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Division of Dockets Management
Food and Drug Administration
5630 Fishers Lane
Room 1061, HFA-305
Rockville, MD 20852

Re: ANDA Suitability Petition
Ascorbic Acid Injection, USP
2,500 mg/5 mL (500 mg/mL)
5,000 mg/10 mL (500 mg/mL)

Dear Sir/Madam:

The undersigned submits this Suitability Petition pursuant to Section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act ("FDCA") and 21 C.F.R. §§ 10.20, 10.30 and 314.93. This Suitability Petition requests that the Food and Drug Administration ("FDA") declare that Ascorbic Acid Injection, USP, 2,500 mg/5 mL (500 mg/mL) and 5,000 mg/10 mL (500 mg/mL) are suitable for submission and subsequent FDA review in an Abbreviated New Drug Application ("ANDA").

The reference listed drug (RLD) for the proposed products is ASCOR® (Ascorbic Acid Injection for intravenous injection), which was approved on October 2, 2017 in NDA 209112 for McGuff Pharmaceuticals Inc. ASCOR® is a solution for injection and is marketed in a Pharmacy Bulk Package with a concentration of 500 mg/mL and a fill volume of 50 mL (25,000 mg/50 mL). While the concentration of the ascorbic acid is the same in the proposed products as in ASCOR® - 500 mg/mL – a Suitability Petition is necessary because the total volumes of the proposed products' containers are different.

In order to facilitate the FDA's review, we wish to call attention to the fact that on March 31, 2021, BPI Labs submitted a similar Suitability Petition concerning ASCOR® and its Ascorbic Acid Injection 5000 mg/10 mL (500 mg/mL) product (see Docket FDA-2021-P-0345-0001). To our knowledge, that Petition is still pending.

A. Action Requested

This petition respectfully requests that FDA declare that Ascorbic Acid Injection, USP, 2,500 mg/5 mL (500 mg/mL) and 5,000 mg/10 mL (500 mg/mL) are suitable for submission in an ANDA. Pursuant to Section 505(j)(2)(C) of the FDCA and 21 C.F.R. § 314.93, the suitability petition process is the appropriate mechanism for securing FDA authorization to submit an ANDA for a drug product that differs in this manner from the RLD.

The active ingredient, dosage form, indications and route of administration of the proposed products are the same as those of the RLD. The proposed products would differ only in total fill volume/total amount of drug (5 mL containing 500 mg/mL for a total amount of 2,500 mg of Ascorbic Acid per vial and 10 mL containing 500 mg/mL for a total amount of 5,000 mg of Ascorbic Acid per vial) from the RLD (50 mL containing 500 mg/mL for a total amount of 25,000 mg of Ascorbic Acid per vial).

It should be noted that there is no change to the concentration of the products (i.e., the drug content per mL is identical to the RLD), and the difference in the proposed total fill volumes is clearly contemplated by the dosing information in the approved labeling for the RLD as detailed in the Statement of Grounds below.

In summary, this suitability petition seeks a determination for an ANDA of the proposed products with a change in total drug content per container in comparison to the RLD.

Approval of this Suitability Petition would allow ANDA applicants to submit Ascorbic Acid Injection, USP, 2,500 mg/5 mL (500 mg/mL) and 5,000 mg/10 mL (500 mg/mL) vials (in addition to the 25,000 mg/50 mL vial presentation) in an ANDA, and would permit convenient dosing and minimize potential waste associated with the 50 mL vial size.. Further, FDA's approval of this Suitability Petition would be consistent with the Agency's well-publicized efforts to encourage generic competition for NDA-approved products.

B. Statement of Grounds

Section 505(j)(2)(C) of the FDCA and 21 C.F.R. § 314.93 provide for the submission of an ANDA for a drug that differs in strength from an RLD, provided that FDA has approved a petition seeking permission to file such an application. FDA has long had a policy of requiring a suitability petition to obtain authorization for an ANDA to be submitted for a parenteral drug in a drug-container size (or volume) in which the total content of the container is different from the total content of a container approved for the listed drug or in a previous suitability petition

for an ANDA. In other words, FDA has determined that "strength" of injectable drug products is not the same if the fill volumes of the solution in the products are different. For that reason we are filing this Suitability Petition to request FDA permission to submit an ANDA for products having a different fill volume (i.e., strength) in comparison to the approved RLD product.

The proposed changes here do not pose questions of safety or effectiveness since the proposed concentration of the products remains aligned with the recommended product doses stated in the RLD's labeling. The uses, dosage form, and route of administration of the proposed drug products remain the same as those of the RLD. As both proposed products are true solutions, if shown to meet bioequivalence requirements, the proposed drug products can be expected to have the same therapeutic effect as the RLD product.

A comparison of the RLD 50 mL vial to the proposed Ascorbic Acid Injection, USP, 2,500 mg/5 mL (500 mg/mL) and 5,000 mg/10 mL (500 mg/mL) vial drug products is provided in **Table 1**.

