CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

125289

CHEMISTRY REVIEW(S)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Center for Drugs Evaluation and Research – Food and Drug Administration
Office of Biotechnology Products / Office of Pharmaceutical Science
Division of Monoclonal Antibodies, NIH Bldg 29B, HFD-123
29B Lincoln Drive, Bethesda, MD 20892

The Quality Team Leader's Executive Summary

From: **David M. Frucht, M.D.,**
Acting Chief, Laboratory of Cell Biology
Division of Monoclonal Antibodies (DMA)

Through: **Kathleen A. Clouse, Ph.D., Director, DMA**

BLA Number: **125289**
Product: **Golimumab (CNTO 148, SIMPONI)**
Sponsor : **Centocor**

Date of Review : **February 19, 2009**

Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The data submitted in this application support the conclusion that the manufacture of golimumab is well controlled, leading to a product that is pure and potent. The product is free from endogenous or adventitious infectious agents sufficient to meet the parameters recommended by FDA. The conditions used in manufacturing have been sufficiently validated, and a consistent product is produced from the multiple production runs presented. It is recommended that this product be approved for human use (under conditions specified in the package insert). Please refer to concluding section for other product quality-related statements to be included in the potential approval letter.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

The current assay for detection of adventitious virus contamination in the unprocessed bulk harvest performed at [redacted] is a sub-optimal legacy assay dating from the 1980's and has an unacceptable percentage of false positives, which may be attributable to subtleties in assay performance. As a temporary safety measure, testing has been transferred to a second contract testing organization, [redacted] where this assay has not been susceptible to matrix effects. As a permanent solution and a post-marketing commitment, the Sponsor will be requested to optimize the existing assay or develop an improved assay for detecting adventitious virus contamination in the unprocessed bulk harvest. b(4)

II. Summary of Quality Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

- Golimumab (CNTO148, SIMPONI) is a human $IgG_1\kappa$ monoclonal antibody directed against human tumor necrosis factor alpha (TNF-α). The submission includes the complete sequence of both the heavy chain and light chain, two of each composing the complete $IgG_1\kappa$ molecule. Each heavy chain contains [redacted] intrachain disulfide bridges, whereas each light chain contains [redacted] intrachain disulfide bridges. Each heavy chain is linked to the other, and to one of two light chains, through interchain disulfide bonds. Golimumab has a β-pleated sheet structure. The carbohydrate structure is typical of that for other monoclonal antibodies. [redacted] Golimumab displays an N-linked glycan structure as expected for a human IgG_1; there is no evidence for O-glycosylation. [redacted] Golimumab is a complex biomolecule that displays microheterogeneity. This heterogeneity results primarily from heavy chain deamidation, terminal galactosylation, b(4)

and [redacted] The mass weight of golimumab is 150-151 kDa. b(4)

- Drug substance manufacture occurs at Centocor B.V., Einsteinweg 101, 2333 CB Leiden, The Netherlands.

- The mechanism of action for golimumab is to neutralize the activity of human TNF-α. Abnormally high levels of soluble TNF-α have been implicated in the pathophysiology of rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis. Binding of soluble TNF-α by golimumab prevents this cytokine from binding to cell surface TNF-α receptors, consequently preventing the initiation of downstream signaling cascades. Golimumab is also capable of binding to TNF-α expressed on the surface of cells. In addition, the Fc region functions to bind FcRn and FcγR1. The binding affinity to FcRn was evaluated by an FcRn competition assay (IC_{50}: 15-17 μg/mL), whereas the binding affinity to FcγR1 was assessed by ELISA (EC_{50}: 0.8 μg/mL). Golimumab has been shown to be capable of binding complement and mediating complement-dependent cytotoxicity (CDC) of $mTNF^{hi}$ transfectomas. However, $mTNF^{lo}$ cells (LPS-stimulated monocytes), which are more representative of leukocytes from patients with activated inflammatory disease, are not susceptible to golimumab-mediated CDC.

- The clinical indications for golimumab include adult rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis. No clinical studies of golimumab have been conducted in pediatric populations.

