晟德大藥廠股份有限公司
CENTER LABORATORIES, INC.

30 November 2020

CITIZEN PETITION

Division of Dockets Management
Department of Health and Human Services
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

Re: CALAN® (verapamil HCl) oral tablets (NDA 018817)

Subject: Citizen Petition requesting the FDA to determine that discontinuation of CALAN (verapamil hydrochloride) 40, 80, 120, and 160 mg tablets (NDA 018817) from Pfizer Inc was not due to safety or efficacy reasons

Dear Sir/Madam:

The attached petition, submitted on behalf of Center Laboratories, Inc., requests the Food and Drug Administration (FDA) determine that the discontinued formulations of CALAN® (verapamil hydrochloride) 40, 80, 120, and 160 mg tablets (NDA 018817) from Pfizer Inc were not discontinued due to safety or efficacy reasons.

The authorized United States (US) agent for Center Laboratories, Inc. for this petition is:

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Vice President, Regulatory Strategy
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This petition is accompanied by a separate, related petition requesting the FDA determine that the discontinued formulations of ISOPTIN® (verapamil hydrochloride) 40, 80, and 120 mg

tablets (NDA 018593) from Mt. Adams Technologies LLC were not discontinued due to safety or efficacy reasons.

Please do not hesitate to contact Dr. Norris should you have any questions or require further information regarding this submission.

Sincerely,

Robert Hsu

Kristi Norris

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CITIZEN PETITION

The undersigned submits this petition on behalf of Center Laboratories, Inc. (hereinafter referred to as Centerlab or the Sponsor) under the Federal Food, Drug, and Cosmetic Act (FD&C Act) and pursuant to 21 CFR §10.30, §10.20, §10.25(a), §314.122, and §314.161 to request the Commissioner of Food and Drugs make a determination that the discontinued formulations of CALAN® (verapamil hydrochloride) 40, 80, 120, and 160 mg oral tablets (NDA 018817) from Pfizer Inc were not discontinued due to safety or efficacy reasons.

A. Action Requested

The petitioner requests the Commissioner of Food and Drugs make a determination that the discontinued formulations of CALAN (verapamil hydrochloride) 40, 80, 120, and 160 mg oral tablets (NDA 018817) from Pfizer Inc were not discontinued due to safety or efficacy reasons.

B. Statement of Grounds

Centerlab plans to submit a New Drug Application (NDA) for its proposed CS02 (R-verapamil hydrochloride) product via the 505(b)(2) regulatory pathway. An application submitted under Section 505(b)(2) of the FD&C Act is an application that contains full reports of investigations of safety and effectiveness but where at least some of the information required for approval comes from studies not conducted by or for the applicant and for which the applicant has not obtained a right of reference. To support the CS02 NDA, Centerlab plans to rely on the Agency's previous findings of safety for one or more listed drugs (LDs), as reflected in the LD labeling, based on a scientific bridge established through a comparative bioavailability study.

CS02 (R-verapamil hydrochloride) is an immediate-release (IR) oral tablet. The active pharmaceutical ingredient in CS02 is the R-enantiomer of verapamil. Verapamil is approved by the FDA as a racemic mixture of the R- and S-enantiomers in various formulations (eg, IR tablet, sustained-release [SR] tablet, SR capsule, and injection) for the treatment of cardiovascular indications. Centerlab plans to use FDA-approved IR oral tablet formulations of verapamil as the LDs for the CS02 505(b)(2) NDA.

