Study Title:	A Double-Blind, Randomized, Parallel-Group, Active-Control Study to Compare the Efficacy and Safety of CHS-1420 Versus Humira® in Subjects With Chronic Plaque Psoriasis (**PsO**sim)
Protocol Number:	CHS-1420-02
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IND Number:	119540
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Development Phase:	Phase 3 Comparative Efficacy and Safety
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SIGNATURE PAGE

STUDY TITLE: A Double-Blind, Randomized, Parallel-Group, Active Control Study to Compare the Efficacy and Safety of CHS-1420 Versus Humira® in Subjects With Chronic Plaque Psoriasis (PsOsim)

COHERUS BIOSCIENCES, INC.

I, the undersigned, have read this protocol and agree that it contains all necessary information required to conduct the study.

Signature

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Chief Medical Officer
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Date: 17 July 2015

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SIGNATURE PAGE

STUDY TITLE: A Double-Blind, Randomized, Parallel-Group, Active Control Study to Compare the Efficacy and Safety of CHS-1420 Versus Humira® in Subjects With Chronic Plaque Psoriasis (**PsO**sim)

INVESTIGATOR

By signing below I agree that:

I have read this protocol and agree to conduct the study as outlined herein in accordance with International Conference on Harmonisation Good Clinical Practice, United States Food and Drug Administration regulations, Institutional Review Board regulations, and regional regulatory requirements.

_____ _____
Principal Investigator Signature Date

_____
Principal Investigator Name and Title (please print)

Institution Address

_____

_____

_____

SYNOPSIS

Study Title	A Double-Blind, Randomized, Parallel-Group, Active Control Study to Compare the Efficacy and Safety of CHS-1420 Versus Humira® in Subjects With Chronic Plaque Psoriasis (**PsO**sim)
Sponsor	Coherus BioSciences, Inc.
Study Objectives	**Primary Objective**: To compare the efficacy (measured by the Psoriasis Area and Severity Index [PASI]) and safety of CHS-1420- and Humira sourced from the United States (US) at 12 weeks in subjects with moderate to severe chronic plaque psoriasis (PsO) **Secondary Objectives**: To compare the safety of and durability of response to CHS-1420 and Humira over 24 weeks as well as efficacy/safety of switching from Humira to CHS-1420. To assess long term safety and efficacy of CHS-1420 during the open label extension over a further 24 weeks (Treatment Period 3).
Study Design	This is a 55-week (including follow-up), randomized, double-blind, active-control, parallel-group, multicenter, global study in subjects with active, moderate to severe, chronic PsO. The study will consist of 23 weeks of administration of blinded study drug over a 24 week period, divided into Treatment Period 1 and Treatment Period 2, followed by 23 weeks of administration of open-label CHS-1420 (Treatment Period 3) over a 24 week period and a Follow-up (or Early Termination [ET]) visit 8 weeks after the last dose. Subjects who meet inclusion/exclusion criteria will be stratified by body mass index (BMI) less than (<) 30 kg/m^2 or greater than or equal to (≥) 30 kg/m^2, and age <65 yrs or ≥ 65 yrs and randomized 1:1 to receive CHS-1420 or Humira in Treatment Period 1. Subjects assigned to CHS-1420 will continue to receive CHS-1420 in Treatment Period 2. Subjects assigned to Humira in Treatment Period 1 will be randomly assigned (1:1) to either continue with Humira in Treatment Period 2 or to switch to CHS-1420 in Treatment Period 2. In Treatment Period 1, subjects will receive 2 subcutaneous (SC) injections of study drug on Week 0/Day 0 followed by single SC injections of study drug every other week (QOW) from Week 1/Day 7 through Week 15/Day 105 For Treatment Period 2, subjects assigned to Humira in Treatment Period 1 will be switched to either CHS-1420 or continue with Humira, and will continue to receive single SC injections of study drug QOW from Week 17/Day 119 through Week 23/Day 161. All subjects that complete Treatment Periods 1 and 2 and achieve at least a 50% improvement in PASI score (PASI-50) at Week 24 will receive 23 weeks of open-label CHS-1420 in Treatment Period 3 QOW from Week 25/Day 185 through Week 47/Day 329. The first dose of study drug on Week 0/Day 0 will be self-administered or administered by a caregiver at the investigative site, and subjects will be monitored for adverse reactions and injection site reactions (ISRs) during the 2 hours after this dose. Subsequent doses will be self-administered or administered by a caregiver at home. Subjects/caregivers will be trained on

	injection technique before administering study drug and on an electronic diary (eDiary), to track compliance and subject-reported ISRs. Subjects/caregivers will contact the eDiary following each injection to document dosing on the day of injection and any possible ISRs after the injection. During site visits, subject questionnaires will be completed by subjects using an electronic diary in the clinic. The primary efficacy endpoint is the proportion of subjects achieving 75% improvement in Psoriasis Area and Severity Index (PASI-75) at week 12. The proportion of subjects achieving PASI-75 at 16 weeks will be a secondary efficacy endpoint. An independent, unblinded Data Monitoring Committee will review Treatment Period 1 study data to determine if there is adequate safety and efficacy to warrant continuing the study to completion. Subjects who discontinue study drug for any reason during Treatment Period 1 will be encouraged to return for all study visits through Week 16 if applicable and for the ET visit 56 days (8 weeks) after the last dose of study drug per the protocol Schedule of Procedures. Subjects who discontinue study drug for any reason during Treatment Period 2 or 3 will be encouraged to return for the Follow-up or ET visit 56 days (8 weeks) after the last dose of study drug (also per the protocol Schedule of Procedures). The Follow-up or ET visit will include evaluation of safety and immunogenicity (formation of anti-drug antibodies [ADAs]).
Study Centers	Approximately 160 active clinical sites worldwide will participate in this clinical trial.
Sample Size	The sample size determination is based on demonstrating a comparable PASI-75 at Week 12. Assuming that 70% of subjects in both the reference group, Humira, and the CHS-1420 group achieve PASI-75, with a statistical margin of 15% (absolute), approximately 250 subjects per treatment group will produce 90% power to establish equivalence at the 5% alpha level (2-sided) for the period 1 comparison. Subjects who lack follow-up data for the week 12 assessment will be considered non-responders in the primary analyses.
Study Population	Adult male and female subjects with moderate to severe chronic PsO.