- Golimumab is administered at a 50 mg dose given as a SC injection once per month, [redacted] After proper training in SC injection technique, a patient may self-administer the injections. For patients with rheumatoid arthritis, golimumab is administered in combination with methotrexate; for patients with psoriatic arthritis or ankylosing spondylitis, co-administration of methotrexate is optional. b(4)

- Golimumab is provided in 1 mL pre-filled syringes that are assembled with a Centocor Autoinjector [redacted] It is intended for single use. Golimumab is supplied in two dosage formats (100 mg/1 mL and 50 mg/0.5 mL). Each dosage format contains 100 mg/mL golimumab, 4.1% (w/v) sorbitol, 5.6 mM l-histidine, and 0.015% polysorbate 80 dissolved in Water for Injection. The excipients used are of compendial grade as follows: L-histidine [United States Pharmacopoeia (USP)/European Pharmacopoeia (EP)], L-histidine monohydrochloride monohydrate (EP), sorbitol [National Pharmacopoeia (NF)], polysorbate 80 (NF/EP), and Water for Injection (USP/EP). b(4)

[redacted] b(4)

- Excipients were chosen based on known formulations for proteins and stability studies as follows:
  - Sorbitol-
  - Histidine

[redacted] b(4)

- Polysorbate 80 (PS 80)- [redacted] b(4)

- The primary container closure is a [redacted] mL long syringe barrel with a 27 G fixed needle, along with a [redacted] There are two secondary packaging modes as follows: [redacted] (2) Centocor Autoinjector (DMF under review at CDRH as a consult review). **Note:** *The needle shield contains latex; this should be reflected in the labeling.*

- PFS and autoinjectors are packaged in individual cardboard carton boxes, protecting the product from light.

- Golimumab is expressed in [redacted] with expression plasmids [redacted] The variable regions were constructed based on the human framework and CDRs from an anti-TNF-α monoclonal antibody isolated from a TNF-α-immunized xenomouse. Post-transfection, there were [redacted] prior to establishment of the Master Cell Bank, [redacted] MCB;02NOV01. The current system of cell banks also includes the Working Cell Banks [redacted] WCB;29MAY02 and [redacted] WCB;29NOV05. These cell banks have been tested for viability upon thaw, identity, sterility, mycoplasma and adventitious agents. Post-production cells were tested for genetic stability; this investigation supports a [redacted] culture period for these cells. b(4)

- Manufacture of the golimumab Drug Substance is divided into [redacted] steps that are grouped into three main areas as follows:

[redacted] b(4)

- The golimumab Drug Substance manufacturing process is based on Centocor's monoclonal antibody platform process. This process has undergone several modifications, including changes to site, scale, cell line and unit operations. Process parameters were subjected to a risk assessment to identify critical process parameters

3 Page(s) Withheld

✓ Trade Secret / Confidential (b4)

_____ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

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- **Clinical indication**

b(4)

Golimumab is administered at a 50 mg dose given as a SC injection once per months, [redacted] After proper training in SC injection technique by the health care provider, a patient may self-administer the injections. For patients with rheumatoid arthritis, golimumab is administered in combination with methotrexate; for patients with psoriatic arthritis or ankylosing spondylitis, co-administration of methotrexate is optional and left to the discretion of the physician.

- **Composition of Drug Product**

Component	100 mg Dose Amount per dose (mg)	50 mg Dose Amount per dose (mg)	Concentration
CNTO 148	100	50	100 mg/mL
Sorbitol	41.0	20.5	4.1% (w/v)
L-Histidine	0.87	0.44	5.6 mM
PS 80	0.15	0.075	0.015% (w/v)
Water for injection (mL)	1	0.5	NA[a]

C. Basis for Approvability or Not-Approval Recommendation

Golimumab is manufactured by a robust process with precautions for contamination by cell substrate or adventitious agents. Golimumab is manufactured consistently, leading to a safe and effective product, and approval is recommended for the proposed clinical indications. In addition, the letter to the Sponsor should also indicate that

b(4)

[redacted]

Quality unit Assessment

I. REVIEW OF COMMON TECHNICAL DOCUMENT-QUALITY (CTD-Q) MODULE 3.2: BODY OF DATA

The review of module 3.2 is attached as a separate document. A consult review regarding the validation reports for those bioassays used human studies (immunogenicity, neutralization, and serum golimumab assays) was provided as a separate memorandum to the clinical pharmacology review team.

