typical range of butylated hydroxytoluene (BHT) content from 100 to 500 ppm, which is a safe and effective antioxidant for polyethers. Figure 1 shows the percent viscosity retained versus storage time for samples stored at 23°C, solution viscosity being directly related to polymer molecular weight. The samples contain zero and 500 ppm BHT, respectively. Note the significant improvement in polymer stability for the BHT containing sample.

**Figure 1**

Effectiveness of BHT as Stabilizer For POLYOX WSR

**Storage Temperature**

The rate of polyether autooxidation is a strong function of temperature. This can be seen in Figure 2, which compares the viscosity loss as a function of storage temperature for 200,000 MW material.

At 23°C the product shows good stability with less than a 10 percent viscosity loss after two years. At 40°C the same material shows a 20% viscosity loss over the same time period.

**Figure 2**

Temperature Effect on Storage Stability

MW = 200,000

**Molecular Weight Effect**

Polymer molecular weight also impacts the viscosity loss as a function of storage time. The number of chain cleavages taking place per unit time is independent of polymer molecular weight. However, each chain cleavage has a larger impact on the measured viscosity for a high molecular weight polymer than found for a low molecular weight grade since it leads to a wider polydispersity. This can be seen in Figure 3, which compares the viscosity change for high and low molecular weight grades stored at 23°C.

**Figure 3**

Storage Stability versus Molecular Weight Measured at 23°C

MW=200,000

MW=5,000,000
**Tablet Stability**

Stable formulations based on POLYOX WSR can be produced utilizing the guidelines presented for the bulk polymer. This is of particular importance for matrix tablets, since the polymer viscosity controls the drug release rate. In this case, it is important to realize that BHT is a volatile antioxidant and typical pharmaceutical processing steps may cause BHT to sublime during processing. This is particularly true when using fluid bed techniques to process POLYOX WSR. Addition of BHT to the product after fluid bed processing will remedy this problem and can be accomplished by dry blending BHT into the final granulation during lubricant addition.

In order to define the storage stability of POLYOX WSR based matrix tablets the following formulation was prepared via wet granulation:

- 15% Theophylline
- 20% POLYOX WSR Coagulant grade (MW = 5,000,000 amu)
- 0.5% Magnesium Stearate
- 64.5% Avicel PH 102
- 1000 ppm BHT

The high molecular weight polymer was selected for the study because any chain cleavage taking place will be more readily apparent in high molecular weight material. In addition, the polymer concentration was kept to a minimum and the tablets were tested uncoated to maximize the effect of changes in polymer viscosity on the release profile. These variables were chosen to demonstrate stability under worst case conditions.

Figure 4 presents the release profiles measured for this formulation at different storage times. Data is presented for tablets stored 0, 28, 58, and 158 days at 40°C and 75% relative humidity. The deviation in the release profile does not exceed 10% at any time point during the 158 day study. Vitamin E is also an effective antioxidant for POLYOX WSR and can be used in place of BHT. When 1000 ppm of vitamin E was used in place of BHT in the above formulation equivalent stability was noted.

**Figure 4**

In-Vitro Release Profile

![Release Profile Graph]

**Recommendations - Bulk Polymer**

- Store product at or below 25°C in sealed drums.
- If stored for prolonged periods, retest product viscosity specification prior to use.

**Recommendations - Tablets**

- Insure that adequate antioxidant concentration is present in the final product prior to tableting.
- Utilize product packaging or a tablet coating to minimize oxygen migration into the tablet if required.

For more information, complete literature, and product samples, you can reach a Dow representative at the following numbers:

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