ISOPTIN® (verapamil hydrochloride; NDA 018593; Mt. Adams Technologies LLC) is the first IR oral tablet formulation of racemic verapamil and was approved by the FDA in 1982. ISOPTIN is a sugar-coated tablet and was replaced by the film-coated version, CALAN (verapamil hydrochloride; NDA 018817; Pfizer Inc), after CALAN was approved by the FDA in 1984, based on its bioequivalence to ISOPTIN (Center for Drugs and Biologics, 1984). ISOPTIN and CALAN were approved by the FDA for the treatment of angina, arrhythmias, and essential hypertension (Knoll Pharmaceuticals, 1986; Pfizer Inc, 2017). According to the FDA's "Approved Drug Products with Therapeutic Equivalence Evaluations" (also known as the "Orange Book"), all strengths of both products have since been discontinued. The 40, 80, and 120 mg strengths of ISOPTIN and the 80 and 120 mg strengths of CALAN continue to be listed as the reference listed drug (RLD) in the Orange Book, but no determination has been made in the Federal Register that the products were not discontinued due to reasons of safety or efficacy. However, per the Orange Book, generics of ISOPTIN and CALAN are still being marketed. In particular, the 120 mg strength of Verapamil Hydrochloride Oral Tablets (ANDA 071881) from

Heritage Pharmaceuticals Inc has been designated as the new reference standard (RS) for the purposes of conducting bioequivalence studies to ISOPTIN and CALAN.

It is also worth noting that two related racemic verapamil products from the same manufacturers, ISOPTIN (verapamil hydrochloride) 2.5 mg/mL intravenous injection (NDA 018485) from Mt. Adams Technologies LLC and CALAN SR (verapamil hydrochloride) 180 mg sustained-release oral tablets (NDA 019152) from Pfizer Inc, have been discontinued, and the FDA determined that both products were not discontinued for reasons due to safety or efficacy (81 FR 78606; 82 FR 43388). Since the discontinuations of these related verapamil products were not a result of safety or efficacy concerns, Centerlab believes the discontinuations of ISOPTIN and CALAN were also not a result of safety or efficacy concerns.

To support the CS02 NDA, Centerlab plans to rely on the Agency's previous findings of safety for ISOPTIN and CALAN. However, in order for the CS02 NDA to be able to rely on information from these discontinued LDs, an FDA determination that states ISOPTIN and CALAN were not discontinued due to reasons of safety or efficacy is needed.

This petition requests the FDA determine that the discontinued formulations of CALAN (verapamil hydrochloride) 40, 80, 120, and 160 mg oral tablets (NDA 018817) from Pfizer Inc were not discontinued due to safety or efficacy reasons. This petition is accompanied by a second, related petition requesting the FDA determine that the discontinued formulations of ISOPTIN (verapamil hydrochloride) 40, 80, and 120 mg oral tablets (NDA 018593) from Mt. Adams Technologies LLC were not discontinued due to safety or efficacy reasons.

C. Environmental Impact

A claim for categorical exclusion from the requirements of an environmental assessment or impact statement is made pursuant to 21 CFR § 25.31(a). As all formulations of CALAN (verapamil hydrochloride) IR oral tablets (NDA 018817) from Pfizer Inc are currently discontinued, issuing a determination that said formulations were not discontinued due to reasons of safety or efficacy would not increase the use of verapamil.

D. Economic Impact

Information regarding economic impact will be made upon request by the Commissioner.

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.

Sincerely,

Camargo Pharmaceutical Services, LLC
(US Agent for Center Laboratories, Inc.)

Kristi Norris

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REFERENCES

81 FR 78606. Determination That CALAN SR (Verapamil Hydrochloride) Extended-Release Oral Tablet, 180 Milligrams, Was Not Withdrawn From Sale for Reasons of Safety or Effectiveness. Federal Register *81,* 78606-78607.

82 FR 43388. Determination That CORTONE (Cortisone Acetate) Tablets and Other Drug Products Were Not Withdrawn From Sale for Reasons of Safety or Effectiveness. Federal Register *82,* 43388-43390.

Center for Drugs and Biologics (1984). Drug Approval Package; Calan (verapamil HCl) oral tablets; NDA 018817.

Knoll Pharmaceuticals (1986). ISOPTIN (verapamil hydrochloride) oral tablets Prescribing Information (NDA 018593).

Pfizer Inc (2017). CALAN (verapamil hydrochloride) oral tablets Prescribing Information (NDA 018817) (New York, NY). https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/018817s033lbl.pdf. 15 Jun 2020.