DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 50-708/S-036 and S-037
NDA 50-709/S-028 and S-030

SUPPLEMENT APPROVAL

Astellas Pharma
Attention: Eva Essig, PhD
Senior Director, Regulatory Affairs
Three Parkway North
Deerfield, IL 60015-2548

Dear Dr. Essig:

Please refer to your Supplemental New Drug Applications (sNDAs) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

NDA Number	Supplement Number	Drug Name	Date of Supplement	Date of Receipt
50-708	036	Prograf® (tacrolimus) Capsules 0.5mg, 1 mg and 5 mg	June 29, 2009	June 30, 2009
50-709	028	Prograf® (tacrolimus) Injection 5mg/ml	June 29, 2009	June 30, 2009

We acknowledge receipt of your amendments dated January 14, March 24, June 24, July 1, July 7, and July 8, 2011. The January 14, 2011 submissions constitute a complete response to our September 30, 2010, action letter.

These prior approval supplemental New Drug Applications provide for revisions to the product labeling in response to our February 25, 2009 letter that outlined the implementation plan for the January 24, 2006, Final Rule titled, R*equirements on Content and Format of Labeling for Human Prescription Drug and Biological Products* (Federal Register Vol. 71, No. 15, 3921-3997). Specifically, these sNDAs provide for the conversion of the current approved labeling to the format required by the Physician Labeling Rule in accordance with 21 CFR 201.56 and 201.57.

We also refer to your Supplemental New Drug Applications (sNDAs) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

NDA Number	Supplement Number	Drug Name	Date of Supplement	Date of Receipt
50-708	037	Prograf® (tacrolimus) Capsules 0.5mg, 1 mg and 5 mg	January 26, 2011	January 27, 2011
50-709	030	Prograf® (tacrolimus) Injection 5mg/ml	January 26, 2011	January 27, 2011

These "Changes Being Effected" (CBE) supplemental New Drug Applications provide for the addition of information on "Pure Red Cell Aplasia" to the product labeling. Specifically, information on pure red cell aplasia is included in the WARNINGS AND PRECAUTIONS section as provided below, and cross-referenced in HIGHLIGHTS OF PRESCRIBING INFORMATION and ADVERSE REACTIONS sections of the contents of labeling.

> **5.16 Pure Red Cell Aplasia**
> Cases of pure red cell aplasia (PRCA) have been reported in patients treated with tacrolimus. A mechanism for tacrolimus-induced PRCA has not been elucidated. All patients reported risk factors for PRCA such as parvovirus B19 infection, underlying disease, or concomitant medications associated with PRCA. If PRCA is diagnosed, discontinuation of Prograf should be considered *[see Adverse Reactions (6.2)]*.

We have completed our review of these supplemental applications, as amended. 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 labeling text submitted on July 8, 2011.

We are also waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

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, 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 for these NDAs, 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 these supplemental applications, as well as annual reportable changes and annotate each change. To facilitate review of your submissions, 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 an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Ms. June Germain, MS, Senior Regulatory Project Manager, at (301) 796-1600.

Sincerely,

{See appended electronic signature page}

Renata Albrecht, MD
Director
Division of Transplant and Ophthalmology Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURE: Content of Labeling

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

/s/

RENATA ALBRECHT
07/14/2011