WHITE PAPER

LoxaSperse®

LoxaSperse – Is it Safe Microbiologically for Use in Sinus/Nasal Irrigations?

Pertinent USP References:

USP NF	Xylitol
USP NF	Poloxamer
USP 5	Inhalation and Nasal Drug Products – General Information and Product Quality Tests
USP 795	Pharmaceutical Compounding – Non-sterile Preparations
USP 1111	Microbiological Examination of Non-sterile Products: Acceptance criteria for Pharmaceutical Preparations and Substances for Pharmaceutical Use.
USP 1112	Application of Water Activity Determination to Non-sterile Pharmaceutical Products
USP 797	Pharmaceutical Compounding – Sterile Preparations

The United States Pharmacopeia and National Formulary (USP-NF) are recognized as official compendia and referenced in various legal statutes as the basis for determining the identity, strength, quality, purity, packaging, and labeling of drugs and related articles. LoxaSperse is a proprietary blend of xylitol and poloxamers, both of which are characterized by official USP-NF monographs.

USP Chapter 795 discusses the required way to safely compound non-sterile preparations as it relates to the quality of ingredients that can be used to compound. Some of the criteria include identity and purity considerations when purchasing from a reliable supplier who follows USP standards. Further requirements stipulate that drug compounding be performed by qualified and trained personnel, using appropriate equipment that is cleaned and maintained according to written procedures and kept from cross contamination of other contaminating drug material. Basically, Chapter 795 requires that qualified people use the correct quantity of material that is documented acceptable, in the right equipment, in the right environment, in a reproducible and traceable operation. Without meeting these basic tenets, any discussions of safety are irrelevant. It is also important to note that Chapter 795 and 797 of the USP do NOT apply to the administration of medications, but rather the preparations themselves and the environment in which they are prepared.

USP Chapter 1111 discusses acceptance criteria for Microbiological Quality of Non-sterile Dosage Forms. Table 1 of this chapter clearly states that non-sterile preparations for nasal use should contain no more than 200 Total Aerobic Microbial Count (TAMC) per g or mL, 20 Total Combined Yeasts and Molds Count (TYMC) per g or mL. In addition, Specified Microorganisms by route of administration are listed to be evaluated. Per USP, nasal use products must be free from Staphylococcus aureus and Pseudomonas aeruginosa in 1 g or 1 mL samples.

USP Chapter 1112 discusses the Application of Water Activity Determination to Non-sterile Pharmaceutical Products. This chapter provides information relating, but not limited to, improving antimicrobial effectiveness and reducing susceptibility of formulations to microbial contamination; it also provides a tool for the rationale setting the frequency of microbial testing to include screening for objectionable microorganisms for product release, listing by name the greatest potential organisms of concern. It is documented in this chapter that a water activity of greater than 0.55 is required for the proliferation of any microbial growth. The water activity of LoxaSperse has been shown to be 0.47 at worst (without a desiccant stored 90 days) at room temperature. With a desiccant the water activity under the same test conditions was 0.32. This USP chapter indicates that there is NO potential for microbial growth at these measured water activity levels. At this level, the USP recommends the reduction of routine testing (as opposed to testing each and every batch).

What does the recommendation for reduced testing mean and why is it important in a discussion of microbiological safety? This chapter clearly states that nasal inhalant commercial products should be tested for TAMC and TCYMC, as well as for the absence of Staphylococcus aureus and Pseudomonas aeruginosa. In addition,

Click the QR to see more PCCA studies and reports.

specific guidance is given for products with low water activity defined as less than 0.75. It states routine testing can be reduced "…when pharmaceutical products are made from ingredients of good microbial quality [e.g. adhere to monograph requirements], when manufacturing environments do not foster microbial contamination [e.g. are compliant with USP <795>], when there are processes that inherently reduce microbial content [e.g. LoxaSperse is mixed with sterile water or saline], when the formulation of the drug product has antimicrobial activity [e.g. LoxaSperse is mixed with antimicrobials], and when manufacturing sites have an established testing history of low bioburden associated with their products [e.g. licensed compounding pharmacy]."

Given this information and taking all guidance together, not any one single element, testing each and every product batch produced is not required. It would not be uncommon for skip lot testing to be at the level of 50%, such that every other batch produced is tested. Regarding LoxaSperse, PCCA chooses to test 100% of batches for TAMC, TCYMC, and the absence of Staphylococcus aureus and Pseudomonas aeruginosa, verifying the quality of each and every LoxaSperse lot shipped.

USP Chapter 5 Inhalation and Nasal Drug Products – General Information and Product Quality Tests specifically discusses quality tests for inhalation drug products. A specific section concerning dry powders for inhalation lists the quality control data that must be known for product acceptability. These include specific and quantifiable information such as identification, content uniformity, water content, assay, impurities, and microbial limits. It is important to point out that approved commercial powders for inhalation are non-sterile products.

LoxaSperse meets or exceeds all USP requirements for chemical and microbiological performance. Every lot released by PCCA prior to shipping is not only reviewed based on specifications in the original certificate of analysis (C of A), but actual testing is performed to guarantee critical parameters. This includes chemical testing of identity, pH, solubility, and visual description. Again, this is testing, not a paper check. Microbial testing is performed on each and every lot of product to include total counts for aerobic organisms, yeast and mold. These are referred to as TAMC and TCYMC. Given that LoxaSperse exhibits a water activity at all times below 0.47, USP would indicate these tests would not be required per Chapter 1112. Microbial growth is not possible at this water activity. PCCA still tests each and every released lot. Given this fact, any active pharmaceutical ingredient (API) mixed with LoxaSperse that itself exhibited antimicrobial activity would be expected to result in a final preparation with an increased, synergistic antimicrobial action within the preparation itself.

The question of microbial safety of a non-sterile powder mixed with sterile water or saline at administration is dependent upon basic considerations undertaken by the health care personnel involved. First and foremost, a sterile diluent must be used to reconstitute immediately prior to administration. Equally important is the use of a compound that has been formulated per the guidelines of USP Chapter 795 for the specific needs of the patient. The compounded preparation's specifications should be verified by testing. LoxaSperse is designed to increase solubility and dispersibility of imbedded actives; that is, it is effective as designed.

LoxaSperse, which has a water activity level of below 0.47, does not support microbial growth; therefore it is safe microbiologically. As tested and released from PCCA, LoxaSperse is documented as both microbiologically safe and chemically effective. From a regulatory perspective, it is important to reiterate that USP 795 and 797 do not apply to administration. These chapters do not prohibit the procedure of preparing a quality non-sterile powder that is ultimately reconstituted for administration as a sinus rinse by the patient.