Table 1: Comparison of RLD Product to Proposed Products

Ingredient	ASCOR® (NDA 209112), 50 mL fill size	Proposed Ascorbic Acid Injection, USP Products	
		5 mL fill size	10 mL fill size
Ascorbic Acid	500 mg/mL (equivalent to 562.5 mg of sodium ascorbate)	500 mg/mL (equivalent to 562.5 mg of sodium ascorbate)	500 mg/mL (equivalent to 562.5 mg of sodium ascorbate)
Edetate disodium	0.25 mg/mL	0.25 mg/mL	0.25 mg/mL
Water for Injection	q.s. to 50 mL	q.s. to 5 mL	q.s. to 10 mL
Hydrochloric acid or sodium hydroxide	For adjusting pH to 5.6 to 6.6	For adjusting pH to 5.6 to 6.6	For adjusting pH to 5.6 to 6.6

Table 1 shows that the proposed products differ from the RLD only in vial size, with a proposed addition of 5 mL and 10 mL vial sizes to the previously approved and marketed 50 mL vial RLD product. The active ingredient is identical to the RLD, and hence, there is no difference in the safety and efficacy between the proposed Ascorbic Acid Injection products and the RLD product. The changes proposed in fill volume do not affect dosing,

administration or conditions of use. The indications, warnings and directions for use of the proposed ANDA products will remain the same as that of the RLD.

ASCOR® is supplied as a Pharmacy Bulk Package (PBP) which is intended for dispensing of single doses to multiple patients in a pharmacy admixture program and is restricted to the preparation of admixtures for infusion. Each vial of ASCOR® contains 25,000 mg (500 mg/mL in 50 mL vial) of ascorbic acid.

As shown in the attached labeling for ASCOR®, the largest recommended single dose is 200 mg. Under its labeling, ASCOR® needs to be dispensed in single doses to multiple patients in a pharmacy admixture program. Once the closure system has been penetrated, all dispensing from the PBP vial needs to be completed within 4 hours. Each dose must be used immediately and unused portion needs to be discarded.

The total drug content in the 50 mL pack is equivalent to 125 doses of 200 mg (for adults and pediatric patients 11 years and older). For the other pediatric dosing options with lower daily dosing requirements, even more doses would be need to be used within 4 hours. Usage of many single dispensed doses within 4 hours in a real-world setting could be highly challenging and may lead to unnecessary wastage of drug product. The proposed fill volumes of 5 mL and 10 mL will be equivalent to ~12.5 and ~25 doses of 200 mg for adults and pediatric patients 11 years and older, respectively, and will thus provide an opportunity to utilize the drug product more efficiently by avoiding wastage of product. The same rationale applies even more so for pediatric patients taking the lower daily doses of 50 mg and 100 mg. In certain probable real-world instances, wherein there are one or fewer patients in need of the drug product, pharmacies will be able to offer the drug product more efficiently by minimizing the wastage of unused portions using the proposed product with fill volumes of 5 mL and 10 mL (instead of the 50 mL RLD). The proposed fill volumes do not pose questions of safety or effectiveness because the dosing information contained in the labeling for the RLD clearly contemplates the instantly proposed vial sizes.

The Exhibits hereto contain proposed product labeling which aligns with the RLD labeling. As such, this petition includes the following Exhibits:

- Exhibit 1: Package Insert for McGuff Pharmaceuticals Inc.'s ASCOR® (Ascorbic Acid Injection, NDA 209112, approved October 2, 2017; latest label approved in October 2017)
- Exhibit 2: Proposed Package Insert for Ascorbic Acid Injection, USP, 2,500 mg/5 mL (500 mg/mL) and 5,000 mg/10 mL (500 mg/mL) Vials (includes 25,000 mg/50 mL Vials as well)

- Exhibit 3: Side by Side Comparison of the RLD's Current Approved Package Insert and the Petitioner's Proposed Package Insert

Approval of this Suitability Petition would allow ANDA applicants to submit Ascorbic Acid Injection, USP, 2,500 mg/5 mL (500 mg/mL) and 5,000 mg/10 mL (500 mg/mL) vials (in addition to the 25,000 mg/50 mL vial size) as an ANDA, and would permit convenient dosing and administration by healthcare providers and minimize potential waste associated with the 50 mL vials. Further, as noted above, FDA's approval of this Suitability Petition would be consistent with the Agency's well-publicized efforts to encourage generic competition for NDA-approved products.

For the foregoing reasons, we request that the FDA determine that Ascorbic Acid Injection, USP, 2,500 mg/5 mL (500 mg/mL) and 5,000 mg/10 mL (500 mg/mL) are suitable for submission in an ANDA.

C. Environmental Impact

The Petitioner claims a categorical exclusion under 21 C.F.R. § 25.31.

D. Economic Impact

In accordance with 21 C.F.R. § 10.30(b), the Petitioner will, upon request by the Commissioner, submit economic impact information.

E. Certification

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Respectfully submitted,

Brian P. Waldman

Exhibits attached

- **Exhibit 1:** Package Insert for McGuff Pharmaceuticals Inc.'s ASCOR® (Ascorbic Acid Injection, NDA 209112, approved October 2, 2017; latest label approved in October 2017)
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- **Exhibit 3:** Side by Side Comparison of the RLD's Current Approved Package Insert and the Petitioner's Proposed Package Insert