Main Inclusion Criteria	Subjects must meet the following criteria to be enrolled in this study:
	1. Male or female adult at least 18 years of age;
	2. Diagnosis of chronic plaque-type psoriasis at least 6 months prior to Screening;
	3. Moderate to severe chronic plaque type psoriasis as defined at Screening by:
	    1. PASI score of greater than or equal to 12,
	    2. Physician's Static Global Assessment (PSGA) score greater than or equal to 3 (based on a scale of 0 to 5), and
	    3. Body surface area affected by chronic plaque-type psoriasis of greater than or equal to 10%;

	4. Considered a candidate by the Investigator to start anti-TNF therapy for PsO; 5. ~~Anti-TNF therapy naïve;~~ (Deleted due to duplication with Exclusion Criteria #2) ~~6. The patient has completed washout period prior to randomization for current or recent psoriasis therapies:~~ ~~a) 2 weeks for disallowed topical therapies (see Section 4.8)~~ ~~b) 4 weeks for ultraviolet B phototherapy~~ ~~c) 4 weeks for psoralen plus ultraviolet A phototherapy; phosphodiesterase type 4 (PDE4) inhibitors (eg., apremilast)~~ d) ~~12 weeks or a period equal to 5 times the half-life of the biologic (other than Anti-TNF) or investigational agent (whichever is longer) for other biologics or experimental therapies~~ Deleted due to duplication with Inclusion Criteria #8 and #9 and Exclusion Criteria #4 7. Able and willing to give written informed consent prior to performance of any study-related procedures 8. The patient has discontinued the use of any biologics or prohibited treatments as listed in Section 4.8 (e.g., systemic corticosteroids, ultraviolet (UV),laser treatments, apremilast [Otezla], other phosphodiesterase type 4 [PDE4] inhibitors and kinase inhibitors) within the 28 days prior to Randomization (Week 0/Day 0); 9. The patient has stopped the use of American Dermatology Association class 1 to 5 topical corticosteroids (Section 4.8) within 15 days prior to Randomization (Week 0/Day 0). 10. ~~Able and willing to give written informed consent prior to performance of any study-related procedures; and~~ (Deleted due to duplication with Inclusion Criteria #7) 11. Women who meet one of the following: a) Women of childbearing potential with a negative urine pregnancy test at Screening who agree to use 1 or more approved methods of birth control during the study. Approved methods of birth control are: hormonal contraception, intrauterine device, diaphragm plus spermicide, condom plus spermicide. Abstinence from heterosexual intercourse will be acceptable only if it is the preferred and usual lifestyle of the subject regardless of study participation; abstinence should be practiced for the duration of the study and until 5 months after taking the last dose of study drug; or b) Women who have been postmenopausal for at least 2 years (with amenorrhea for at least 1 year/12 consecutive months) or have had a hysterectomy, bilateral salpingo-oophorectomy, or tubal ligation prior to signing the informed consent form.
Main Exclusion Criteria	Those who meet any of the following criteria will be excluded from participation in this study: 1. Forms of psoriasis other than chronic PsO (e.g., pustular erythrodermic, guttate psoriasis); 2. Previous receipt of anti-TNF therapies (and biosimilars to anti-TNF-therapies) for any indication at any time, including infliximab, etanercept, adalimumab, golimumab, certolizumab pegol, pentoxifyllene. 3. Initiation of a drug that is known to cause or exacerbate psoriasis (including, but not limited to, beta-blockers, lithium, and anti-malarials),

	within the 6 months prior to Randomization (Week 0/Day 0); those who have been on a stable dose for at least 6 months prior to Randomization (Week 0/Day 0) without exacerbation of psoriasis may be enrolled and do not need to discontinue these medications; 4. Receipt of an investigational drug or investigational device within the 28 days prior to Randomization (Week 0/Day 0) or a period equal to 5 times the half-life of the investigational agent (whichever is longer); 5. History of alcohol or drug abuse within 2 years prior to Screening; 6. Diagnosis of rheumatic disease, autoimmune disease, connective tissue disease, or immune deficiency disease (e.g., primary Sjögren's syndrome, systemic lupus erythematosus, demyelinating diseases such as multiple sclerosis); Note: Psoriatic arthritis is allowed. 7. White blood cell count less than 3500 cells/mm^3, lymphocyte count less than 1000 cells/mm^3, platelet count less than or equal to 125,000 cells/mm^3, serum creatinine greater than or equal to 2 mg/dL (177 μmol/L), alanine transaminase or aspartate transaminase greater than or equal to 2 × the upper limit of normal (ULN), or hemoglobin less than or equal to 8.5 g/dL at Screening; 8. Presence or history of malignancy, except for successfully treated non-metastatic basal or squamous cell carcinoma of the skin and carcinoma in-situ of the cervix; 9. Presence of active or latent tuberculosis (TB) based on positive blood test (QuantiFERON®-TB Gold test) during Screening or known exposure to a patient with active TB. Note: QuantiFERON® - TB Gold test can be repeated once using a fresh sample in subjects with an indeterminate result or low positivity (defined as QuantiFERON TB Antigen minus Nil value = 0.35 - 2 IU/mL); if the repeat test result is negative, the subject may participate in the study; 10. History of positive test results for fungal or other infections (e.g., histoplasmosis, coccidiomycosis) required by regional guidelines within 3 months prior to Randomization (Week 0/Day 0); 11. Chest x-ray (CXR) obtained within 6 months before Screening suggestive of an active or latent TB or another active disease process; If a chest x-ray has not been obtained within the past 6 months one should be obtained during the Screening process; 12. Major systemic infections, including human immunodeficiency virus (HIV); 13. Unresolved Hepatitis B or Hepatitis C infection (defined as positive hepatitis B surface antigen [HBsAg], hepatitis B core antibody [HBcAb], or hepatitis C virus [HCV] RNA);

Exclusion Continued	14. Presence of any significant comorbid medical condition(s), including, but not limited to: a) Uncontrolled diabetes mellitus (Hemoglobin A1C [HgbA1c] greater than or equal to 8% within the 3 months prior to Screening or history of diabetic ketoacidosis or hypoglycemic reactions requiring hospitalization within the 12 months prior to Screening), b) Uncontrolled hypertension (systolic blood pressure greater than 160 mmHg and diastolic blood pressure greater than 100 mmHg) within the 3 months prior to Screening, c) Severe kidney disease requiring hemodialysis or peritoneal dialysis, d) Advanced liver disease, such as liver cirrhosis or severe non-alcoholic steatohepatitis (NASH) e) Severe congestive heart failure or history of ejection fraction less than or equal to 30%, f) Severe lung disease requiring home oxygen, g) Active unstable angina requiring daily treatment with nitrates or other medications; 15. Presence of any other major medical or psychiatric illness that in the opinion of the Investigator would put the subject at increased risk or affect the ability to participate in the study; 16. Known or suspected sensitivity or allergic reactions to latex or latex-containing products; or 17. Women who are pregnant or nursing. 18. Administration of a live vaccination within 4 weeks prior to Randomization (Week 0/Day 0), or a known need for live vaccination during the study and for 3 months after the last dose of study drug
Study Drug Dosage and Administration	Humira will be provided in Humira commercial pre-filled syringes, each containing 40 mg of adalimumab/0.8 mL. CHS-1420 will be provided in pre-filled syringes that match the Humira commercial pre-filled syringes, each containing 40 mg of CHS-1420/0.8 mL. Subjects will receive blinded study drug in pre-filled syringes. Each syringe will contain Humira or CHS-1420. The initial dose of CHS-1420 or Humira is 2 SC injections (2 pre-filled syringes) of study drug administered on the same day (Week 0/Day 0). A single SC injection (1 pre-filled syringe) of study drug will then be administered QOW from Week 1/Day 7 through Week 23/Day 161. At Week 24/Day 168, all subjects who have achieved at least a PASI-50 will be assigned CHS-1420 and continue with administration QOW until Week 47/Day 329.
Study Endpoints	**Efficacy Endpoints:** **Primary endpoint:** • 75% improvement in Psoriasis Area and Severity Index (PASI-75) at week 12 **Secondary efficacy endpoints:** • PASI-75 at Weeks 2, 4, 6, 8, 10, 16, 20, 24, 32, 40 and 48; • Percentage change from Baseline in PASI at Weeks 2, 4, 6, 8, 10, 12, 16, 20, 24, 32, 40 and 48; • 50% improvement in Psoriasis Area and Severity Index (PASI-50) at Weeks 2, 4, 6, 8, 10, 12, 16, 20, 24, 32, 40 and 48 • 90% improvement in Psoriasis Area and Severity Index (PASI-90) at Weeks 2, 4, 6, 8, 10, 12, 16, 20, 24, 32, 40 and 48;

