

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

50-722/S-007

50-723/S-004

50-759/S-005

ADMINISTRATIVE DOCUMENTS

Certification Statement for Generic Drug Enforcement Act of 1992

On behalf of Syntex (U.S.A.) Inc., Roche Global Development has made a diligent effort to insure that no person debarred under Section 306(a) or 306(b) of the Federal Food, Drug and Cosmetic Act has provided any services in connection with this application. Relying on this effort, Roche certifies that it did not and will not use in capacity the services of any person debarred under Section 306(a) or 306(b) of the Federal Food, Drug and Cosmetic Act in connection with this application.

PEDIATRIC PAGE (Complete for all original application and all efficacy supplements) [View Word Document](#)

NDA Number: 050722 **Trade Name:** CELLCEPT (MYCOPHENOLATE MOFETIL) 250MG C
Supplement Number: 007 **Generic Name:** MYCOPHENOLATE MOFETIL
Supplement Type: SE5 **Dosage Form:**
Regulatory Action: OP **COMIS Indication:** PROPHYLAXIS OF ORGAN REJECTION AND TREATMENT OF REFRACTORY ORGAN REJECTION IN PATIENTS RECEIVING ALLOGENEIC RENAL TRANSPLANTS
Action Date: 2/22/00

Indication # 1 Prevention of acute rejection in pediatric renal transplant patients
Label Adequacy: Adequate for ALL pediatric age groups
Formulation Needed: NO NEW FORMULATION is needed
Comments (if any): (12-14-00): Roche studied children between the ages of 3 months and 18 years.

	<u>Lower Range</u>	<u>Upper Range</u>	<u>Status</u>	<u>Date</u>
	3 months	18 years	Completed	12/22/00
	0 months	3 months	Waived	12/22/00

Comments: (12-14-00) From Dr. Marc Cavaille-Coll: With respect to pediatric renal transplant patients, we should keep in mind that renal transplant recipients aged 0 to 5 years old represent less than 0.5% of all renal transplant recipients in the US, and a total number of less than 200 to date. Recipients less than 3 months old are extremely rare. It would not be realistic to expect that the firm could study a meaningful number of subjects less than 3 months old. I would recommend waiving this group and extrapolating from information in the next older group in renal transplantation. It is already remarkable that they were able to study children between ages 3 months and 18 years.

This page was last edited on 12/14/00

Signature

Date

PEDIATRIC PAGE (Complete for all original application and all efficacy supplements) [View Word Document](#)

NDA Number: 050723 **Trade Name:** CELLCEPT (MYCOPHENOLATE MOFETIL) 500MG T
Supplement Number: 004 **Generic Name:** MYCOPHENOLATE MOFETIL
Supplement Type: SE5 **Dosage Form:**
Regulatory Action: OP **COMIS Indication:** PROPHYLAXIS OF ORGAN REJECTION AND TREATMENT OF REFRACTORY ORGAN REJECTION IN PATIENTS RECEIVING ALLOGENEIC RENAL TRANSPLANTS
Action Date: 5/24/00

Indication # 1 Prevention of acute rejection in pediatric renal transplant patients
Label Adequacy: Adequate for ALL pediatric age groups
Formulation Needed: NO NEW FORMULATION is needed
Comments (if any): (12-14-00): Roche studied children between the ages of 3 months and 18 years.

	<u>Lower Range</u>	<u>Upper Range</u>	<u>Status</u>	<u>Date</u>
	3 months	18 years	Completed	12/22/00
	0 months	3 months	Waived	12/22/00

Comments: (12-14-00) From Dr. Marc Cavaille-Coll: With respect to pediatric renal transplant patients, we should keep in mind that renal transplant recipients aged 0 to 5 years old represent less than 0.5% of all renal transplant recipients in the US, and a total number of less than 200 to date. Recipients less than 3 months old are extremely rare. It would not be realistic to expect that the firm could study a meaningful number of subjects less than 3 months old. I would recommend waiving this group and extrapolating from information in the next older group in renal transplantation. It is already remarkable that they were able to study children between ages 3 months and 18 years.