II. REVIEW OF COMMON TECHNICAL DOCUMENT-QUALITY (CTD-Q) MODULE 1

A. ENVIRONMENTAL ASSESSMENT OR CLAIM OF CATEGORICAL EXCLUSION

Golimumab meets the criteria for a categorical exclusion defined in the regulations 21 CFR 25.31(c).

III. LIST OF DEFICIENCIES TO BE COMMUNICATED

There are no CMC-related deficiencies precluding approval of this BLA.

IV. ADMINISTRATIVE

A. Reviewer's Signature

2/26/09

Product Quality Reviewer: Kurt Brorson, Ph.D.

B. Endorsement Block

2/26/09

Product Division Team Leader: David M. Frucht, M.D.

02/26/09

Product Division Director: Kathleen A. Clouse, Ph.D.

C. CC Block

OBP Office Director: Steven Kozlowski, M.D.
Clinical Deputy Division Director: Rigoberto Roca, M.D.
Clinical Division Director: Bob Rappaport, M.D.
Division of Monoclonal Antibodies File/BLA STN 125289

2/26/09

PRODUCT QUALITY REVIEW

BLA #125289

Golimumab
(SIMPONI)

Centocor Inc.

Kurt Brorson, Ph.D.
Division of Monoclonal Antibodies

Product Quality Review Data Sheet

1. BLA 125289

2. REVIEW #: 1

3. REVIEW DATE: 14-Feb-2009

4. REVIEWER: Kurt Brorson, Ph.D.

5. COMMUNICATIONS AND PREVIOUS CMC-RELATED DOCUMENTS:

Previous Documents	Document Date
End of phase 2 meeting (comparability plan)	4/21/05
Correspondence regarding dosage form	4/25/06
Pre-BLA meeting (combined CMC & clinical)	8/21/07
Pre-BLA meeting correspondence (immunogenicity discussion)	8/29/07
Telecon to discuss AVA event (Centocor)	10/14/08
Telecon to discuss AVA event [redacted]	10.21/08
Telecon to discuss AVA event (Centocor)	10/23/08
Telecon to discuss AVA event (Centocor)	11/7/08
Telecon to discuss AVA event (Centocor)	11/20/08
Telecon to discuss AVA event (Centocor)	12/11/08

b(4)

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
0000 (original submission)	6/25/08
0014 (Stability amendment)	12/30/08
00xx (Response to inspection observations)	pending

7. NAME & ADDRESS OF APPLICANT:

Name:	Centocor, Inc.
Address:	200 Great Valley Parkway, Malvern PA 19355
Representative:	Bethany Paxson
Telephone:	610-651-6000

8. DRUG PRODUCT NAME/TYPE:

a) Proprietary Name: SIMPONI
b) Non-Proprietary Name (USAN): Golimumab
c) Other names: CNTO148, rTNV148B
d) Submission Priority: Standard

9. PHARMAC. CATEGORY: Anti-TNF-α monoclonal antibody

10. DOSAGE FORM: Prefilled syringe in either a passive delivery system or an autoinjector device with either a 50 mg/syringe (0.5 mL) or a 100 mg/syringe (1.0 mL)

11. STRENGTH/POTENCY: Golimumab is provided in two dosage formats: 50 mg and 100 mg deliverable.

Table 1. Quantitative and Qualitative Composition

Component	100 mg Dose Amount per dose (mg)	50 mg Dose Amount per dose (mg)	Concentration
CNTO 148	100	50	100 mg/mL
Sorbitol	41.0	20.5	4.1% (w/v)
L-Histidine	0.87	0.44	5.6 mM
PS 80	0.15	0.075	0.015% (w/v)
Water for injection (mL)	1	0.5	NA[a]

Note: *PS 80 is polysorbate 80,* [redacted]

b(4)

2 Page(s) Withheld

✓ Trade Secret / Confidential (b4)

_____ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

Withheld Track Number: Chemistry- 3

15. RELATED/SUPPORTING DOCUMENTS:

Drug Master File (DMF) and Master File for Devices (MAF):