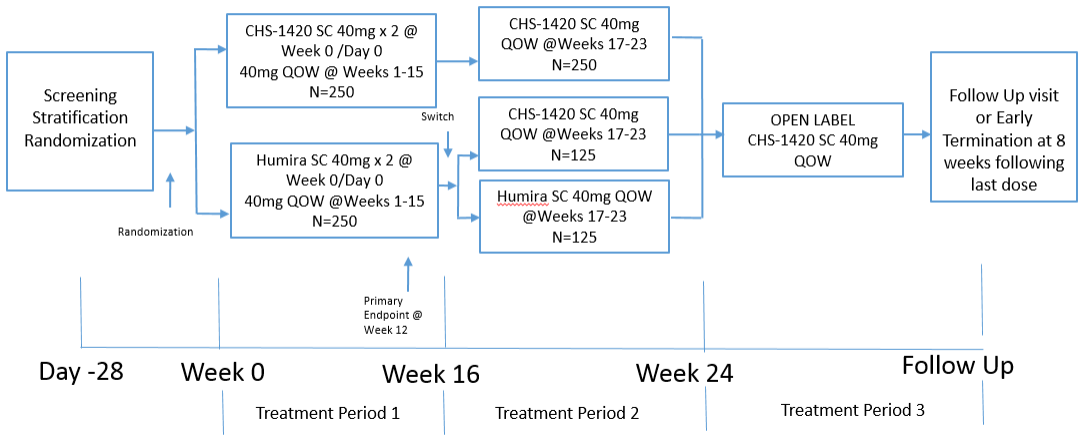
	• Changes in physician's static global assessment (PSGA) of disease activity on a scale from 0 to 5 from Baseline to Weeks 2, 4, 6, 8, 10, 12, 16, 20, 24, 32, 40, 48 and, as applicable, the Follow-up or ET visit; • Change in PSGA = 0 to 1, demonstrating clear or almost clear skin at Weeks 2, 4, 6, 8, 10, 12, 16, 20, 24, 32, 40, 48 and, as applicable, the Follow-up or ET visit; **Other efficacy endpoints:** • Changes in Subject's Global Assessment (SGA) of Psoriasis on a scale from 0 to 5 from Baseline to Weeks 2, 4, 6, 8, 10, 12, 16, 20, 24, 32, 40 and 48 and, as applicable, the Follow-up or ET visit; • Changes in Dermatology Life Quality Index from Baseline to Weeks 12 and 24; • Changes in EuroQol 5-Dimension Health Status Questionnaire from Baseline to Weeks 12 and 24; • Changes in Health Assessment Questionnaire–Disability Index from Baseline to Weeks 12, 16 24, 40 and 48 for subjects with self-reported PsA history only; and • Changes in highly sensitive C-reactive protein from Baseline to Weeks 12,16 24, 40 and 48 for subjects with self-reported PsA history only. **Safety:** Safety will be assessed in all Treatment Periods by: • Monitoring of treatment-emergent adverse events; • Evaluation of subject discontinuation and withdrawal information; • Assessment of ISRs; • Assessment of changes in safety laboratory parameters, including hematology, clinical chemistry • Assessment of changes in vital signs, physical examination and electrocardiogram findings. • Monitoring for conversion to positive TB with regular QuantiFERON-TB Gold test at Baseline and Week 24 or 56 days (8 weeks) after the last dose.

	Immunogenicity: Serum samples for ADAs will be collected prior to the first injections of study drug, at all visits during the treatment periods, and at follow-up 8 weeks after the last administration of study drug. Immunogenicity will be assessed using screening and confirmatory ADA assays. An assay to determine if ADAs are neutralizing may be used. **Retained samples:** Serum samples will be collected prior to the first injections of study drug, at all visits during the treatment periods, and at follow-up 8 weeks after the last administration of study drug. Retained serum may be used to determine serum concentrations or for other tests required to evaluate adverse events (AEs), loss of response, or compliance; to correlate with ADA assay results; or to meet any other regulatory requirement. No other biomarkers or genetic testing will be performed on these samples. Samples will be destroyed 2 years after the completion of the clinical study (final database lock).
Statistical Analysis	The analysis populations consist of the following: • The Randomized Population will include all randomized subjects. Subjects will be allocated to the treatment arm they are randomized to for a particular Treatment Period of analysis. • The Full Analysis Population (FAP): all randomized subjects who receive at least 1 dose of study drug. The FAP is the primary efficacy analysis population. Subjects will be allocated to the treatment arm they are randomized to for a particular Treatment Period of analysis. • The Safety Population: those subjects in the FAP, but subjects will be allocated to the treatment arm by period based upon actual treatment received. • The Per Protocol Population: those subjects in the FAP completing at least 12 weeks of treatment and follow-up with respect to the PASI and have no protocol violations that may affect the interpretation of the primary efficacy endpoint. These violations will be identified by the Sponsor prior to study unblinding. Subjects will be allocated to the treatment arm they are randomized to for a particular Treatment Period of analysis. • Open Label Extension Population: those subjects receiving at least 1 dose of open label treatment. The primary statistical analyses will be : • The difference between the percentages of subjects in the CHS-1420 and Humira groups achieving PASI-75 at Week 12 Equivalence will be based upon the 95% (2-sided) confidence interval for the difference in PASI-75 rates. If both the lower and upper bounds of the 95% confidence interval exclude ±15%, equivalence will be established. The difference between the mean percent change from Baseline in PASI between the CHS-1420 and Humira (US) arms at Week 12 will be assessed as a supporting secondary endpoint. Subjects who lack a Week 12 assessment will be considered non-responders in the primary analyses. As a sensitivity analysis, the last available score will be used.

