September 21, 2006 1556 06 SEP 27 P2:11

Dockets Management Branch (HFA-305)
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

SUITABLILITY PETITION

On behalf of our client Kendle International respectfully submits this suitability petition pursuant to 21 U.S.C.§ 355(j)(2)(C) and 21 C.F.R.§ 10.30 and 314.93. Kendle requests that the Food and Drug Administration (FDA) determine that 12.5 mg tablets of Metoprolol Tartrate are suitable for an Abbreviated New Drug Application (ANDA), or supplemental ANDA, based on the reference listed drug (RLD), Metoprolol Tartrate Tablets 100 mg from Mylan. This RLD is identified in Approved Products with Therapeutic Equivalence evaluation (Orange Book)

ACTION REQUESTED

Kendle International seeks a determination that a 12.5 mg Metoprolol Tartrate tablet drug product is suitable for an ANDA, or ANDA supplement, based on the listed drug Metoprolol Tartrate Tablets100 mg from Mylan.

STATEMENT OF GROUNDS

The reference-listed drug (RLD) for the proposed generic drug product will be Metoprolol Tartrate Tablets 100 mg from Mylan. Metoprolol Tartrate Tablets are approved for use at daily doses up to approximately 400 mg per day. Metoprolol Tartrate Tablets are labeled for individualized doses based on diagnosis (hypertension, angina pectoris and Myocardial infarction) and patient tolerance.

The approved Metoprolol Tartrate Tablets, myocardial infarction labeling, however, states:

> "Patients who appear not to tolerate the full intravenous dose should be started on Lopressor ® tablets either 25 mg or 50 mg every 6 hours (depending on the degree of intolerance) 15 minutes after the last intravenous dose or as soon as their clinical condition allows."

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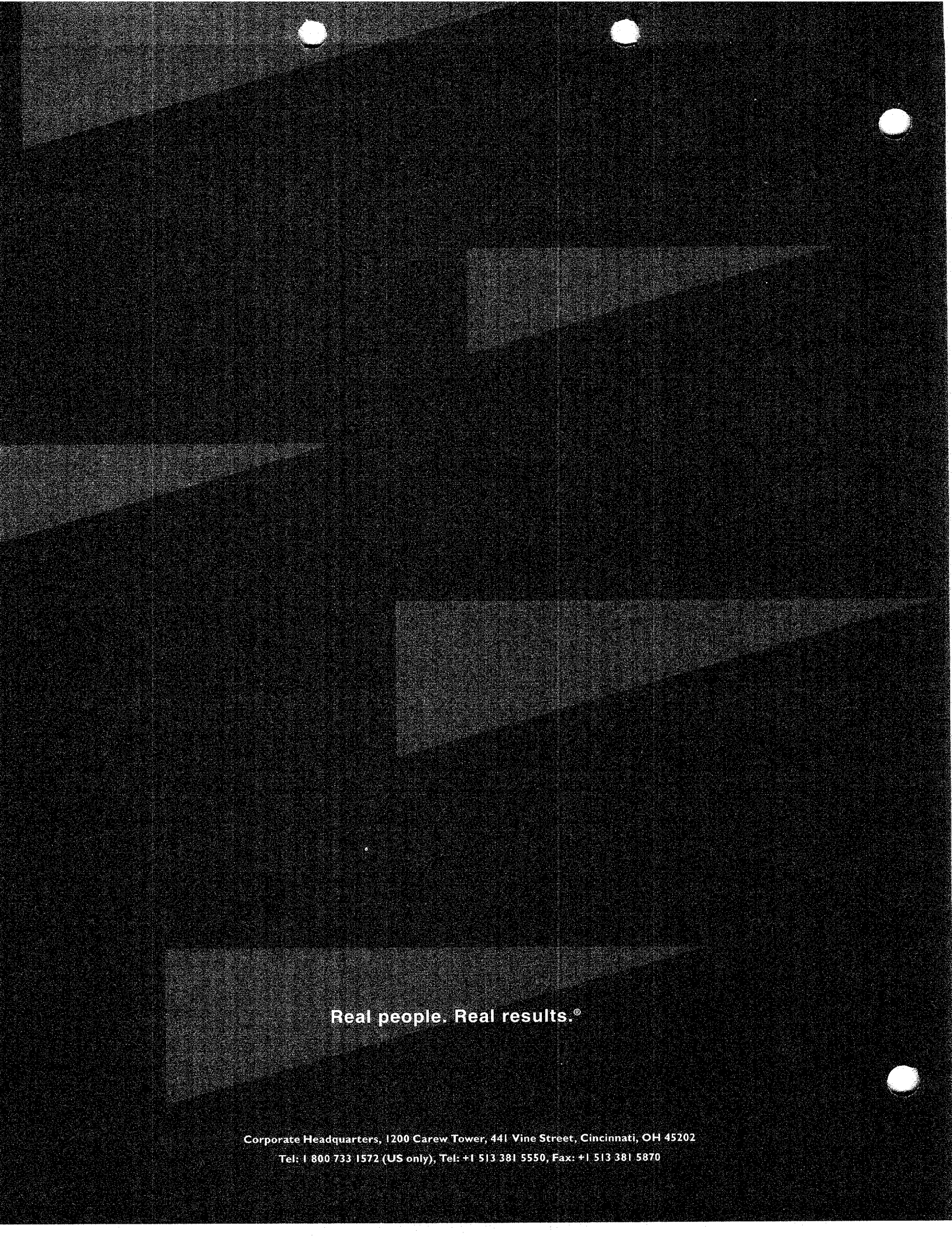