This page was last edited on 12/14/00

Signature

Date

PEDIATRIC PAGE (Complete for all original application and all efficacy supplements) [View Word Document](#)

NDA Number: 050759 **Trade Name:** CELLCEPT(MYCOPHENOLATE MOFETIL)200MG/ML
Supplement Number: 005 **Generic Name:** MYCOPHENOLATE MOFETIL
Supplement Type: SE5 **Dosage Form:**
Regulatory Action: OP **COMIS Indication:** PROPHYLAXIS OF TRANSPLANT REJECTION AND INCREASED PATIENT AND GRANT SURVIVAL IN PATIENTS RECEIVING ALLOGENIC RENAL TRANSPLANTS
Action Date: 5/24/00

Indication # 1 Prevention of acute rejection in pediatric renal transplant patients.
Label Adequacy: Adequate for ALL pediatric age groups
Formulation Needed: NO NEW FORMULATION is needed
Comments (if any): (12-14-00): Roche studied children between the ages of 3 months and 18 years.

Lower Range	Upper Range	Status	Date
3 months	18 years	Completed	12/22/00
0 months	3 months	Waived	12/22/00

Comments: (12-14-00) From Dr. Marc Cavaille-Coll: With respect to pediatric renal transplant patients, we should keep in mind that renal transplant recipients aged 0 to 5 years old represent less than 0.5% of all renal transplant recipients in the US, and a total number of less than 200 to date. Recipients less than 3 months old are extremely rare. It would not be realistic to expect that the firm could study a meaningful number of subjects less than 3 months old. I would recommend waiving this group and extrapolating from information in the next older group in renal transplantation. It is already remarkable that they were able to study children between ages 3 months and 18 years.

This page was last edited on 12/14/00

Signature

Date



February 18, 2000

Division of Special Pathogens and Immunologic Drug Products, HFD-590
Food and Drug Administration
Center for Drug Evaluation and Research
9201 Corporate Blvd., 4th Floor
Rockville, MD 20850

SUBJECT: **NDA 50-722 / S-007 - CellCept[®] 250 mg Capsules (mycophenolate mofetil)
Pediatric Use Supplement**

Dear Reviewers:

On behalf of Syntex (U.S.A.), Inc., and pursuant to Section 21 CFR 314.70(b), we are herewith submitting a Supplemental New Drug Application to extend the current use of CellCept (mycophenolate mofetil) in the prophylaxis of acute rejection to pediatric patients receiving allogeneic renal transplants. This supplemental application also fulfills the request for further characterization of the pharmacokinetics of mycophenolate mofetil in pediatric patients made by the Agency in the approval letter for CellCept 250 mg capsules (NDA 50-722) on May 3, 1995.

Pursuant to 21 CFR 201.57(f)(9)(iv), the proposed revision to the "Pediatric Use" subsection of the CellCept label is based on adequate and well-controlled studies in adult renal transplant patients with supporting data from 140 patients from pediatric studies. Furthermore, the data included in this submission supports the premise that the course of acute rejection and the mechanism of action of CellCept in the prevention of acute rejection are sufficiently similar in adults and the pediatric populations to permit extrapolation from the adult efficacy data to pediatric patients.

Supported by pharmacokinetic and safety information contained in this supplement, the proposed revisions to the CellCept package insert include the recommendation for the use of 600mg/m² of CellCept oral suspension as the dose for pediatric patients. Guidance for the use of capsules and tablets in this population is also provided. We believe that the approval of this important supplement will enable the pediatric transplant community to correctly dose pediatric renal allograft patients.

This supplement is being submitted to the CellCept 250 mg capsules (NDA 50-722) as part of a phase IV commitment. Letters of cross-reference will be submitted to the approved NDAs for CellCept oral suspension (NDA 50-759) and CellCept tablets (NDA 50-723) to seek approval for extending the use of these dosage forms in pediatric patients receiving renal transplants in accordance with the corresponding dosing recommendations.

The content and format of this supplement follows the Guidance for Industry for "The Content and Format for Pediatric Use Supplements" (CDER, May 1996) which was discussed and agreed

upon with the Division at the Pre-NDA teleconference on January 21, 1999. An outline of the organization of this supplement is presented below.