- [redacted] b(4)
- [redacted]

16. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Establishment Status	Complete	Q4 2008	Patricia Hughes
Carton and Vial Labeling	Pending		Kimberly Rains
Environmental Assessment	Approve	2/13/09	Kurt Brorson
BMT-Centocor BV DS facility inspection	EIR complete	2/20/09	Kurt Brorson, Patricia Hughes & Kalavarti Suvarna
BMT- [redacted] DS safety testing facility inspection	EIRcomplete	2/20/09	Kurt Brorson, Patricia Hughes & Kalavarti Suvarna
BMT-DP & autoinjector facilities	Inspections waived	Q3 2008	Patricia Hughes
Trade name review	Pending		

b(4)

17. CMC Inspectional Activities:

Two inspections were performed:

1. **Centocor BV, Leiden Holland. This is the drug substance manufacturer and the main testing site for DS and DP release and stability. The site was inspected Jan 28- Feb 3, 2009 by Kurt Brorson (DMA), Patricia Hughes (DMPQ) and Kalavarti Suvarna (DMPQ). A form 483 with five items was issued; responses are pending.**
2. **[redacted] This is testing site for drug substance microbial safety (i.e., mycoplasma and adventitious viruses. The site was inspected Feb 4-6, 2009 by Kurt Brorson (DMA), Patricia Hughes (DMPQ) and Kalavarti Suvarna (DMPQ). A form 483 with four items was issued; responses are pending.**

b(4)

Inspections for other sites (i.e., Drug Product fill, cell bank testing, autoinjector assembly) were waived, as they are frequently inspected by ORA.

Review Memo

Ref:	**125289**
Prepared by:	Kurt Brorson, Ph.D., Staff Scientist, DMA 2/26/09
Through:	David Frucht, M.D., Acting Chief, Laboratory of Cell Biology, DMA 2/26/09 Kathleen Clouse, Ph.D., Director, DMA Kathleen Clouse 02/26/09
CSO:	Sharon Turner-Rinehardt, DAARP
Sponsor:	Centocor
Product:	Golimumab (CNTO148, SIMPONI)
Date of submission:	**6/24/08**
Date of Review:	**1/10/08**

Summary

CNTO 148 is a human $IgG_1\kappa$ monoclonal antibody specific for human tumor necrosis factor alpha (TNFα), thereby neutralizing the biological activity of TNFα. The CNTO 148 drug substance is manufactured at Centocor B.V. (Leiden, The Netherlands) by

[redacted] b(4)

The CNTO 148 PFS formulation is composed of 100 mg/mL CNTO 148 with excipient concentrations of 5.6 mM L-histidine, 4.1% (w/v) sorbitol, and 0.015% (w/v) polysorbate 80, pH 5.5. It is manufactured in two dosage formats, a 50 mg/syringe (0.5 mL) and a 100 mg/syringe (1.0 mL).

Each heavy chain contains [redacted] ntra chain disulfide bridges, whereas each light chain contains [redacted] intrachain disulfide bridges. Each heavy chains is linked to the other, and to one of two light chains, through interchain disulfide bonds. The molecular mass is 150-151 kD. It contains N-linked glycan structures as expected for a recombinant human IgG_1: biantennary, core-fucosylated species with galactose heterogeneity. [redacted] b(4)

35 Page(s) Withheld

✓ Trade Secret / Confidential (b4)

_____ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

Withheld Track Number: Chemistry- 4

Kurt Brorson

STN 125289 Product Golimumab

Part B – Product/CMC/Facility Reviewer(s)

CTD Module 2 Contents	Present?		If not, justification, action & status
Overall CTD Table of Contents [2.1]	(Y)	N	
Introduction to the summary documents (1 page) [2.2]	(Y)	N	
Quality overall summary [2.3]	(Y)	N	
◻ Drug Substance	(Y)	N	
◻ Drug Product	(Y)	N	
◻ Facilities and Equipment	(Y)	N	
◻ Adventitious Agents Safety Evaluation	(Y)	N	
◻ Novel Excipients	Y	N	} N/A This information is submitted in module 3
◻ Executed Batch Records	Y	N	
◻ Method Validation Package	Y	N	
◻ Comparability Protocols	Y	N	