	For confidence interval involving binary outcomes, the Cochran-Mantel-Haenszel weights will be used to combine the stratum-specific differences where the strata will be based upon the factors used to assign subjects to treatment for involving continuous outcomes, the stratum-specific differences will be combined using an analysis of variance approach with weights proportionate to the stratum sizes. Other secondary continuous variables will be summarized using descriptive statistics (N, mean, standard deviation, 95% confidence interval, median, range, minimum, and maximum, where appropriate). Discrete variables will be summarized using frequency counts and percentages. Starting with Treatment Period 2, data summaries for efficacy will be presented by the particular treatment sequence received in Treatment Periods 1 and 2: CHS-1420/CHS-1420, Humira/Humira and Humira/CHS-1420. Safety data for Treatment Period 1 will be presented by the treatment received. Safety data for the study period as a whole (ie, time spanning Treatment Periods 1 to 3) will be presented for those randomized and receiving the same treatment in Treatment Periods 1 and 2. Separate summaries will be presented for Treatment Period 2 based upon the particular treatment sequence received in Treatment Periods 1 and 2: CHS-1420/CHS-1420, Humira/Humira and Humira/CHS-1420. Safety data for the open-label extension (Treatment Period 3) will be summarized based primarily upon events first recorded (or worsened in severity) during the open-label extension.
Study Duration	Screening: up to 28 days Treatment Period 1: 16 weeks (Week 0 to Week 16) Treatment Period 2: 8 weeks (Week 17 to Week 24) Treatment Period 3: 24 weeks (Week 25 to Week 48) Follow-up: 8 weeks after last dose of study drug Subjects may be considered completers if the subjects complete 48 weeks of treatment and the Follow-up visit 8 weeks following the last dose in this trial (completes the study); Subjects may be withdrawn from study therapy for any of the following reasons: • The subject experiences a serious adverse event (SAE) or medically important AE (e.g., serious or opportunistic infection) that would preclude further treatment with study drug;

	• The subject develops a malignancy while on study; • The subject requires medical treatment excluded by the protocol or that could present a safety risk to the subject; • The subject is not willing to continue participation in the study (withdraws consent); • The subject experiences an increase in disease activity that requires additional or different therapy; • The subject develops active TB or a positive response to QuantiFERON-TB Gold test anytime during the study. If the QuantiFERON-TB Gold test yields low positive results (defined as QuantiFERON TB Antigen minus Nil value = 0.35 - 2 IU/mL), a repeat test should be done. If the repeat test is negative and there is no evidence of active TB, the patient can continue on the study, subject to the clinical judgment of the Investigator; • The female subject becomes pregnant; • The subject is lost to follow up; • The subject demonstrates a consistent lack of compliance with the provisions of the protocol; • In the opinion of the Investigator it is in the best interest of the subject to discontinue participation; or The subject can also be discontinued if the sponsor decides to terminate the study for any reason (e.g., an unexpected SAE not previously observed with adalimumab occurs).

Figure 1:Study Design



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LIST OF ABBREVIATIONS AND DEFINITION OF TERMS

ADA	Anti-drug antibody
AE	Adverse event
AS	Ankylosing spondylitis
BMI	Body Mass Index
BSA	Body surface area
CD	Crohn's disease
CFR	Code of Federal Regulations
CRA	Clinical Research Associate
CXR	Chest x-ray
DLQI	Dermatology Life Quality Index
DMARD	disease modifying anti-rheumatic drug
DMC	Data Monitoring Committee
EC	Ethics Committee
eCRF	Electronic Case Report Form
ECG	Electrocardiogram
eDiary	Electronic diary
ECL	electrochemiluminescent
EDC	Electronic data capture
EMA	European Medicines Agency
EQ-5D	EuroQol 5-Dimension Health Status Questionnaire
ET	Early Termination
EU	European Union
FAP	Full Analysis Population
FDA	United States Food and Drug Administration
GCP	Good Clinical Practice
HAQ-DI	Health Assessment Questionnaire–Disability Index
HBcAb	Hepatitis B core antibody
HBsAg	Hepatitis B surface antigen
HgbA1c	Hemoglobin A1C
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus

hs-CRP	highly sensitive C-reactive protein
ICF	Informed consent form
ICH	International Conference on Harmonisation
ID	Identification number
IMID	Immune-mediated inflammatory disease
IRB	Institutional Review Board
ISR	Injection site reaction
IxRS	Interactive Voice or Web-based Response System
JIA	Juvenile idiopathic arthritis
MedDRA	Medical Dictionary for Regulatory Activities
mTNFα	transmembrane tumor necrosis factor alpha
NAB	Neutralizing anti-drug antibody
NASH	Nonalcoholic steatohepatitis
NINR	National Institute of Nursing Research
NP	Nurse Practitioner
NSAID	Non-steroidal anti-inflammatory drug
p75	75 kilodalton protein
PASI	Psoriasis Area and Severity Index
PASI-50	50% improvement in Psoriasis Area and Severity Index
PASI-75	75% improvement in Psoriasis Area and Severity Index
PASI-90	90% improvement in Psoriasis Area and Severity Index
PDE4	Phosphodiesterase type 4
PK	Pharmacokinetic(s)
PsA	Psoriatic arthritis
PSGA	Physician's Static Global Assessment
PsO	Plaque psoriasis
PUVA	Psoralen plus ultraviolet A
QOW	Every other week
RA	Rheumatoid arthritis
SAE	Serious adverse event
SC	Subcutaneous(ly)
SGA	Subject's Global Assessment
SOP	Standard Operating Procedure

SUSAR	Suspected unexpected serious adverse reaction
TB	Tuberculosis
TEAE	Treatment-emergent adverse event
TNF	Tumor necrosis factor
TNFR	Tumor necrosis factor receptor
TNFα	tumor necrosis factor alpha
TNFβ	tumor necrosis factor beta
UC	Ulcerative colitis
ULN	Upper limit of normal
US	United States
UV	Ultraviolet
UVB	Ultraviolet B
WCT	Worldwide Clinical Trials
WHO-DD	World Health Organization Drug Dictionary

1 INTRODUCTION

1.1 Overview

Coherus is developing CHS-1420 drug product (CHS-1420) as a proposed biosimilar to Humira® (adalimumab) under a global development strategy for chronic plaque psoriasis (PsO) and other indications for which Humira is approved in various regulatory territories.

CHS-1420 is being developed initially as a proposed biosimilar to Humira (US). Appropriate bridging studies (analytical, non-clinical, and clinical) will be performed that will allow filing of CHS-1420 as a proposed biosimilar to Humira sourced from the European Union, (EU) (Humira [EU]).

1.2 Background

The purposes of this study are to compare the efficacy and safety of biosimilar adalimumab (CHS-1420) developed by Coherus BioSciences, Inc. and an approved reference drug, Humira in subjects with chronic PsO and to compare the durability of responses to CHS-1420 and Humira.