<u>NDA Section</u>	<u>Volume</u>	<u>Reviewers Copies</u>
I. Application Forms and Index	1	All
II. Labeling	2	All
III. Application Summary	2	All
IV. Chemistry, Manufacturing and Controls	2	Technical
VI. Human Pharmacokinetics/Bioavailability	3-7	Biopharmaceutics
VIII/X. Clinical / Statistical Data	8 - 19	Medical / Statistical
XI. Case Report Tabulations	CD-ROM CRTs - patient profiles for study MYCS2675 in .pdf format CRTs - domain listings for all studies in the supplement in .pdf format CRTs - data sets for study MYCS2675	N/A
XII. Case Report Forms	CD-ROM Electronic copies of deaths and terminations due to AE in .pdf format	N/A

In addition, as requested by the Division on January 21, 2000, electronic copies (.pdf) of the three study reports contained within this submission, the Application Summary, the Integrated Summary of Safety, and the Summary of Human Bioavailability and Pharmacokinetics will be submitted to the Division two weeks following the filing.

In accordance with 21 CFR 314.50(d)(5), the 4-month safety update for this supplement will be provided in June 2000. The clinical data cut-off for this update will be March 10, 2000. The update will include narratives and tabulations of malignancies graft loss (re-transplantation or death), and AEs leading to study termination for patients in study MYCS2675. The update will be formatted as an addendum to the ISS included herewith.

The archival copy of this NDA supplement is being sent to the Central Document Room for CDER. Reviewer's copies and desk copies are being sent to the Document Control Room for the Division to the attention of Mr. Bacho.

CellCept®
Mycophenolate Mofetil



NDA Pediatric Use Supplement
February 18, 2000

Roche appreciates the continuous support the Division has provided on the development program for CellCept. We look forward to extending this long-standing collaboration to the review of this supplement.

Should you have any questions during the course of the review period, please do not hesitate to contact me by phone at (650) 354-2370 or by fax at (650) 852-1861.

Sincerely,

A handwritten signature in cursive script that reads "Carmen R. Rodriguez".

Carmen R. Rodriguez, M.Sc.
Regulatory Program Director
Roche Global Development

Archival Copy:

CDER Central Document Room
12229 Wilkins Avenue
Rockville, MD 20852

Reviewers / Desk Copies:

Division of Special Pathogens and
Immunologic Drug Products
Document Control Room
(Attn: Mr. Matthew Bacho)
9201 Corporate Blvd. 4th Floor
Rockville, MD 20852

Via: Fed-Ex

**MEMORANDUM OF TELEFACSIMILE CORRESPONDENCE**

DATE: April 13, 2000

TO: Carmen Rodriguez, M.Sc.
Regulatory Program Director
Roche Pharmaceuticals
(650) 354-2370
(650) 852-1861 (fax)

FROM: Matthew A. Bacho, Regulatory Project Manager

THROUGH: Joyce A. Korvick, M.D., M.P.H., Medical Officer
Kofi A. Kumi, Ph.D., Clin. Pharm. & Biopharmaceutics Reviewer

NDA: NDA 50-722/S-007 (CellCept®)

SUBJECT: Request for Information

With reference to your supplemental new drug application for the use of CellCept® to prevent organ rejection in pediatric patients receiving allogeneic renal transplants, our reviewing medical officer and clinical pharmacologist request the following information:

- 1) Please provide us with the date of submission and location within the supplemental NDA of the pilot study MYC2190.
- 2) Could you provide the meaning behind "Master Reference Number" and whether we can use this information to locate specific pieces of information?
- 3) Please send a data set that includes the outcome/efficacy of CellCept® in pediatric kidney transplant patients in study MYCS2675. Review of the current SAS transport sets does not reveal an "efficacy" file. Although this study is not powered to describe the efficacy of CellCept® in pediatric patients, it is important for us to review outcomes to ensure that the rejection rates are no worse than that which would be expected in this group of patients.
- 4) Finally, we determined that NDA 50-722/S-007 was fileable.

We are providing the above information via telephone facsimile for your convenience. Please feel free to contact me at (301) 827-2127 if you have any questions regarding the contents of this transmission.

/S/

Matthew A. Bacho
Regulatory Project Manager
Division of Special Pathogen and Immunologic Drug Products