

STN 125160/0

Product Certolizumab pegol

Part A Page 1

**APPEARS THIS WAY  
ON ORIGINAL**

STN 125160/0

Product Certolizumab pegol

**Part A. Regulatory Project Manager (RPM)**

CTD Module 1 Contents	Present?	If not, justification, action & status
Cover Letter	(Y) N	
Form 356h completed	(Y) N	
<input checked="" type="checkbox"/> including list of all establishment sites and their registration numbers	(Y) N	
<input checked="" type="checkbox"/> If foreign applicant, US Agent signature.	(Y) N	
Comprehensive Table of Contents	(Y) N	
Debarment Certification with correct wording (see * below)	(Y) N	
User Fee Cover Sheet	(Y) N	
User Fee payment received	(Y) N	
Financial certification &/or disclosure information	(Y) N	
Environment assessment or request for categorical exclusion (21 CFR Part 25)	(Y) N	
Pediatric rule: study, waiver, or deferral	(Y) N	
Labeling:	Y N	
<input type="checkbox"/> PI –non-annotated	Y N	
<input checked="" type="checkbox"/> PI –annotated	Y N	
<input checked="" type="checkbox"/> PI (electronic)	Y N	
<input type="checkbox"/> Medication Guide	Y N	N/A
<input checked="" type="checkbox"/> Patient Insert	Y N	
<input checked="" type="checkbox"/> package and container	Y N	
<input type="checkbox"/> diluent	Y N	N/A
<input type="checkbox"/> other components	Y N	N/A
<input checked="" type="checkbox"/> established name (e.g. USAN)	Y N	
<input checked="" type="checkbox"/> proprietary name (for review)	Y N	

\* The Debarment Certification must have correct wording , e.g. "I, the undersigned, hereby certify that XXX Co. did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food Drug, and Cosmetic Act in connection with the studies listed in Appendix XXX." Applicant may not use wording such as "To the best of my knowledge..."

Examples of Filing Issues	Yes?	If not, justification, action & status
Content, presentation, and organization of paper and electronic components sufficient to permit substantive review?: Examples include:	(Y) N	
<input checked="" type="checkbox"/> legible	(Y) N	
<input checked="" type="checkbox"/> English (or translated into English)	(Y) N	
<input checked="" type="checkbox"/> compatible file formats	(Y) N	
<input checked="" type="checkbox"/> navigable hyper-links	(Y) N	
<input checked="" type="checkbox"/> interpretable data tabulations (line listings) & graphical displays	(Y) N	
<input checked="" type="checkbox"/> summary reports reference the location of individual data and records	(Y) N	

Examples of Filing Issues	Yes?		If not, justification, action & status
<input checked="" type="checkbox"/> protocols for clinical trials present	<input checked="" type="checkbox"/> Y	N	
<input checked="" type="checkbox"/> all electronic submission components usable (e.g. conforms to published guidance)	<input checked="" type="checkbox"/> Y	N	
companion application received if a shared or divided manufacturing arrangement	Y	N	N/A
if CMC supplement:			
<input type="checkbox"/> description and results of studies performed to evaluate the change	Y	N	N/A This is a BLA.
<input type="checkbox"/> relevant validation protocols	Y	N	
<input type="checkbox"/> list of relevant SOPs	Y	N	
if clinical supplement:			
<input type="checkbox"/> changes in labeling clearly highlighted	Y	N	N/A This is a BLA.
<input type="checkbox"/> data to support all label changes	Y	N	
<input type="checkbox"/> all required electronic components, including electronic datasets (e.g. SAS)	Y	N	
if electronic submission:			
<input checked="" type="checkbox"/> required paper documents (e.g. forms and certifications) submitted	<input checked="" type="checkbox"/> Y	N	

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).

N/A

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Has orphan drug exclusivity been granted to another drug for the same indication?

If yes, review committee informed? \_\_\_\_\_

Does this submission relate to an outstanding PMC? No.

If an Advisory Committee (AC) discussion may be needed, list applicable AC meetings scheduled to occur during the review period:

- Name: \_\_\_\_\_
- Dates: N/A

Recommendation (circle one): File RTF

RPM Signature: [Signature]

Branch Chief concurrence: [Signature]

6 Page(s) Withheld

Trade Secret / Confidential

Draft Labeling

Deliberative Process

**Part C – Non-Clinical Pharmacology/Toxicology Reviewer(s)**

CTD Module 2 Contents	Present?	If not, justification, action & status
Overall CTD Table of Contents [2.1]	<input checked="" type="checkbox"/> Y N	
Introduction to the summary documents (1 page) [2.2]	<input checked="" type="checkbox"/> Y N	
Non-clinical overview [2.4]	<input checked="" type="checkbox"/> Y N	
Non-clinical summary [2.6]	<input checked="" type="checkbox"/> Y N	
<input type="checkbox"/> Pharmacology	<input checked="" type="checkbox"/> Y N	
<input type="checkbox"/> Pharmacokinetics	<input checked="" type="checkbox"/> Y N	
<input type="checkbox"/> Toxicology	<input checked="" type="checkbox"/> Y N	

CTD Module 4 Contents	Present?	If not, justification, action & status
Module Table of Contents [4.1]	<input checked="" type="checkbox"/> Y N	
Study Reports and related info. [4.2]	<input checked="" type="checkbox"/> Y N	
<input type="checkbox"/> Pharmacology	<input checked="" type="checkbox"/> Y N	
<input type="checkbox"/> Pharmacokinetics	<input checked="" type="checkbox"/> Y N	
<input type="checkbox"/> Toxicology	<input checked="" type="checkbox"/> Y N	
Literature references and copies [4.3]	<input checked="" type="checkbox"/> Y N	