Psoriasis is a chronic, autoimmune disease that appears on the skin. It occurs when the immune system sends out faulty signals that speed up the growth cycle of skin cells. Psoriasis is not contagious. There are 5 types of psoriasis. The most common form, PsO, appears as raised, red patches covered with a silvery white buildup of dead skin cells. Psoriasis can occur on any part of the body and is associated with other serious health conditions, such as arthritis, inflammatory bowel disease, diabetes, heart disease, and depression. Psoriasis is the most common autoimmune disease in the US. As many as 7.5 million Americans have psoriasis and 125 million people worldwide suffer with psoriasis (National Psoriasis Foundation, 2014).

Up to 30% of people with psoriasis also develop psoriatic arthritis (PsA), which causes pain, stiffness, and swelling in and around the joints. Psoriatic arthritis can develop at any time, but it most commonly appears between the ages of 30 and 50. Genes, the immune system, and environmental factors are all believed to play a role in the onset of the disease. Early recognition, diagnosis, and treatment of PsA are critical to relieve pain and inflammation and help prevent progressive joint damage.

Tumor necrosis factor (TNF) is a naturally occurring cytokine that plays an important role in the inflammatory processes of immune-mediated inflammatory diseases (IMIDs) such as PsO, PsA, juvenile idiopathic arthritis (JIA), polyarticular JIA, enthesitis-related arthritis, axial spondyloarthritis, ankylosing spondylitis (AS), axial spondyloarthritis without radiographic evidence of AS, psoriasis, Crohn's disease (CD), ulcerative colitis (UC), and rheumatoid arthritis (RA). Elevated levels of TNF are found in involved tissues and fluids of subjects with PsO and other IMIDs (Kruege, Krane, Carter, & Gottlieb, 1990) (Brotas, Cunha, Lago, Machado, & Carneir, 2012) (Keystone & Ware, 2010). Two distinct tumor necrosis factor receptors (TNFRs), a 55 kilodalton protein and a 75 kilodalton protein (p75), exist naturally as monomeric molecules on cell surfaces and in soluble forms. Biological activity of TNF is dependent upon binding to either cell surface TNFR. Accumulating evidence suggests differential effects of p75 TNFR in the pathogenesis of inflammatory and autoimmune disorders (Bluml, Scheinecker, Smolen, & Redlich, 2012). In addition to soluble tumor necrosis factor alpha (TNFα), its precursor form, transmembrane tumor necrosis factor alpha (mTNFα), is involved in the inflammatory response (Horiuchi, Mitoma, Harashima, Tsukamoto, & Shimoda, 2010).

Adalimumab inhibits binding of TNFα, but not tumor necrosis factor beta (TNFβ), to cell surface tumor necrosis factor receptors TNFRs, rendering TNFα biologically inactive.

Humira was approved by the United States Food and Drug Administration (FDA) in 2002 for RA. Humira is indicated for reducing signs and symptoms, inducing major clinical response, inhibiting the progression of structural damage, and improving physical function in adult patients with moderate to severe active RA. Humira can be used alone or in combination with methotrexate or other non-biologic disease modifying anti-rheumatic drugs (DMARDs). Subsequently Humira has been approved for PsA, AS, JIA, PsO, CD, and UC (AbbVie US, 2014) as follows:

- PsA: Humira is indicated for reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with active PsA. Humira can be used alone or in combination with non-biologic DMARDs.
- AS: Humira is indicated for reducing signs and symptoms in adult patients with active AS.
- JIA: Humira is indicated for reducing signs and symptoms of moderately to severely active polyarticular JIA in pediatric patients 2 years of age and older. Humira can be used alone or in combination with methotrexate.

- PsO: Humira is indicated for the treatment of adult patients with moderate-to-severe chronic PsO who are candidates for systemic therapy or phototherapy, and when other systemic therapies are medically less appropriate. Humira should only be administered to patients who will be closely monitored and have regular Follow-up visits with a physician.
- CD: Humira is indicated for reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active CD who have had an inadequate response to conventional therapy. Humira is indicated for reducing signs and symptoms and inducing clinical remission in these patients if they have also lost response to or are intolerant to infliximab. Humira is also indicated for reducing signs and symptoms and inducing and maintaining clinical remission in patients 6 years of age and older with moderately to severely active Crohn's disease who have had an inadequate response to corticosteroids or immunomodulators such as azathioprine, 6-mercaptopurine, or methotrexate.
- UC: Humira is indicated for inducing and sustaining clinical remission in adult patients with moderately to severely active UC who have had an inadequate response to immunosuppressants such as corticosteroids, azathioprine, or 6-mercaptopurine. The effectiveness of Humira has not been established in patients who have lost response to or were intolerant to TNF blockers.

The recommended dosage of Humira for subjects with moderate to severe chronic PsO is 80 mg by subcutaneous (SC) injection followed by 40 mg by SC injection every other week (QOW). The most common adverse events (AEs) reported in clinical studies with adalimumab were injection site reactions (ISRs), infections, headache, and rash. Because the needle guards for both Humira and CHS-1420 contain latex, subjects with allergies to latex should not be enrolled in the study. Further details are provided in the prescribing information for Humira (Appendix A).

1.3 Development of CHS-1420

Unlike generic drugs, which are relatively simple chemical structures, biologic drugs are manufactured in cultured cells and vary lot to lot depending on the culture conditions. Because of these variations, biologic drugs cannot be considered "identical," but may be considered "biosimilar." Determination of biosimilarity is akin to determining the similarity of identical twins. Whereas identical twins are genetically identical, there may be minor differences in appearance, such as height or weight, which would allow them to be identified as unique and separate but biosimilar.

In order to be considered biosimilar, 2 biologics must meet the following criteria:

- Identical primary structures (i.e., amino acid sequence, and disulfide bonding)
- Highly similar post translational modifications (e.g., glycosylation)
- Highly similar 3-dimensional structures (e.g., α helix, β-sheet)
- Similar purity profiles
- Similar nonclinical in vitro pharmacology and in vivo pharmacokinetics (PK), toxicokinetics, and toxicity
- Similar responses in clinical trials including PK, safety, immunogenicity, and efficacy

See the Investigator's Brochure for more details.

2 STUDY OBJECTIVES

The primary objective of this study is to compare the efficacy (measured by the Psoriasis Area and Severity Index [PASI]) and safety of CHS-1420 and Humira at 12 weeks in subjects with moderate to severe chronic PsO. The secondary objectives are to compare the safety of and response to CHS-1420 over 24 weeks as well as efficacy/safety of switching from Humira to CHS-1420. Long term safety and efficacy of CHS-1420 during the open label extension over a further 24 weeks (Treatment Period 3) will be assessed.

