



**Q&A Session Questions from November 18th, 2009 Webinar
POLYOXTM, Water Soluble Resin – New Applications in ER Matrices
Presented by Colorcon, Inc.**

Speakers:

**Dr. Ali Rajabi-Siahboomi – Sr. Director of Scientific Affairs - Colorcon, Inc.
Dr. Robert L. Schmitt –R&D Fellow – The Dow Chemical Company
Dr. Hiep Huatan – Pharmaceutical Consultant & Managing Director – H2 Pharma**

	QUESTION	ANSWER
1.	What is the tablet size or compression pressure?	Metformin: 1 g at compression force of 20 kN
2.	What grade of PEO was used for the metformin % polymer data?	POLYOX WSR 1105 and POLYOX WSR 303
3.	Does the release profile of matrix formulation with MCC PH 102 reduce viscosity of PEO?	No, our data show that MCC, Starch 1500 [®] (partially pregelatinized maize starch) and DCP are all compatible with POLYOX in tablet formulations.
4.	I had experience that when PEO used with K4M in matrix, initially it had desired release, but at accelerated condition dissolution slips. Formulation doesn't have lactose? Can you justify?	Check final dosage form to see if viscosity drop of the polymer is the mechanism. If yes, test for BHT in the final dosage form to ensure suitable antioxidant levels in tablets.
5.	Main concern for matrix formulation is food effect	This may be the case depending on the formulation and properties of the API. May be good to evaluate Osmotic systems, which generally do not show food effects.
6.	Recovery of API is approximately 5% low in POLYOX matrices. How can we improve the recovery?	Try Osmotic separation of the polymer and drug prior to Liquid Chromatography.
7.	What is your recommendation with respect to processing equipment with PEO, i.e. Rapid mixer granulation or fluid bed processing?	Need to assess the necessity of wet granulation, as direct compression is enhanced when using POLYOX. For wet granulation, easiest way is to use low or high shear granulation with nozzle adapted to produce fine spray to generate even and controlled granulation. When using high-shear we need to step down on energy input, i.e. use slower mixing speed and without chopper.
8.	What about the stability of POLYOX against oxidation?	POLYOX is stabilized for storage with BHT (an antioxidant used within the polymer). It may be required to include additional antioxidant in the final dosage form. BHT and Vit E are effective antioxidants.
9.	Any data, for which type of drug (acidic or basic) PEO is recommended as far as stability is concerned?	We have not seen any specific pH effects on stability profile.
10.	PEO being high molecular weight polymer liable to react with drug molecules at many sites. Is there any method to prevent this interaction?	When processed in the solid state (i.e. granulation, direct compression or dry granulation) the crystalline nature of the polymer limits direct reaction via chain binding with the drug.
11.	I am concerned about oxidation and polymer degradation. What does the stability of oxidatively labile APIs look like in POLYOX?	This is a drug specific question and more information is required before an educated answer can be given. Our current understanding is that POLYOX is not known to increase oxidation of an oxidatively liable API.

12.	Are there any low viscosity grades of POLYOX, which can be used in wet granulation?	Yes, POLYOX WSR N-10 and WSR N-80 are low MW grades. Both can be used in wet granulation.
13.	I missed part of the presentation. It is possible that this was already discussed. What is the level of peroxides in your polymers?	There are no published data on this. Internal data shows peroxide levels are very low and very difficult to measure. <50 ppm is best estimate for internal use.
14.	How stable is the POLYOX 303? How much loss in the viscosity is there and in how many months?	Please request for a POLYOX stability package, which has been developed by Colorcon and Dow Chemical Company (CR Alliance partners).
15.	You mentioned that for soluble drugs, particle size of POLYOX does not play any role, what about insoluble drugs? For insoluble drugs, particles size of the drug would play any role?	This is a phenomenon that requires further study. Our current data indicate that in some cases particle size may have an influence on drug release of APIs with poor solubility.
16.	Do you have any study done in vivo food effect METHOCEL™ (premium cellulose ethers) versus PEO?	Although we do not have in vivo data or most specifically data on food effect, there are products in the market that have used POLYOX matrix technology.
17.	Suppose API is in about 20% in the formulation along with POLYOX, but blend doesn't have sufficient flow, therefore wet granulation was adapted as the alternative route for ER tablets? My question is what will happen as POLYOX takes up water?	POLYOX will granulate very quickly using just water. If over-granulated, lumps and large proportion of ungranulated fines may appear in the final product. Hence, the rate of granulation is slowed down when using alcohol, typically 80:20 alcohol:water mix.
18.	Is oxidation a major concern for POLYOX?	HH - POLYOX is subject to auto-oxidation, which is well recognized, but is preventable and effectively controlled with the use of BHT. With the appropriate inclusion and maintenance of the BHT level through the shelf-life of the product then POLYOX oxidation should not pose a major problem.
19.	The question is related to the supply of POLYOX. As a policy, how old may material be when it is sent out, especially in India? Please do not correlate it to the fact that it will be within the retest period.	The policy around the age of product before being shipped out is under review.
20.	What are the levels of Starch 1500 and lactose used in the stability studies slides	44.5% of the formulation was filler in this study. A copy of the CRS abstract, where the initial data was presented is available on our web site.
21.	Although POLYOX polymers are hydrophilic, but do they display detergency like some other hydrophilic polymers?	No, POLYOX does not show a detergency property.
22.	Does the %fines >200 mesh of the final granulation have an effect on drug release?	The %fines >200 would likely affect compression profile and overall hardness of the matrix. POLYOX formulations generally have low susceptibility to hardness related dissolution variation. Hence, can surmise that if hardness is controlled then dissolution variability should be limited.
23.	Can we use this polymer for highly oxidizing molecules and hydrolytic molecules?	If the oxidizing molecule liberates a free radical this is not a good choice. Otherwise this polymer can be used.
24.	What are the differences between standard and FP grades?	Fine particle (FP) grades are designed to have a smaller particle size than standard grades. This is helpful when matching the particle distribution of the active or for high polymer containing granulations.
25.	Is there any in vitro - in vivo correlation data available using POLYOX in a formulation?	SCOLR have published in this area - refer to publication Turner et al., Drug Dev. Ind. Pharm., 2004, 30:8, 797-807

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