Examples of Filing Issues	Yes?	If not, justification, action & status
content, presentation, and organization sufficient to permit substantive review?	<input checked="" type="checkbox"/> Y N	
<input type="checkbox"/> legible	<input checked="" type="checkbox"/> Y N	
<input type="checkbox"/> English (or translated into English)	<input checked="" type="checkbox"/> Y N	
<input type="checkbox"/> compatible file formats	<input checked="" type="checkbox"/> Y N	
<input type="checkbox"/> navigable hyper-links	<input checked="" type="checkbox"/> Y N	
<input type="checkbox"/> interpretable data tabulations (line listings) & graphical displays	<input checked="" type="checkbox"/> Y N	
<input type="checkbox"/> summary reports reference the location of individual data and records	<input checked="" type="checkbox"/> Y N	
<input type="checkbox"/> protocol-specified (as opposed to a different, post-hoc analysis) and other critical statistical analyses included	<input checked="" type="checkbox"/> Y N	
<input type="checkbox"/> all electronic submission components usable	<input checked="" type="checkbox"/> 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)	<input checked="" type="checkbox"/> Y N	
for each non-clinical laboratory study, either a statement that the study was conducted in compliance with the good laboratory practice requirements set forth in 21 CFR Part 58 or, if the study was not conducted in compliance with such regulations, a brief statement justifying the non-compliance	<input checked="" type="checkbox"/> Y N	

Examples of Filing Issues	Yes?		If not, justification, action & status
animal reproduction studies included, if the biological product is to be administered to people with reproductive potential, unless an explanation of why such studies are not applicable	(Y)	N	
includes carcinogenicity and/or reproductive and developmental toxicology studies deemed necessary by well established agency interpretation or communication during the IND review process	(Y)	N	

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).

*The sponsor provided Interim Study Report for the "52-week study with recovery period in cynomolgus monkeys to examine the effects of CDP 870 on hematological and morphological parameters following repeat subcutaneous dosing" (Study # 506771)*

*The sponsor needs to provide the final report for the study.*

Recommendation (circle one): (File) RTF

Pharm/Tox reviewer: Sushanta Ka Choudhary 4/20/06  
(signature/ date)

Branch Chief concurrence: [Signature] 4/20/06  
(signature/ date)

Division Director concurrence: \_\_\_\_\_  
(signature/ date)

## Part D – Clinical (Pharmacology, Efficacy, Safety, and Statistical) Reviewers

CTD Module 2 Contents	Present?	If not, justification, action & status
Overall CTD Table of Contents [2.1]	<input checked="" type="radio"/> Y <input type="radio"/> N	
Introduction to the summary documents (1 page) [2.2]	<input checked="" type="radio"/> Y <input type="radio"/> N	
Clinical overview [2.5]	<input checked="" type="radio"/> Y <input type="radio"/> N	
Clinical summary [2.7] (summary of individual studies; comparison and analyses across studies)	<input checked="" type="radio"/> Y <input type="radio"/> N	
<input type="checkbox"/> Biopharmaceutics and associated analytical methods	<input checked="" type="radio"/> Y <input type="radio"/> N	
<input type="checkbox"/> Clinical pharmacology [includes immunogenicity]	<input checked="" type="radio"/> Y <input type="radio"/> N	
<input type="checkbox"/> Clinical Efficacy [for each indication]	<input type="radio"/> Y <input type="radio"/> N	
<input type="checkbox"/> Clinical Safety	<input type="radio"/> Y <input type="radio"/> N	
<input type="checkbox"/> Synopses of individual studies	<input checked="" type="radio"/> Y <input type="radio"/> N	

CTD Module 5 Contents	Present?	If not, justification, action & status
Module Table of Contents [5.1]	<input checked="" type="radio"/> Y <input type="radio"/> N	
Tabular Listing of all clinical studies [5.2]	<input checked="" type="radio"/> Y <input type="radio"/> N	
Study Reports and related information [5.3]	<input type="radio"/> Y <input type="radio"/> N	
<input type="checkbox"/> Biopharmaceutic	<input checked="" type="radio"/> Y <input type="radio"/> N	
<input type="checkbox"/> Studies pertinent to Pharmacokinetics using Human Biomaterials	<input checked="" type="radio"/> Y <input type="radio"/> N	
<input type="checkbox"/> Pharmacokinetics (PK)	<input checked="" type="radio"/> Y <input type="radio"/> N	
<input type="checkbox"/> Pharmacodynamic (PD)	<input checked="" type="radio"/> Y <input type="radio"/> N	
<input type="checkbox"/> Efficacy and Safety	<input type="radio"/> Y <input type="radio"/> N	
<input type="checkbox"/> Postmarketing experience	<input type="radio"/> Y <input type="radio"/> N	
<input type="checkbox"/> Case report forms	<input type="radio"/> Y <input type="radio"/> N	
<input type="checkbox"/> Individual patient listings (indexed by study)	<input type="radio"/> Y <input type="radio"/> N	
<input type="checkbox"/> electronic datasets (e.g. SAS)	<input checked="" type="radio"/> Y <input type="radio"/> N	
Literature references and copies [5.4]	<input checked="" type="radio"/> Y <input type="radio"/> N	

Examples of Filing Issues	Yes?	If not, action & status
Content, presentation, and organization sufficient to permit substantive review?	<input type="radio"/> Y <input type="radio"/> N	
<input type="checkbox"/> legible	<input checked="" type="radio"/> Y <input type="radio"/> N	
<input type="checkbox"/> English (or certified translation into English)	<input checked="" type="radio"/> Y <input type="radio"/> N	
<input type="checkbox"/> compatible file formats	<input checked="" type="radio"/> Y <input type="radio"/> N	
<input type="checkbox"/> navigable hyper-links	<input checked="" type="radio"/> Y <input type="radio"/> N	
<input type="checkbox"/> interpretable data tabulations (line listings) & graphical displays	<input checked="" type="radio"/> Y <input type="radio"/> N	

Examples of Billing Issues	Yes	If not, action & status
<input type="checkbox"/> summary reports reference the location of individual data and records	(Y) N	
<input type="checkbox"/> protocols for clinical trials present	(Y) N	
<input type="checkbox"/> all electronic submission components usable	(Y) N	
statement for each clinical investigation:		
<input type="checkbox"/> conducted in compliance with IRB requirements	(Y) N	
<input type="checkbox"/> conducted in compliance with requirements for informed consent	(Y) N	
adequate and well-controlled clinical study data (e.g. not obviously inappropriate or clinically irrelevant study design or endpoints for efficacy)	Y N	
adequate explanation of why results from what appears to be a single controlled trial (or alternate method for demonstrating efficacy) should be accepted as scientifically valid without replication	Y N	
study design not clearly inappropriate (as reflected in regulations, well-established agency interpretation or correspondence) for the particular claim	Y N	
study(ies) assess the contribution of each component of a combination product [21 CFR 610.17]	Y N	
total patient exposure (numbers or duration) at relevant doses is not clearly inadequate to evaluate safety (per standards communicated during IND review, or ICH or other guidance documents)	Y N	
adequate data to demonstrate safety and/or effectiveness in the population intended for use of the biological product based on age, gender, race, physiologic status, or concomitant therapy	Y N	
drug interaction studies communicated as during IND review as necessary are included	Y N	
assessed drug effects whose assessment is required by well established agency interpretation or communicated during IND review	Y N	
comprehensive analysis of safety data from all current world-wide knowledge of product	Y N	