3 INVESTIGATIONAL PLAN

3.1 Overall Study Design and Plan

This is a 48 week study with a follow up visit 8 weeks after the last dose, randomized, double-blind, active-control followed by open label safety, parallel group, multicenter, study in subjects with active, moderate to severe, chronic PsO. Approximately 500 subjects will be randomized at approximately 160 sites worldwide.

The study will consist of 23 weeks of administration of blinded study drug over a 24 week period, divided into Treatment Period 1 (16 weeks) and Treatment Period 2 (8 weeks), 23 weeks of open label CHS-1420 during 24 weeks of Treatment Period 3 and a Follow-up visit 56 days (8 weeks) after the last dose of study drug. Subjects who meet inclusion/exclusion criteria will be stratified by body mass index (BMI) < 30 kg/m^2 or ≥ 30 kg/m^2 and by age < 65 years or ≥ 65 years. Within these strata, subjects will be randomized to receive either CHS-1420 or Humira. Half of the subjects assigned to Humira will be assigned to receive CHS-1420 in Treatment Period 2 with the remainder continuing on Humira. For simplicity, the assignments for Treatment Period 1 and Treatment Period 2 will be made at the beginning of Treatment Period 1.

In Treatment Period 1, subjects will receive 2 subcutaneous (SC) injections of study drug on Week 0/Day 0 followed by single SC injections of study drug every other week (QOW) from Week 1/Day 7 through Week 15/Day 105.

For Treatment Period 2, subjects will: 1) continue on CHS-1420 or 2) Humira or 3) will be switched from Humira to CHS-1420 and they will continue to receive single SC injections of study drug QOW from Week 17/Day 119 through Week 23/Day 161.

For Treatment Period 3, all subjects that complete Treatment Periods 1 and 2 and achieve at least a 50% improvement in PASI score (PASI-50) at Week 24 will receive 23 weeks of open-label CHS-1420 in Treatment Period 3 QOW from Week 25/Day 185 through Week 47/Day 329.

The first dose of study drug on Week 0/Day 0 will be self-administered or administered by a caregiver at the investigative site, and subjects will be monitored for adverse reactions and ISRs during the 2 hours after this dose. Subsequent doses will be self-administered or administered by a caregiver at home. Subjects/caregivers will be trained on injection techniques and the electronic diary (eDiary) used to track compliance and subject-reported ISRs. Subjects/caregivers will contact the eDiary following each injection to document dosing on the day of injection and any possible ISRs after the injection.

The primary efficacy endpoint is the proportion of subjects achieving 75% improvement in Psoriasis Area and Severity Index (PASI-75) at Week 12. When an adequate amount of data are available for the primary endpoint, an independent, unblinded Data Monitoring Committee (DMC) will review the accumulating safety and efficacy to determine if the data are adequate to warrant continuing the study.

Subjects who discontinue study drug for any reason during Treatment Period 1 will be encouraged to return for all study visits through Week 16 and for the ET visit 56 days (8 weeks) after the last dose per the protocol Schedule of Procedures, and subjects who discontinue study drug for any reason during Treatment Period 2 or 3 will be encouraged to return for a Follow-up or ET visit 56 days (8 weeks) after the last dose of study drug (also per the protocol Schedule of Procedures). This Follow-up or ET visit will include evaluation of safety and immunogenicity (formation of anti-drug antibodies [ADAs]).

3.2 Rationale for Study Design/Dose Level

No clinical trials to evaluate the efficacy and safety of CHS-1420 in subjects with PsO have been performed to date. The design of this study is based on 2 clinical studies comparing adalimumab 80 mg ×1 followed by 40 mg QOW to placebo in subjects with moderate to severe psoriasis (Menter, et al., 2008), (Gordon, et al., 2006).

In a 52-week, randomized, double-blind, placebo-controlled, multicenter study, 1212 subjects with moderate or severe psoriasis were randomized 2:1 to receive either adalimumab or placebo at an initial dose of 80 mg followed by 40 mg QOW for the first 15 weeks (Menter, et al., 2008). Main exclusion criteria included exposure to anti-TNF therapy, other skin disease or infection that could interfere with evaluation, allergy to adalimumab or its constituents, current oral or injectable corticosteroid use, untreated tuberculosis (TB), poorly controlled medical conditions, history of neurologic symptoms suggestive of central nervous system demyelinating disease, and history of cancer or lymphoproliferative disease (other than successfully treated nonmelanoma skin cancer or localized carcinoma in situ of the cervix). Subjects achieving a PASI-75 response at Week 16 were eligible to continue in an open-label study and receive adalimumab 40 mg QOW for Weeks 17 through 31. Subjects who maintained a PASI-75 response at Week 33 were re-randomized to adalimumab or placebo QOW for an additional 19 weeks. The primary efficacy endpoints for this study were percentages of subjects achieving PASI-75 response at Week 16 relative to baseline and percentages of subjects losing adequate response after Week 33. At Week 16, 580/814 (71%) of adalimumab-treated versus 26/398 (7%) of placebo-treated subjects achieved at least PASI-75 scores. PASI-75 results at 12 weeks were also reported with 68% of subjects on Humira and 5% of subjects on placebo achieving PASI-75. The mean % change in PASI at 12 weeks for Humira was 76 compared to 15 for placebo. From Week 33 to Week 52, 5% of adalimumab-treated and 28% of placebo-treated subjects lost adequate responses.

In a 12-week, double-blind, placebo-controlled, multicenter study, 147 subjects with moderate to severe psoriasis were randomized to receive either an initial dose of 80 mg adalimumab followed by 40 mg adalimumab QOW, every week, or placebo (Gordon, et al., 2006). Subjects who completed the initial 12-week trial were eligible to continue in a 48-week extension trial. The primary efficacy analysis was the percentages of subjects achieving at least PASI-75 relative to baseline at Week 12 (for the initial trial) and at Week 24 (for the extension trial).

At 12 weeks, 53% of subjects receiving adalimumab QOW and 80% of subjects receiving adalimumab every week achieved PASI-75 compared to 4% of subjects receiving placebo (P<0.001).

Menter (Menter, et al., 2008) and Gordon (Gordon, et al., 2006) used the PASI-75 as the primary outcome measure with the PASI-75 evaluated at 16 weeks and 12 weeks, respectively. Both studies reported mean % change in PASI at Week 12: 76% Humira vs. 15% Placebo and 70% Humira vs. 14% placebo for Menter, 2008 and Gordon, 2006, respectively.

In this study (CHS-1420-02), eligible subjects are those who have a diagnosis of chronic PsO for at least 6 months that is moderate to severe as defined by a PASI score of greater than or equal to 12, Physician's Static Global Assessment (PSGA) score of greater than or equal to 3 (based on a scale of 0 to 5), and body surface area (BSA) affected by chronic PsO of greater than or equal to 10%. Subjects will be stratified by BMI < 30 kg/m2 or ≥ 30 kg/m2 and age < 65 years or ≥ 65 years (Menter, 2010).