CTD Module 3 Contents	Present?		If not, justification, action & status
Module Table of Contents [3.1]	(Y)	N	
Drug Substance [3.2.S]			
◻ general info	(Y)	N	
o nomenclature			
o structure (e.g. sequence, glycosylation sites)			
o properties			
◻ manufacturers (names, locations, and responsibilities of all sites involved)	(Y)	N	
◻ description of manufacturing process	(Y)	N	
o batch numbering and pooling scheme			
o cell culture and harvest			
o purification			
o filling, storage and shipping			
◻ control of materials	(Y)	N	
o raw materials and reagents			
o biological source and starting materials			
o cell substrate: source, history, and generation			
o cell banking system, characterization, and testing			
◻ control of critical steps and intermediates	(Y)	N	
o justification of specifications			
o analytical method validation			
o reference standards			
o stability			
◻ process validation (prospective	(Y)	N	

CTD Module 3 Contents	Present?	If not, justification, action & status
plan, results, analysis, and conclusions)		
❑ manufacturing process development (describe changes during non-clinical and clinical development; justification for changes)	(Y) N	
❑ characterization of drug substance	(Y) N	
❑ control of drug substance	(Y) N	
o specification		
o justification of specs.		
o analytical procedures		
o analytical method validation		
o batch analyses		
o consistency (3 consecutive lots)		
o justification of specs.		
❑ reference standards	(Y) N	
❑ container closure system	(Y) N	
❑ stability	(Y) N	
❑ summary		
❑ post-approval protocol and commitment		
❑ pre-approval		
o protocol		
o results		
o method validation		
Drug Product [3.2.P]		
❑ description and composition	(Y) N	
❑ pharmaceutical development	(Y) N	
❑ manufacturers (names, locations, and responsibilities of all sites involved)	(Y) N	
❑ batch formula	(Y) N	
❑ description of manufacturing process for production through finishing, including formulation, filling, labeling and packaging (including all steps performed at outside [e.g., contract] facilities)	(Y) N	
❑ controls of critical steps and intermediates	(Y) N	
❑ process validation including aseptic processing & sterility assurance:	(Y) N	
o 3 consecutive lots		
o other needed validation data		
❑ control of excipients (justification of specifications; analytical method	(Y) N	

CTD Module 3 Contents	Present?	If not, justification, action & status
validation; excipients of human/animal origin) ❑ control of drug product (justification of specifications; analytical method validation) ❑ container closure system [3.2.P.7] o specifications (vial, elastomer, drawings) o availability of DMF o closure integrity o administration device(s) ❑ stability ❑ summary ❑ post-approval protocol and commitment ❑ pre-approval o protocol o results o method validation	(Y) N (Y) N (Y) N	
Diluent (vials or filled syringes) [3.2P'] ❑ description and composition of diluent ❑ pharmaceutical development ❑ manufacturers (names, locations, and responsibilities of all sites involved) ❑ batch formula ❑ description of manufacturing process for production through finishing, including formulation, filling, labeling and packaging (including all steps performed at outside [e.g., contract] facilities) ❑ controls of critical steps and intermediates ❑ process validation including aseptic processing & sterility assurance: o 3 consecutive lots o other needed validation data ❑ control of excipients (justification of specifications; analytical method validation; excipients of human/animal origin, other novel excipients) ❑ control of diluent (justification of specifications; analytical method validation, batch analysis, characterization of impurities)	Y N Y N Y N Y N Y N Y N Y N Y N	Not Applicable, liquid dosage form