Examples of filing issues	Yes?		If not, action & status
data supporting the proposed dose and dose interval	<input checked="" type="radio"/> Y	<input type="radio"/> N	
appropriate (e.g. protocol-specified) and complete statistical analyses of efficacy data	<input type="radio"/> Y	<input type="radio"/> N	
adequate characterization of product specificity or mode of action	<input type="radio"/> Y	<input type="radio"/> 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	<input checked="" type="radio"/> Y	<input type="radio"/> N	
inadequate efficacy and/or safety data on product to be marketed when different from product used in clinical studies which are the basis of safety and efficacy determinations	<input type="radio"/> Y	<input type="radio"/> N	
all information reasonably known to the applicant and relevant to the safety and efficacy described?	<input type="radio"/> Y	<input type="radio"/> N	

List of Clinical Studies (protocol number)	Final study report submitted?		Financial disclosure or certification submitted?			SAS & other electronic datasets complete & usable?		BIMOs sites identified?		
	Y	N	Y	N	NR	Y	N	Y	N	NR
	Y	N	Y	N	NR	Y	N	Y	N	NR
	Y	N	Y	N	NR	Y	N	Y	N	NR
	Y	N	Y	N	NR	Y	N	Y	N	NR
	Y	N	Y	N	NR	Y	N	Y	N	NR
	Y	N	Y	N	NR	Y	N	Y	N	NR
	Y	N	Y	N	NR	Y	N	Y	N	NR
	Y	N	Y	N	NR	Y	N	Y	N	NR
	Y	N	Y	N	NR	Y	N	Y	N	NR
	Y	N	Y	N	NR	Y	N	Y	N	NR

Y= yes; N=no; NR=not required



**Part D – Clinical (Pharmacology, Efficacy, Safety, and Statistical)****Reviewers**

CTD Module 2 Contents	Present?	If not, justification, action & status
Overall CTD Table of Contents [2.1]	<input checked="" type="checkbox"/> Y N	
Introduction to the summary documents (1 page) [2.2]	<input checked="" type="checkbox"/> Y N	
Clinical overview [2.5]	<input checked="" type="checkbox"/> Y N	
Clinical summary [2.7] (summary of individual studies; comparison and analyses across studies)	<input checked="" type="checkbox"/> Y N	
<input type="checkbox"/> Biopharmaceutics and associated analytical methods	<input checked="" type="checkbox"/> Y N	
<input type="checkbox"/> Clinical pharmacology [includes immunogenicity]	<input checked="" type="checkbox"/> Y N	
<input type="checkbox"/> Clinical Efficacy [for each indication]	<input checked="" type="checkbox"/> Y N	
<input type="checkbox"/> Clinical Safety	<input checked="" type="checkbox"/> Y N	
<input type="checkbox"/> Synopses of individual studies	<input checked="" type="checkbox"/> Y N	

CTD Module 5 Contents	Present?	If not, justification, action & status
Module Table of Contents [5.1]	<input checked="" type="checkbox"/> Y N	
Tabular Listing of all clinical studies [5.2]	<input checked="" type="checkbox"/> Y N	
Study Reports and related information [5.3]	Y N	
<input type="checkbox"/> Biopharmaceutic	Y N	
<input type="checkbox"/> Studies pertinent to Pharmacokinetics using Human Biomaterials	Y N	
<input type="checkbox"/> Pharmacokinetics (PK)	Y N	
<input type="checkbox"/> Pharmacodynamic (PD)	Y N	
<input checked="" type="checkbox"/> Efficacy and Safety	<input checked="" type="checkbox"/> Y N	
<input checked="" type="checkbox"/> Postmarketing experience	Y N	
<input checked="" type="checkbox"/> Case report forms	Y N	
<input type="checkbox"/> Individual patient listings (indexed by study)	Y N	
<input checked="" type="checkbox"/> electronic datasets (e.g. SAS)	<input checked="" type="checkbox"/> Y N	
Literature references and copies [5.4]	Y N	

Examples of Filing Issues	Yes?	If not, action & status
Content, presentation, and organization sufficient to permit substantive review?	<input checked="" type="checkbox"/> Y N	
<input type="checkbox"/> legible	<input checked="" type="checkbox"/> Y N	
<input type="checkbox"/> English (or certified translation into English)	<input checked="" type="checkbox"/> Y N	
<input type="checkbox"/> compatible file formats	<input checked="" type="checkbox"/> Y N	
<input type="checkbox"/> navigable hyper-links	<input checked="" type="checkbox"/> Y N	
<input type="checkbox"/> interpretable data tabulations (line listings) & graphical displays	<input checked="" type="checkbox"/> Y N	

Examples of Filing Issues	Yes?		If not, action & status
data supporting the proposed dose and dose interval	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N	
appropriate (e.g. protocol-specified) and complete statistical analyses of efficacy data	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N	
adequate characterization of product specificity or mode of action	<input type="checkbox"/> Y	<input type="checkbox"/> 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	<input type="checkbox"/> Y	<input type="checkbox"/> N	
inadequate efficacy and/or safety data on product to be marketed when different from product used in clinical studies which are the basis of safety and efficacy determinations	<input type="checkbox"/> Y	<input type="checkbox"/> N	
all information reasonably known to the applicant and relevant to the safety and efficacy described?	<input type="checkbox"/> Y	<input type="checkbox"/> N	