The proposed dose level and dose regimen are consistent with that in the Humira (EU) Summary of Product Characteristics (AbbVie EU, 2014) and the Humira package insert (AbbVie US, 2014). In this study, 2 SC injections (2 pre-filled syringes, [80 mg]) of study drug will be administered on Week 0/Day 0. From Week 1/Day 7 through up to Week 23/Day 161, 1 SC injection (1 pre-filled syringe [40 mg]) of study drug will be administered QOW.

3.3 Selection of Study Population

3.3.1 Inclusion Criteria

Subjects must meet the following criteria to be enrolled in this study:

1. Male or female adult at least 18 years of age;
2. Diagnosis of chronic plaque-type psoriasis at least 6 months prior to Screening;
3. Moderate to severe chronic plaque type psoriasis as defined at Screening by:
   a) PASI score of greater than or equal to 12,
   b) PSGA score greater than or equal to 3 (based on a scale of 0 to 5), and
   c) BSA affected by chronic plaque-type psoriasis of greater than or equal to 10%;
4. Considered a candidate by the Investigator to start Anti-TNF therapy for PsO;
5. ~~Anti-TNF therapy naïve;~~ (Deleted due to duplication with Exclusion Criteria #2)
6. ~~The patient has completed washout period prior to randomization for current or recent psoriasis therapies:~~
   ~~a. 2 weeks for disallowed topical therapies (see Section 4.8)~~
   ~~b. 4 weeks for ultraviolet B phototherapy~~

~~c. 4 weeks for psoralen plus ultraviolet A phototherapy; phosphodiesterase type 4 (PDE4) inhibitors (eg., apremilast)~~
~~d. 12 weeks or a period equal to 5 times the half-life of the biologic (other than anti-TNF) or investigational agent (whichever is longer) for other biologics or experimental therapies~~

Deleted Due to duplication with Inclusion Criteria #8 and #9 and Exclusion Criteria #4.

7. Able and willing to give written informed consent prior to performance of any study-related procedures; and
8. The patient has discontinued the use of any biologics or prohibited treatments as listed in Section 4.8 (e.g., systemic corticosteroids, ultraviolet (UV),laser treatments, apremilast [Otezla], other phosphodiesterase type 4 [PDE4] inhibitors and kinase inhibitors) within the 28 days prior to Randomization (Week 0/Day 0);
9. The patient hasstopped the use of American Dermatology Association class 1 to 5 topical corticosteroids (Section 4.8) within 15 days prior to Randomization (Week 0/Day 0).
10. ~~Able and willing to give written informed consent prior to performance of any study-related procedures; and~~ (Deleted due to duplication with Inclusion Criteria #7)
11. Women who meet one of the following:
    a) Women of childbearing potential with a negative urine pregnancy test at Screening who agree to use 1 or more approved methods of birth control during the study. Approved methods of birth control are: hormonal contraception, intrauterine device, diaphragm plus spermicide, condom plus spermicide. Abstinence from heterosexual intercourse will be acceptable only if it is the preferred and usual lifestyle of the subject regardless of study participation; abstinence should be practiced for the duration of the study and until 5 months after taking the last dose of study drug; or
    b) Women who have been postmenopausal for at least 2 years (with amenorrhea for at least 1 year/12 consecutive months) or have had a hysterectomy, bilateral salpingo-oophorectomy, or tubal ligation prior to signing the informed consent form (ICF).

3.3.2 Exclusion Criteria

Those who meet any of the following criteria will be excluded from participation in the study:

1. Forms of psoriasis other than chronic PsO (e.g., pustular erythrodermic, guttate psoriasis);

2. Previous receipt of anti-TNF therapies (and biosimilars to anti-TNF-therapies) for any indication at any time, including infliximab,etanercept, adalimumab, golimumab , certolizumab pegol , pentoxifyllene;
3. Initiation of a drug that is known to cause or exacerbate psoriasis (including, but not limited to, beta-blockers, lithium, and anti-malarials), within the 6 months prior to Randomization (Week 0/Day 0); those who have been on a stable dose for at least 6 months prior to Randomization (Week 0/Day 0) without exacerbation of psoriasis may be enrolled and do not need to discontinue these medications;
4. Receipt of an investigational drug or investigational device within the 28 days prior to Randomization (Week 0/Day 0) or a period equal to 5 times the half-life of the investigational agent (whichever is longer);
5. History of alcohol or drug abuse within 2 years prior to Screening;
6. Diagnosis of rheumatic disease, autoimmune disease, connective tissue disease, or immune deficiency disease (e.g., primary Sjögren's syndrome, systemic lupus erythematosus, demyelinating diseases such as multiple sclerosis); Note: Psoriatic Arthritis is allowed.
7. White blood cell count less than 3500 cells/mm^3, lymphocyte count less than 1000 cells/mm^3, platelet count less than or equal to125,000 cells/mm^3, serum creatinine greater than or equal to 2 mg/dL (177 µmol/L), alanine transaminase or aspartate transaminase greater than or equal to 2 × the upper limit of normal (ULN), or hemoglobin less than or equal to 8.5 g/dL at Screening;
8. Presence or history of malignancy, except for successfully treated non-metastatic basal or squamous cell carcinoma of the skin and carcinoma in situ of the cervix;
9. Presence of active or latent tuberculosis (TB) based on positive blood test (QuantiFERON®-TB Gold test) during Screening or known exposure to a patient with active TB. Note: QuantiFERON® - TB Gold test can be repeated once using a fresh sample in subjects with an indeterminate result or low positivity defined as Quantiferon TB Antigen minus Nil value = 0.35 - 2 IU/mL; if the repeat test result is negative, the subject may participate in the study;
10. History of positive test results for fungal or other infections (e.g., histoplasmosis, coccidiomycosis) required by regional guidelines within 3 months prior to Randomization (Week 0/Day 0);
11. Chest x-ray (CXR) obtained within 6 months before Screening suggestive of an active or latent TB or another active disease process; If a chest x-ray has not been obtained within the past 6 months one should be obtained during the Screening process;
12. Major systemic infections, including human immunodeficiency virus (HIV);

13. Unresolved Hepatitis B or Hepatitis C infection (defined as positive hepatitis B surface antigen [HBsAg], hepatitis B core antibody [HBcAb], or hepatitis C virus [HCV] RNA);
14. Presence of any significant comorbid medical condition(s), including, but not limited to:
    a) Uncontrolled diabetes mellitus (Hemoglobin A1C [HgbA1c] greater than or equal to 8% within the 3 months prior to Screening or history of diabetic ketoacidosis or hypoglycemic reactions requiring hospitalization within the 12 months prior to Screening),
    b) Uncontrolled hypertension (systolic blood pressure greater than 160 mmHg and diastolic blood pressure greater than 100 mmHg) (Mancia, et al., 2013) within the 3 months prior to Screening,
    c) Severe kidney disease requiring hemodialysis or peritoneal dialysis,
    d) Advanced liver disease, such as liver cirrhosis or severe non-alcoholic steatohepatitis (NASH)
    e) Severe congestive heart failure or history of ejection fraction less than or equal to 30%,
    f) Severe lung disease requiring home oxygen,
    g) Active unstable angina requiring daily treatment with nitrates or other medications;
15. Presence of any other major medical or psychiatric illness that in the opinion of the Investigator would put the subject at increased risk or affect the ability to participate in the study;
16. Known or suspected sensitivity or allergic reactions to latex or latex containing products; or
17. Women who are pregnant or nursing.
18. Administration of a live vaccination within 4 weeks prior to Randomization (Week 0/Day 0), or a known need for live vaccination during the study and for 3 months after the last dose of study drug

3.3.3 Completed Subjects

Subjects may be considered completers if the subjects complete 48 weeks of treatment and the Follow-up visit 8 weeks following the last dose in this trial (completes the study).