STN 125289 Product _____

CTD Module 3 Contents	Present?		If not, justification, action & status
❑ reference standards	Y	N	N/A
❑ container closure system	Y	N	
o specifications (vial, elastomer, drawings)			
o availability of DMF			
o closure integrity			
❑ stability	Y	N	
❑ summary			
❑ post-approval protocol and commitment			
❑ pre-approval			
o protocol			
o results			
Other components to be marketed (full description and supporting data, as listed above):			
❑ other devices	(Y)	N	
❑ other marketed chemicals (e.g. part of kit)	(Y)	N	
Appendices for Biotech Products [3.2.A]			
❑ facilities and equipment	(Y)	N	
o manufacturing flow; adjacent areas			
o other products in facility			
o equipment dedication, preparation and storage			
o sterilization of equipment and materials			
o procedures and design features to prevent contamination and cross-contamination			
❑ adventitious agents safety evaluation (viral and non-viral) e.g.:	(Y)	N	
o avoidance and control procedures			
o cell line qualification			
o other materials of biological origin			
o viral testing of unprocessed bulk			
o viral clearance studies			
o testing at appropriate stages of production			
❑ novel excipients	Y	N	N/A, there are none
USA Regional Information [3.2.R]			
❑ executed batch records	(Y)	N	
❑ method validation package	(Y)	N	

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CTD Module 3 Contents	Present?	If not, justification, action & status
☐ comparability protocols	(Y) N	
Literature references and copies [3.3]	(Y) N	

Examples of Filing Issues	Yes?	If not, justification, action & status
content, presentation, and organization sufficient to permit substantive review?	(Y) N	
☐ legible	(Y) N	
☐ English (or translated into English)	(Y) N	
☐ compatible file formats	(Y) N	
☐ navigable hyper-links	(Y) N	
☐ interpretable data tabulations (line listings) & graphical displays	(Y) N	
☐ summary reports reference the location of individual data and records	(Y) N	
☐ all electronic submission components usable	(Y) N	
includes appropriate process validation data for the manufacturing process at the commercial production facility?	(Y) N	
includes production data on drug substance and drug product manufactured in the facility intended to be licensed (including pilot facilities) using the final production process(es)?	(Y) N	
includes data demonstrating consistency of manufacture	(Y) N	
includes complete description of product lots and manufacturing process utilized for clinical studies	(Y) N	
describes changes in the manufacturing process, from material used in clinical trial to commercial production lots	(Y) N	
data demonstrating comparability of product to be marketed to that used in clinical trials (when significant changes in manufacturing processes or facilities have occurred)	(Y) N	
certification that all facilities are ready for inspection	(Y) N	
data establishing stability of the product through the proposed dating period and a stability protocol describing the test methods used and time intervals for product assessment.	(Y) N	
if not using a test or process specified by regulation, data is provided to show the	Y N	N/A, there are none

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Examples of Filing Issues	Yes?	If not, justification, action & status
alternate is equivalent (21 CFR 610.9) to that specified by regulation. List: ☐ LAL instead of rabbit pyrogen ☐ mycoplasma ☐ sterility ☐ ☐	 Y N Y N Y N	
identification by lot number, and submission upon request, of sample(s) representative of the product to be marketed; summaries of test results for those samples	Y N	
floor diagrams that address the flow of the manufacturing process for the drug substance and drug product	(Y) N	
description of precautions taken to prevent product contamination and cross-contamination, including identification of other products utilizing the same manufacturing areas and equipment	(Y) N	
information and data supporting validity of sterilization processes for sterile products and aseptic manufacturing operations	(Y) N	
if this is a supplement for post-approval manufacturing changes, is animal or clinical data needed? Was it submitted?	Y N	N/A

List any issue not addressed above which should be identified as a reason for not filing the BLA/BLS. Also provide additional details if above charts did not provide enough room (or attach separate memo).

Recommendation (circle one): (File) RTF

Reviewer: [signature] 8-5-08 (signature/ date) Type (circle one): (Product (Chair)) Facility (DMPQ)

Concurrence:
Branch/Lab Chief: [signature] (signature/ date) 8/05/08

Division. Director: Kathleen Clowse (signature/ date) 08/05/08

TBP Version: 2/22/07

1 CATEGORICAL EXCLUSION

Centocor, Inc., Horsham, PA, certifies that the above referenced action meets the criteria for a categorical exclusion defined in the regulations 21 CFR 25.31(c), and that to the knowledge of Centocor, Inc., no extraordinary circumstances exist. Thus, no environmental assessment needs to be performed.

2 Page(s) Withheld

✓ Trade Secret / Confidential (b4)

_____ Draft Labeling (b4)

_____ Draft Labeling (b5)

_____ Deliberative Process (b5)

Withheld Track Number: Environmental Assessment- 5