List of Clinical Studies (protocol number)	Final study report submitted?		Financial disclosure or certification submitted?			SAS & other electronic datasets complete & usable?		BiMo sites identified?		
031	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N	NR	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> Y	<input type="checkbox"/> N	NR
032	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> Y	<input type="checkbox"/> N	NR	<input checked="" type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> Y	<input type="checkbox"/> N	NR
	<input type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> Y	<input type="checkbox"/> N	NR	<input type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> Y	<input type="checkbox"/> N	NR
	<input type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> Y	<input type="checkbox"/> N	NR	<input type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> Y	<input type="checkbox"/> N	NR
	<input type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> Y	<input type="checkbox"/> N	NR	<input type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> Y	<input type="checkbox"/> N	NR
	<input type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> Y	<input type="checkbox"/> N	NR	<input type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> Y	<input type="checkbox"/> N	NR
	<input type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> Y	<input type="checkbox"/> N	NR	<input type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> Y	<input type="checkbox"/> N	NR
	<input type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> Y	<input type="checkbox"/> N	NR	<input type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> Y	<input type="checkbox"/> N	NR
	<input type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> Y	<input type="checkbox"/> N	NR	<input type="checkbox"/> Y	<input type="checkbox"/> N	<input type="checkbox"/> Y	<input type="checkbox"/> N	NR

Y=yes; N=no; NR=not required

## Part D – Clinical (Pharmacology, Efficacy, Safety, and Statistical) Reviewers

CTD Module 2 Contents	Present?	If not, justification, action & status
Overall CTD Table of Contents [2.1]	<input checked="" type="radio"/> Y <input type="radio"/> N	
Introduction to the summary documents (1 page) [2.2]	<input checked="" type="radio"/> Y <input type="radio"/> N	
Clinical overview [2.5]	<input checked="" type="radio"/> Y <input type="radio"/> N	
Clinical summary [2.7] (summary of individual studies; comparison and analyses across studies)	<input checked="" type="radio"/> Y <input type="radio"/> N	
<input checked="" type="checkbox"/> Biopharmaceutics and associated analytical methods	<input checked="" type="radio"/> Y <input type="radio"/> N	
<input checked="" type="checkbox"/> Clinical pharmacology [includes immunogenicity]	<input checked="" type="radio"/> Y <input type="radio"/> N	
<input checked="" type="checkbox"/> Clinical Efficacy [for each indication]	<input checked="" type="radio"/> Y <input type="radio"/> N	
<input checked="" type="checkbox"/> Clinical Safety	<input checked="" type="radio"/> Y <input type="radio"/> N	
<input checked="" type="checkbox"/> Synopses of individual studies	<input checked="" type="radio"/> Y <input type="radio"/> N	

CTD Module 5 Contents	Present?	If not, justification, action & status
Module Table of Contents [5.1]	<input checked="" type="radio"/> Y <input type="radio"/> N	
Tabular Listing of all clinical studies [5.2]	<input checked="" type="radio"/> Y <input type="radio"/> N	
Study Reports and related information [5.3]	<input checked="" type="radio"/> Y <input type="radio"/> N	
<input type="checkbox"/> Biopharmaceutic	<input type="radio"/> Y <input type="radio"/> N	
<input type="checkbox"/> Studies pertinent to Pharmacokinetics using Human Biomaterials	<input type="radio"/> Y <input type="radio"/> N	
<input checked="" type="checkbox"/> Pharmacokinetics (PK)	<input checked="" type="radio"/> Y <input type="radio"/> N	
<input checked="" type="checkbox"/> Pharmacodynamic (PD)	<input checked="" type="radio"/> Y <input type="radio"/> N	
<input checked="" type="checkbox"/> Efficacy and Safety	<input checked="" type="radio"/> Y <input type="radio"/> N	
<input type="checkbox"/> Postmarketing experience	<input type="radio"/> Y <input type="radio"/> N	
<input checked="" type="checkbox"/> Case report forms	<input checked="" type="radio"/> Y <input type="radio"/> N	
<input checked="" type="checkbox"/> Individual patient listings (indexed by study)	<input checked="" type="radio"/> Y <input type="radio"/> N	
<input type="checkbox"/> electronic datasets (e.g. SAS)	<input checked="" type="radio"/> Y <input type="radio"/> N	
Literature references and copies [5.4]	<input type="radio"/> Y <input type="radio"/> N	

Examples of Filing Issues	Yes?	If not, action & status
Content, presentation, and organization sufficient to permit substantive review?	<input checked="" type="radio"/> Y <input type="radio"/> N	
<input type="checkbox"/> legible	<input checked="" type="radio"/> Y <input type="radio"/> N	
<input type="checkbox"/> English (or certified translation into English)	<input checked="" type="radio"/> Y <input type="radio"/> N	
<input type="checkbox"/> compatible file formats	<input checked="" type="radio"/> Y <input type="radio"/> N	
<input type="checkbox"/> navigable hyper-links	<input checked="" type="radio"/> Y <input type="radio"/> N	
<input type="checkbox"/> interpretable data tabulations (line listings) & graphical displays	<input checked="" type="radio"/> Y <input type="radio"/> N	

Examples of Billing Issues	Yes?		If not, action & status
<input type="checkbox"/> summary reports reference the location of individual data and records	(Y)	N	
<input type="checkbox"/> protocols for clinical trials present	(Y)	N	
<input type="checkbox"/> all electronic submission components usable	(Y)	N	
statement for each clinical investigation:			
<input type="checkbox"/> conducted in compliance with IRB requirements	(Y)	N	
<input type="checkbox"/> conducted in compliance with requirements for informed consent	(Y)	N	
adequate and well-controlled clinical study data (e.g. not obviously inappropriate or clinically irrelevant study design or endpoints for efficacy)	(Y)	N	
adequate explanation of why results from what appears to be a single controlled trial (or alternate method for demonstrating efficacy) should be accepted as scientifically valid without replication	Y	N	N/A
study design not clearly inappropriate (as reflected in regulations, well-established agency interpretation or correspondence) for the particular claim	Y	N	N/A
study(ies) assess the contribution of each component of a combination product [21 CFR 610.17]	Y	N	N/A
total patient exposure (numbers or duration) at relevant doses is not clearly inadequate to evaluate safety (per standards communicated during IND review, or ICH or other guidance documents)	Y	N	N/A
adequate data to demonstrate safety and/or effectiveness in the population intended for use of the biological product based on age, gender, race, physiologic status, or concomitant therapy	(Y)	N	
drug interaction studies communicated as during IND review as necessary are included	(Y)	N	
assessed drug effects whose assessment is required by well established agency interpretation or communicated during IND review	(Y)	N	
comprehensive analysis of safety data from all current world-wide knowledge of product	(Y)	N	

