DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 50708/S045
NDA 50709/S038

SUPPLEMENT APPROVAL

Astellas Pharma US, Inc.
Attention: Mary Jo Pritza, MBA, PharmD
Director, Regulatory Affairs
1 Astellas Way
Northbrook, IL 60062

Dear Dr. Pritza:

Please refer to your Supplemental New Drug Applications (sNDAs) dated and received February 20, 2015, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) as follows:

NDA/Supplement #	Product Name	Dosage Form
50708/S045	PROGRAF (tacrolimus)	Capsules, 0.5 mg, 1 mg and 5 mg
50709/S038	PROGRAF (tacrolimus)	Injection, 5 mg/mL

We acknowledge receipt of your April 22, 2015, submission.

These "Prior Approval" supplemental new drug applications provide for the following revision to the 7 DRUG INTERACTIONS/7.11 Others, section of the package insert (deletion is noted by ~~strikethrough~~ and additions are noted by underlined text).

> **7.11 Others**
> Bromocriptine, nefazodone, metoclopramide, danazol, ethinyl estradiol, amiodarone, ~~and~~ methylprednisolone, and herbal products containing schisandra sphenanthera extracts may inhibit CYP3A metabolism of tacrolimus and increase tacrolimus whole blood concentrations. Monitoring of blood concentrations and appropriate dosage adjustments of tacrolimus are recommended when these drugs and tacrolimus are co-administered.

We also note numerous editorial changes, including the deletion of outdated information in the **HIGHLIGHTS OF PRESCRIBING INFORMATION**/RECENT MAJOR CHANGES.

APPROVAL & LABELING

We have completed our review of these supplemental applications. They are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text, which is identical to the package inserts submitted February 20 and April 22, 2015.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling text for the package insert, with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that includes labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for approved NDAs (21 CFR 314.80 and 314.81).

If you have any questions, call Judit Milstein, Chief, Project Management Staff at 301-796-0763.

Sincerely,

{See appended electronic signature page}

Ozlem Belen, MD, MPH
Deputy Director for Safety
Division of Transplant and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURE: Package Insert

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

OZLEM A BELEN
05/19/2015