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For many patients, 12.5 mg is a sufficient dose and, in fact, more than 7% of patients receiving metoprolol tartrate take the drug at a dose below 25 mg. See IMS Audit (May 2006), copy attached as (Attachment 1). Another small percentage, 0.45 %, takes a 1-½ tablet dose. Apparently 25 mg version of the metoprolol tartrate tablets is being cut or broken in half by the patients. The availability of 12.5 mg metoprolol tartrate tablets will ensure a more uniform dosage. The 12.5 mg tablet will also make it easier and more convenient for patients prescribed smaller daily doses of metoprolol tartrate tablets to take their medication and in turn ensure better patient compliance.

In accordance with FDA regulations and policies, our client will request a bioequivalency waiver in its ANDA (or ANDA Supplement) submission. Because the proposed drug product is dose proportional and contains the same active and inactive ingredients as previously approved Metoprolol Tartrate table products, it should be bioequivalent to the RLD. The proposed drug product is expected to have the same therapeutic effect as the RLD, when administered to patients under the same conditions of use. The proposed drug product's route of administration and recommendations of use are the same as those of the RLD.

Clinically, Metoprolol Tartrate is classified as highly soluble and high permeable and is Class 1 as per the Biological Classification System (BCS) for which there is no potential for a bio-problem wit this drug.

Pursuant to 21 CFR § 314.93 (d), a copy of the approved labeling for Mylan's Metoprolol Tartrate Tablets is attached (Attachment 2). A copy of the labeling for Caraco's approved 25 mg strength of that drug product is also attached (Attachment 3). No changes to the labeling are necessary other than those necessitated by the different strength and manufacturer. The descriptions of the strength and tablet and references to the manufacturer of Lopressor ® Tablets will be modified.

ENVIRONMENTAL IMPACT

Pursuant to 21 C.F.R. § 25.31(a), this petition qualifies for a categorical exclusion from the requirement for submission of an environmental assessment.

ECONOMIC IMPACT

According to 21 CFR § 10.30 (b), information on economic impact is to be submitted only when requested by the Commissioner following review of this petition.

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 is unfavorable to the petition.

Respectfully submitted,

Anthony C. Celeste

Kendle International