Examples of Filing Issues	Yes?		If not, action & status
data supporting the proposed dose and dose interval	<input checked="" type="radio"/> Y	<input type="radio"/> N	
appropriate (e.g. protocol-specified) and complete statistical analyses of efficacy data	<input checked="" type="radio"/> Y	<input type="radio"/> N	
adequate characterization of product specificity or mode of action	<input checked="" type="radio"/> Y	<input type="radio"/> 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	<input type="radio"/> Y	<input type="radio"/> N	
inadequate efficacy and/or safety data on product to be marketed when different from product used in clinical studies which are the basis of safety and efficacy determinations	<input type="radio"/> Y	<input checked="" type="radio"/> N	
all information reasonably known to the applicant and relevant to the safety and efficacy described?	<input checked="" type="radio"/> Y	<input type="radio"/> N	

List of Clinical Studies (protocol number)	Final study report submitted?		Financial disclosure or certification submitted?			SAS & other electronic datasets complete & usable?		BiMo sites identified?		
	Y	N	Y	N	NR	Y	N	Y	N	NR
CDP 870-004	<input checked="" type="radio"/> Y	<input type="radio"/> N	<input checked="" type="radio"/> Y	<input type="radio"/> N	NR	<input checked="" type="radio"/> Y	<input type="radio"/> N	<input type="radio"/> Y	<input type="radio"/> N	NR
CDP 870-005	<input checked="" type="radio"/> Y	<input type="radio"/> N	<input checked="" type="radio"/> Y	<input type="radio"/> N	NR	<input checked="" type="radio"/> Y	<input type="radio"/> N	<input type="radio"/> Y	<input type="radio"/> N	NR
CDP 870-008	<input checked="" type="radio"/> Y	<input type="radio"/> N	<input checked="" type="radio"/> Y	<input type="radio"/> N	NR	<input checked="" type="radio"/> Y	<input type="radio"/> N	<input type="radio"/> Y	<input type="radio"/> N	NR
* CDP 870-031	<input checked="" type="radio"/> Y	<input type="radio"/> N	<input checked="" type="radio"/> Y	<input type="radio"/> N	NR	<input checked="" type="radio"/> Y	<input type="radio"/> N	<input type="radio"/> Y	<input type="radio"/> N	NR
* CDP 870-032	<input checked="" type="radio"/> Y	<input type="radio"/> N	<input checked="" type="radio"/> Y	<input type="radio"/> N	NR	<input checked="" type="radio"/> Y	<input type="radio"/> N	<input type="radio"/> Y	<input type="radio"/> N	NR
CDP 870-033	<input checked="" type="radio"/> Y	<input type="radio"/> N	<input checked="" type="radio"/> Y	<input type="radio"/> N	NR	<input checked="" type="radio"/> Y	<input type="radio"/> N	<input type="radio"/> Y	<input type="radio"/> N	NR
CDP 870-034	<input checked="" type="radio"/> Y	<input type="radio"/> N	<input checked="" type="radio"/> Y	<input type="radio"/> N	NR	<input checked="" type="radio"/> Y	<input type="radio"/> N	<input type="radio"/> Y	<input type="radio"/> N	NR
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Y=yes; N=no; NR=not required

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).

Multiple horizontal lines for text entry.

Is clinical site(s) inspection (BiMo) needed?

Yes

Is an Advisory Committee needed?

T.B.D.

Recommendation (circle one): File RTF

Reviewer: \_\_\_\_\_ Type (circle one) Clinical Clin/Pharm Statistical

(signature/ date)

Concurrence:

Branch Chief: \_\_\_\_\_ Division Director: \_\_\_\_\_

(signature/ date)

(signature/ date)

4/21/06

Food and Drug Administration  
Rockville, MD 20852

MAR 10 2006

UCB, Inc.  
Attention: Patricia Fritz  
Vice President, Global Regulatory Affairs  
1950 Lake Park Drive  
Smyrna, Georgia 30080

Dear Ms. Fritz:

We have received your biologics license application (BLA) submitted under section 351 of the Public Health Service Act for the following biological product:

**Our Submission Tracking Number (STN):** BL 125160/0.

**Name of Biological Product:** Certolizumab pegol

**Indication:** \_\_\_\_\_

**Date of Application:** February 28, 2006

**Date of Receipt:** March 1, 2006

**User Fee Goal Date:** December 30, 2006

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We note that you have not fulfilled the requirement. We acknowledge receipt of your request for a deferral of pediatric studies for this application. Once the application has been filed, we will notify you whether we have deferred the pediatric study requirement for this application.

If you have not already done so, promptly submit the *content of labeling* (21 CFR 601.14(b)) in electronic format as described at the following website:

<http://www.fda.gov/oc/datacouncil/spl.html>.

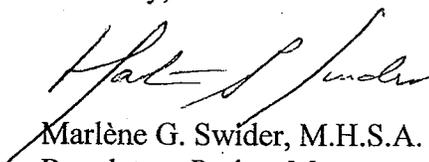
We will notify you within 60 days of the receipt date if the application is sufficiently complete to permit a substantive review.

We request that you submit all future correspondence, supporting data, or labeling relating to this application in triplicate, citing the above STN number. Please refer to <http://www.fda.gov/cder/biologics/default.htm> for important information regarding therapeutic biological products, including the addresses for submissions. Effective August 29, 2005, the new address for all submissions to this application is:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Therapeutic Biological Products Document Room  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

If you have any questions, please contact the Regulatory Project Manager, Marlène G. Swider, at (301) 796-2104.

Sincerely,

A handwritten signature in black ink, appearing to read "Marlene G. Swider". The signature is written in a cursive style with a large initial "M" and "S".

Marlène G. Swider, M.H.S.A.  
Regulatory Project Manager  
Division of Gastroenterology Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research



DEPARTMENT OF HEALTH AND HUMAN SERVICES  
Public Health Service  
Food and Drug Administration  
Center for Biologics Evaluation and Research

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Memorandum

Date: DEC 29 2005  
From: <sup>ab</sup> Cristi Stark, DGP, ODEIII  
To: IND 11197  
Subject: Type B Meeting Summary

---

Meeting Date: December, 2005

Time: 1:00-2:00pm

Location: White Oak Conference Room 1315

Meeting Requestor/Sponsor: UCB Pharma, Inc.

