CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-357

21-358

ENVIRONMENTAL ASSESSMENT

MEMORANDUM **DEPARTMENT OF HEALTH & HUMAN SERVICES**
Public Health Service
Food & Drug Administration
Center for Biologics Evaluation & Research

DATE: April 27, 2001

TO: BLA file STN 103948
Millenium and Ilex Partners, CAMPATH 1H

FROM: Walter Lange, HFM-675

SUBJECT: Categorical exclusion under 21 CFR 25.31(c)
Millenium and Ilex Partners, CAMPATH 1H

I have reviewed pertinent sections of the BLA application (STN 103948) from Millenium and Ilex Partners, for CAMPATH-1H, and find that their request for a categorical exclusion from an environmental assessment under 21 CFR 25.31(c) is justified as the product is composed of naturally occurring substances, and that no extraordinary circumstances exist.

4/27/01
Date

Walter Lange
EA Reviewer for the BLA

5/2/01
Date

Kurt A. Brorson, Ph.D.
Chair, BLA Review Committee

Concurrence:

4/30/01
Date

John A. Eltermann, Jr. R. Ph., M.S.
Director

4.5 Environmental Assessm ent

L&I Partners, LP claims categorical exclusion from preparation of an Environmental Assessment under 21 CFR 25.31 (c). All operations for manufacturing, processing, testing, labeling, packaging, distribution and disposal of CAMPATH® as well as treatment of waste from the production of CAMPATH® are performed in accordance with applicable local and federal environmental regulations. Approval of L&I Partners' BLA for manufacture of CAMPATH® will not alter significantly the concentration or distribution of the substance, its metabolites, or degradation products in the environment. To the best of the knowledge of L&I Partners, LP and BI, no extraordinary circumstances exist that could significantly affect the quality of the human environment upon approval of this BLA (21 CFR 25.21).

05/02/01

Review Memo

Ref:	**STN 103948/1010**
Prepared by:	Kurt Brorson, Ph.D., Staff Scientist, DMA
Through:	Kathryn Stein, Ph.D., Director, DMA Keith Webber Ph.D., Deputy Director, DMA
Cc:	Sharon Sickafuse, DARP
Sponsor:	Millenium & Ilex partners (MPI)
Product:	Campath
Date of submission:	April 24, 2000
Date of review:	May 2, 2001

Background

MPI has submitted a BLA for their anti-CD52 mAb, Campath, for use in CLL. The original BLA contained — months of drug product and drug substance stability data. This amendment contains — month update of stability data for both drug product and drug substance. It also contains a description of an amended sterility test for drug substance.

Conclusions

- Both drug product and drug substance were within specifications after — months of storage at 2-8°C. **Recommendation:** approve 24 months as an initial expiry period for Campath.
- The amended sterility method for drug substance is a — method which complies with 21CFR 610.12. **Recommendation**: approve sterility test method for drug substance.

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Memorandum

Food and Drug Administration
Center for Biologics Evaluation and Research
Bethesda, MD 20892

Date : 5/31/00

To : File

From : Mark Brunswick, Division of Monoclonal Antibodies - HFM-555

Through : Deputy Division Director, Division of Monoclonal Antibodies
K Webb 4-24-01

Subject : BLA 990786

THERAPEUTIC AGENT(S): CAMPATH-1H

SPONSOR(S): L & I Partners, LP
11550 IH 10 West, Suite 100
San Antonio
TX 78230-1064

(210)-949-8274

Contact Kelly Tate

CLINICAL INDICATION(S): The proposed indication for CAMPATH is for the treatment of patients with B-Cell Chronic Lymphocytic Leukemia (CLL) who have received an alkylating agent and have failed fludarabine therapy.

This review will contain information that has been taken directly from the CALA submission. **Reviewer notes and comments will be identified in the review.**

Attached are the history of culture thaws and the lot release data for formulated bulk and final product. There have been thaws that have resulted in released product.

Based on my review of the original BLA, Inspection of the facility, the Sponsor is capable of making the product in a consistent manner. Their production yields a product that is well characterized and has an acceptable low level of contaminants and acceptable level of viral

clearance.

Introduction:

CAMPATH-1H is a humanized monoclonal antibody directed against the human CD52 antigen. CD52 is a membrane glycoprotein expressed predominantly on peripheral blood lymphocytes, monocytes, and tissue macrophages. Clinical development of CAMPATH-1H has focused on the ability of the antibody to lyse lymphocytes. In this application, CAMPATH-1H is the proprietary name applied to Drug Substance or antibody molecule while CAMPATH is applied to Drug Product. A United States Adopted Name (USAN) has been requested **(Reviewer's Note: the USAN name is alemtuzumab)**. CAMPATH Drug Product contains [redacted] Polysorbate 80). CAMPATH Drug [redacted] glass ampoules and is packaged in packs of ampoules. It is stored under refrigeration. CAMPATH is administered by intravenous (IV) infusion after dilution of the ampoule contents in normal saline or 5% dextrose.

CAMPATH-1H antibody is expressed in Chinese Hamster Ovary (CHO) cells in culture, [redacted] CAMPATH Drug Product is prepared by [redacted] ampoules. The entire commercial manufacturing process, [redacted] under contract with the Sponsor. The Sponsor retains responsibility for release and distribution of both Drug Substance and Drug Product.

[redacted]

The Sponsor, L&I Partners, LP, (L&I) has continued the development of CAMPATH . The formulation of CAMPATH was modified from that used [redacted] The Sponsor has conducted the confirmatory clinical trial (CAM211) in CLL that is described in this application. Subsequently, the Sponsor has modified the scale of CAMPATH-1H manufacture from [redacted] as described in the application.

Description and Characterization

Overview