Product: CDP-870 (Certolizumab pegol)

Proposed Use: \_\_\_\_\_

Type of meeting: pre-BLA for CMC

Meeting Purpose: To discuss the content and format for a BLA for CMC

FDA Attendees: John Hyde, Li-Ching Liang, Brian Harvey, Gilbert Salud, Gurpreet Gill-Sangha, Cristi Stark, Patrick Swann

Sponsor Attendees: Anthony Phillips, Andy Hooker, Bernard Chan, Spencer Oliver, Phil Challis, Michael Fairbanks, Stephen Brown, Marline Dragnet, Deborah Hogerman

Note: FDA provided UCB Pharma with draft responses to questions via fax on December 2, 2005. The following minutes include those responses along with additional comments from the meeting discussions.

7 Page(s) Withheld

Trade Secret / Confidential

Draft Labeling

Deliberative Process





Food and Drug Administration  
Rockville, MD 20852

Our Reference: BB-IND 11197

DEC 29 2005

UCB Pharma, Inc.  
Attention: Deborah Hogerman  
Director, Regulatory Affairs  
755 Jefferson Road  
PO Box 31710  
Rochester, NY 14603

Dear Ms. Hogerman:

Please refer to your **Investigational New Drug Application (IND)** for "CDP-870 (Certolizumab)" and to the meeting held on December 5, 2005, between representatives of your firm and this agency. As requested in your letter of October 3, 2005, a copy of our memorandum of that meeting (or telephone conversation) is attached for your information.

Please refer to <http://www.fda.gov/cder/biologics/default.htm> for important information regarding therapeutic biological products, including the addresses for submissions. Effective Oct. 4, 2004, the new address for all submissions to this application is:

CDER Therapeutic Biological Products Document Room  
Center for Drug Evaluation and Research  
Food and Drug Administration  
12229 Wilkins Avenue  
Rockville, Maryland 20852

If you have any questions, please contact me at (301) 796-1007.

Sincerely yours,

Cristi L. Stark, M.S.  
Regulatory Project Manager  
Division of Gastroenterology Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

Enclosure: Meeting Summary





Our Reference: BB-IND 11197

OCT 26 2005

UCB Pharma, Inc.  
Attention: Deborah Hogerman  
Director, Regulatory Affairs  
755 Jefferson Road  
PO Box 31710  
Rochester, NY 14603

Dear Ms. Hogerman:

Please refer to your **Investigational New Drug Application (IND)** for "CDP-870 (Certolizumab)" and to the meeting held on September 27, 2005, between representatives of your firm and this agency. As requested in your letter of July 27, 2005, a copy of our memorandum of that meeting (or telephone conversation) is attached for your information.

Please refer to <http://www.fda.gov/cder/biologics/default.htm> for important information regarding therapeutic biological products, including the addresses for submissions. Effective Oct. 4, 2004, the new address for all submissions to this application is:

CDER Therapeutic Biological Products Document Room  
Center for Drug Evaluation and Research  
Food and Drug Administration  
12229 Wilkins Avenue  
Rockville, Maryland 20852

If you have any questions, please contact me at (301) 796-1007.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Cristi L. Stark".

Cristi L. Stark, M.S.  
Regulatory Project Manager  
Division of Gastroenterology Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

Enclosure: Meeting Summary

OTRR:DARP:CLStark:10.26.2005  
(N:\Stark\UCB Pharma\11197\preBLA clin and non clin Meeting summary letter.doc)

MEETING SUMMARY ENCLOSED (MS)

Division	Name/Signature	Date
DGP		10/26/05



DEPARTMENT OF HEALTH AND HUMAN SERVICES  
Public Health Service  
Food and Drug Administration  
Center for Biologics Evaluation and Research

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Memorandum

**Date:** OCT 26 2005  
**From:** *Cristi Stark, DGP, ODEIII*  
**To:** IND 11197  
**Subject:** Type B Meeting Summary

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**Meeting Date:** September 27, 2005

**Time:** 3:00-4:30pm

**Location:** White Oak Conference Room 1415

**Meeting Requestor/Sponsor:** UCB Pharma, Inc.

**Product:** CDP-870 (Certolizumab pegol)

**Proposed Use:** \_\_\_\_\_

**Type of meeting:** pre-BLA for clinical/non-clinical

**Meeting Purpose:** To discuss the content and format for a BLA for clinical/non-clinical

**FDA Attendees:** John Hyde, Li-Ching Liang, Brian Harvey, Jasti Choudary, Zei-Pao Huang, Stella Grosser, Brian Strongin, Cristi Stark

**Sponsor Attendees:** Patty Fritz, David Mason, Sue Stephens, Michael Canning, Reny Von Frencuell, Alison Innes, Juliet McColm, Deborah Hogerman

**Note:** *FDA provided UCB Pharma with draft responses to questions via fax on September 26, 2005. The following minutes include those responses along with additional comments from the meeting discussions.*

**Sponsor questions and FDA response:**

***Non-Clinical:***

1. *Are the non-clinical studies proposed for inclusion in the BLA, and outlined in the briefing package, adequate for the filing and review of this application?*

They are adequate.

2. *Do the reproductive toxicity studies using the parallel reagent adequately support a Pregnancy Category B in the product label?*

The studies need to be thoroughly reviewed and evaluated during the review cycle of the BLA. An answer will be provided at that time.

***Clinical:***

3. *Are the clinical studies planned for inclusion in the BLA, and outlined in the briefing package, adequate to support the proposed indication?*

The clinical studies planned for inclusion in the BLA appear to be adequate to support the submission of a BLA for your proposed indication.

4. *Is the size of the proposed safety database from the Crohn's program sufficient to support filing and review of the application?*

The size of the proposed safety database from the Crohn's program appears to be sufficient to support filing of the application.

5. *Does the division concur with this proposal for the submission of safety data from studies in rheumatoid arthritis?*

The plan to submit safety data from rheumatoid arthritis studies is acceptable.

6. *Does the division concur with the use of NCI Grade 3 and 4 toxicity criteria to classify markedly abnormal laboratory parameters for the studies in Crohn's disease and RA?*

The use of NCI grade 3 and 4 toxicity criteria is acceptable.

7. *Does the division concur with the plans for providing the 120-day safety update?*

Please clarify what you intend to submit as a 120-day safety update given your new BLA

submission timeline. The safety data in the initial submission need to be as complete and timely as possible.

*Discussion at meeting:* UCB presented information (please see handout) for their 120-day safety update.

- BLA submission = 1<sup>st</sup> quarter 2006
- Clinical cut-off = August 19
- Safety cut-off = October 21
- 120 Day Safety Update = Cut-off 1 month after original filing

FDA stated that this was acceptable; however, if the BLA submission is delayed, then the safety cut-off date must also shift accordingly.

8. *Does the division concur with these proposed analyses for antibody formation?*

These proposed analyses for antibody formation are acceptable.

*Statistics:*

9. *Does the division concur with the proposed sensitivity analysis methods to investigate the impact of region and country differences on response rates for both studies CDP870-031 and CDP870-032? Does the division concur with the method of investigating the impact of non-stratification by site; in particular, the impact of sites recruiting very small numbers of patients, large numbers of patients and sites with marked treatment imbalance?*

Yes.

*Discussion at Meeting:* FDA made a comment regarding gross imbalance. If there is an oddity or warning that arises, UCB may need to treat 4 to 1 as another sensitivity analysis.

10. *Does the division concur with the proposed strategy for pooling studies for the Summary of Clinical Safety? In particular, with reference to the handling of patients randomized to placebo after open-label induction with CDP870 in study CDP870-032?*

Yes.

*Discussion at Meeting:* FDA made a comment regarding gross imbalance. If there is an oddity or warning that arises, UCB may need to treat 4 to 1 as another sensitivity analysis.

**Regulatory:**

11. *Based on the justification provided above and in Section 6.7, would the division consider granting priority review of this application?*

This will be determined at the time of filing based upon the criteria in MAPP 6020.3, *Priority Review Policy*. However, the efficacy results appear modest and the increased compliance has not been documented.

*Discussion at meeting:* UCB acknowledged that they did not provide enough information to justify priority review. This will be included in the BLA.

12. *Is the proposed Table of Contents for the clinical/non-clinical sections of the CTD adequate for the filing and review of this application?*

Yes.

13. *Does the division concur with the proposal for submitting reports from studies in Crohn's disease?*

Please clarify your proposal.

*Discussion at meeting:* UCB presented additional information (please see handout). In the study reports all content will still be submitted; however, they will not be compliant with ICHE3 format. To help accommodate reviewers, an ICHE3 compliant table of contents will accompany each report.

FDA agreed.

14. *Does the division concur with the proposal for submitting reports from studies in RA?*

Please clarify your proposal.

15. *Does the division concur with the proposal for submitting reports from studies in healthy volunteers?*

Please clarify your proposal and explain why reports from studies in healthy volunteers will not be presented in the ICHE3 format. The format must meet the Agency's requirement.

*Discussion at meeting:* UCB stated that their intent was related to format rather than content. They are not planning to file separate ISS/ISE. Everything will be included in Module 5.

FDA agreed and instructed UCB to follow the FDA's guidelines for formatting as on the website. If there are any additional questions they can contact the project manager.

*16. The ISS/CSS and ISE/CSE will be prepared in accordance with FDA's guideline for the Format and Content of Clinical and Statistical Sections of Applications. The text will be incorporated into the Summary of Clinical Safety in Module 2.7.5, with supporting appendices in Module 5. The same format is proposed for the ISE. The text of the ISE will be incorporated into the Summary of Clinical Efficacy in Module 2.7.4, with supporting appendices in Module 5. Does the division concur with this approach?*

Safety data need to be complete.

*17. Is the plan for the submission of CRFs acceptable to the Division?*

Yes.

*18. Is the proposed content of the domain and patient profiles adequate for the review of this BLA?*

Yes.

*19. Is the proposed submission of the domain profiles and patient profiles in conjunction with the CRFs sufficient to meet the requirements?*

Yes.

*20. Are the analysis datasets and domain profiles submitted in electronic form as SAS transport files acceptable for the archival copy of the application? Patient profiles will be submitted as PDF.*

Safety and efficacy data should be submitted in SAS files.

*21. Are the plans concerning the electronic submission and the folder structure of this BLA acceptable to the division?*

Yes.

*22. A Risk Management Plan will be submitted to the BLA as per ICH E2E guidance. Can the division offer additional advice as to an acceptable Risk Management Plan?*

- If the BLA application includes RiskMAPs or pharmacovigilance plans and will be submitted in the Common Technical Document format, please submit as follows:

**RiskMAPs**

2.5.5 Overview of Safety with appropriate cross references to section 2.7.4 Summary of Clinical Safety and any other relevant sections of the Common Technical Document for the BLA application.

**Pharmacovigilance plans**

2.5.5 Overview of Safety, with any protocols for specific studies provided in 5.3.5.4 Other Clinical Study Reports or other sections as appropriate (e.g., module 4 if the study is a nonclinical study).

If the application is not being submitted as a Common Technical Document, include proposed RiskMAPs in the BLA Clinical Data Section (21 CFR 601.25(b)(3)) and clearly label and index them.

- For the most recent publicly available information on CDER's views on RiskMAPs, please refer to the following Guidance documents:

Premarketing Risk Assessment: <http://www.fda.gov/cder/guidance/6357fnl.htm>

Development and Use of Risk Minimization Action Plans:  
<http://www.fda.gov/cder/guidance/6358fnl.htm> >

Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment:  
<http://www.fda.gov/cder/guidance/6359OCC.htm>

- If there is any information on product medication errors from the premarketing clinical experience, Office of Drug Safety requests that this information be submitted with the BLA application.
- You are encouraged to submit the proprietary name and all associated labels and labeling for review as soon as available.

*Discussion at meeting:* UCB has submitted a proprietary name under the IND and will also include the proprietary name with all associated labels in the BLA.

23. *Is the division willing to review and comment on a completed Risk Management Plan before the BLA is filed in order to ensure it meets the requirements?*

No. A review of the proposed Risk Management Plan will be conducted with the BLA review since the specifics of the plan must depend on the data.

24. *Does the division concur with the proposal to defer pediatric studies until after approval of the application as outlined in Section 6.8?*

Please submit your plan for deferral under the BLA. This decision will be deferred until safety data from the adult studies are reviewed.

**Additional Comments/Recommendations:**

Please be sure to include the following items in your BLA submission:

- Relevant background information
- Important regulatory actions in other countries or important information contained in foreign labeling
- Less common adverse events
- Occurrence of adverse events over entire phase 2-3 database, grouped by incidence and body system: between 0.1% and 1%; > 1%
- Special assessments
- Comment on hepatotoxicity
- Overview of vital signs testing in the development program
- Analysis of vital signs focused on measures of central tendencies
- Analysis of vital signs focused on outliers or shifts from normal to abnormal
- Marked outliers for vital signs and dropouts for vital sign abnormalities
- Overview of ECG testing in the development program, including brief review of preclinical results
- Standard analyses and explorations of ECG data
- Overdose experience
- Demographics
- Tables of demographic information for phase 1 and phase 2-3 studies separately

Page 8, IND 11197 - preBLA clinical and non-clinical

- Explorations for dose dependency for adverse findings
- Explorations for time dependency for adverse findings
- Explorations for drug-demographic interactions
- Explorations for drug-disease interactions
- Drug-drug interactions
- Special populations
  - Discuss special dosing considerations based on demographics: race, gender, age for adults, age for pediatrics
  - Special dosing considerations based on coexisting states (e.g., hepatic, renal insufficiency)
  - Special dosing considerations in pregnancy or lactation



DEPARTMENT OF HEALTH AND HUMAN SERVICES  
Public Health Service  
Food and Drug Administration  
Center for Biologics Evaluation and Research

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Memorandum

**Date:** April 15, 2003  
**From:** Karen D. Jones, CBER/OTRR/DARP, HFM-588  
**To:** The pre-IND File  
Participants  
**Subject:** Pre-IND, End of Phase 2 Meeting

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**Meeting Date:** April 15, 2003      **Time:** 1:00-2:30 PM  
**Location:** WOC 1, Conference Room 2  
**Meeting Requestor/Sponsor:** G.D. Searle, LLC wholly owned subsidiary of  
Pharmacia Corporation  
**Product:** CDP-870 (PEGylated Humanized Fab' Fragment to TNF alpha  
**Indication:** Treatment of Crohn's Disease  
**Type of meeting:** Pre-IND, End-of Phase 2  
**Meeting Purpose:** To obtain feedback on the strategy to support an  
indication

**Discussion:**

Following introductions, representatives of G.D. Searle, LLC (Searle) conducted a slide presentation that provided background information on the goals of the CDP-870 clinical development program for treatment of Crohn's disease, an overview of Phase 2 efficacy data and the proposed Phase 3 clinical plan.

Protocols CDP-870-009 and CDP-870-010 are designed to confirm Phase 2 study results. Subjects in studies 009 and 010 are eligible to enter study CDP-870-011 (a re-induction

study). Searle is proposing to modify the 011 study design presented in the briefing package to collect CDAI for all subjects that includes durability of response and efficacy on re-treatment as well as to collect 12 months of safety and efficacy data on all patients. The plan is to submit 6 months post study entry efficacy data on all patients and follow that with an additional 52 weeks safety data at the time of submission of a BLA.

**FDA Comments/Questions and Searle Response:**

1. *Regarding study CDP-870-010, open induction therapy, responders will be eligible to enter study 011. CBER recommends that Searle discuss with FDA how to handle non-responders. Both open-label use or discontinuation are possible.*
  - Searle agrees to consult FDA on this issue.
  
2. *Phase 2 data show that placebo response rate increases over time. Has Searle done dose modeling to determine when the optimal timepoint is likely to occur?*
  - Searle: the literature experience shows that each four week follow-up increment is associated with a 25% rise in the placebo response.

3.

• / / / / /  
/ / /

**Sponsor Questions and FDA response:**

***Preclinical:***

5. *(Searle question 1) Does the Agency concur that the existing and planned non-clinical studies will be adequate to support a BLA submission in Crohn's disease?*
  - *CBER: CBER cannot address the adequacy of the clinical studies until the data are reviewed, however Searle's updated plan for nonclinical studies is consistent with*

that which CBER expects for this indication. The planned \_\_\_\_\_ assay measuring anti-CDP-870 antibody appears to be a reasonable approach. Prior to submission of the BLA, this assay should be validated according to ICH recommendations.

- Searle: We agree to validate the \_\_\_\_\_ assay

**Clinical:**

*Dr. Siegel noted that the proposals presented this date are somewhat different than those provided in the briefing document. Therefore, CBER may not be prepared to provide definitive answers to all questions proposed by Searle.*

6. *(Searle question 2) Does the Agency concur that data from dose ranging studies (-005 and -0 08) and pharmacokinetic modeling support subcutaneous dosing regimens based on 400 mg (0,2,4 compared to 0,4 weeks) for the proposed Phase 3 program induction therapy?*
  - *CBER: The two dose ranging studies, as presented at today's meeting, are an acceptable proposal.*
7. *(Searle question 3) The design of the Phase 3 induction studies (-009 and -0 10) will be based on demonstrating efficacy in patients with active Crohn's disease as evidenced by a C-reactive Protein  $\geq 10$  mg/L and Crohn's Disease Activity Index (CDAI) 22–45 abaseline. Does the Agency concur that the proportion of responders at Week 6 in this patient population, with response defined as a decrease of 100 points or more in the baseline CDAI score, is an acceptable primary endpoint?*
  - *CBER: The response definition proposed (a decrease of 100 points or more in baseline CDAI score) is acceptable. The week 6 timepoint will not be acceptable to support licensure of the Crohn's disease indication. CBER does not see why this biologic should only will work in a subset of Crohn's disease patients (those patients with  $> 10$  mg/mL CRP levels).*
    - *Searle: The signal seen in the Phase 2 studies is supported by the literature. In addition, patients with higher CRP levels have demonstrated more stable placebo response rates. Studies 009 and 010 are intended to confirm the hypothesis. At this time, Searle has not determined whether the therapy should be restricted to this subset of patients. The plan is to run the studies in parallel. Study 010 will be stratified on CRP level.*



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  /   Page(s) Withheld

  ✓   Trade Secret / Confidential

       Draft Labeling

       Deliberative Process

***Agreements:***

*Searle and CBER (Drs. Liang and Siegel) will hold informal teleconferences to reach agreement on a clinical development approach that may include two randomized, controlled studies in patients with high and low CRP, with dual endpoints and require safety data collection out to at least 6 months. The proposed indication will be discussed further at a future time.*

*The meeting concluded.*