3.3.4 Removal of Subjects from Therapy

Subjects will be advised that they are free to withdraw from the study at any time for any reason; however, subjects who discontinue study drug for any reason prior to the end of Treatment Period 1 will be encouraged to return for all study visits through Week 16 and for an ET visit 56 days (8 weeks) after the last dose of study

drug per the protocol Schedule of Procedures (if applicable), and subjects who discontinue study drug for any reason during Treatment Period 2 or 3 will be encouraged to return for the Follow-up or ET visit 56 days (8 weeks) after the last dose of study drug (also per the protocol Schedule of Procedures). This Follow-up or ET visit will include evaluation of safety and immunogenicity (formation of ADAs).

Subjects may be withdrawn from study therapy for any of the following reasons:

- The subject experiences a serious adverse event (SAE) or medically important AE (e.g., serious or opportunistic infection) that would preclude further treatment with study drug;
- The subject develops a malignancy while on study;
- The subject requires medical treatment excluded by the protocol or that could present a safety risk to the subject;
- The subject is not willing to continue participation in the study (withdraws consent);
- The subject experiences an increase in disease activity that requires additional or different therapy;
- The subject develops active TB or a positive response to QuantiFERON-TB Gold test anytime during the study. If the QuantiFERON-TB Gold test yields low positive results (defined as QuantiFERON TB Antigen minus Nil value = 0.35 - 2 IU/mL), a repeat test should be done. If the repeat test is negative, the patient can continue on the study, subject to the clinical judgment of the Investigator);
- The female subject becomes pregnant;
- The subject is lost to follow up;
- The subject demonstrates a consistent lack of compliance with the provisions of the protocol;
- In the opinion of the Investigator it is in the best interest of the subject to discontinue participation; or

The subject can also be discontinued if the sponsor decides to terminate the study for any reason (e.g., an unexpected SAE not previously observed with adalimumab occurs).

4 TREATMENTS

4.1 Treatments Administered

2 SC injections (2 pre-filled syringes, [80 mg]) of study drug will be administered on Week 0/Day 0. From Week 1/Day 7 through up to Week 47/Day 329, 1 SC injection (1 pre-filled syringe [40 mg]) of study drug will be administered QOW.

4.2 Identity of Investigational Product

The following will be supplied by the Sponsor:

- Humira sourced from the US in commercial pre-filled syringes, each containing 40 mg of adalimumab/0.8 mL.
- CHS-1420 in pre-filled syringes that match the Humira commercial pre-filled syringes, each containing 40 mg of CHS-1420/0.8 mL.

Both the CHS-1420 and Humira syringes have needle covers that contain latex. Thus, study drug syringes should not be handled by anyone with a known sensitivity or allergy to latex; this may include caregivers and study staff.

Study drug should be refrigerated between 2° and 8°C (36° and 46°F) in the carton provided to protect it from exposure to light. Subjects/caregivers should transport cartons/syringes to and from the clinic in insulated carriers with cold packs and refrigerate the syringes/cartons as soon as possible.

4.2.1 Labeling

Each carton and syringe will be labeled according to Title 21 of the FDA Code of Federal Regulations (CFR) and/or country specific requirements.

4.3 Method of Assigning Subjects to Treatment Groups

Once the subject has signed the ICF at Screening, site personnel will assign a subject identification number (ID). The subject ID will include the site number (3 digits), and 3 digit subject number, assigned sequentially starting with 001.This number will be utilized to identify the subject throughout the study period. Once the subject ID has been assigned, the site will contact the Interactive Voice Response System/Interactive Web-based Response System (IXRS) to register the subject ID. Dropouts (subjects who discontinue study treatment early, and subjects who are randomized but not treated) will not be replaced. No individual is allowed to re-enter the study if previously randomized and dosed.

Subjects will be assigned to study drug in accordance with the randomization schedule generated using permuted block randomization by an independent statistician.

Approximately 500 subjects will be randomly assigned in a 1:1 ratio (approximately 250/arm) to receive 1 of the following treatments in Treatment Period 1:

- 2 SC injections (2 pre-filled syringes, [80 mg]) of Humira on Week 0/Day 0 and 1 SC injection (1 pre-filled syringe [40 mg]) of Humira QOW from Week 1/Day 7 through up to Week 15/Day 105.
- 2 SC injections (2 pre-filled syringes, [80 mg]) of CHS-1420 on Week 0/Day 0 and 1 SC injection (1 pre-filled syringe [40 mg]) of CHS-1420 QOW from Week 1/Day 7 through up to Week 15/Day 105.

Subject randomization will be stratified by body mass index (BMI) (less than (<) 30 kg/m2 or greater than or equal to (≥) 30 kg/m2), age (<65 yrs or ≥ 65 yrs) and region.

At the end of Treatment Period 1 (Week 16), subjects taking Humira will either begin dosing with CHS-1420 or continue with Humira during Treatment Period 2. A single randomization will be used to determine treatment in Treatment Periods 1 and 2. In effect, a 2:1:1 randomization will be used where for each 2 subjects randomized to receive CHS-1420 an additional 2 will be assigned to receive Humira in Treatment Period 1. For the subjects assigned to Humira in Treatment Period 1, 1/2 of these will be randomly assigned to continue with Humira for Treatment Period 2 and 1/2 will be assigned to switch to CHS-1420 for Treatment Period 2.

At the end of Treatment Period 2 (Week 24), all subjects that achieve at least a PASI-50 score will be assigned CHS-1420 for Treatment Period 3 and continue QOW administration from Week 25/Day 175 through Week 47/Day 329.

4.4 Selection of Doses in the Study

The recommended dosage of Humira for subjects with moderate to severe chronic PsO is an 80 mg initial SC dose followed by 40 mg SC QOW starting 1 week after the initial dose (AbbVie US, 2014). In this study, CHS-1420 or Humira will be administered per the approved dosing regimen for moderate to severe chronic PsO.

4.5 Selection and Timing of Dosing for Each Subject

Study drug will consist of Humira or CHS-1420. Each kit provided to the subjects will contain 4 syringes each.

In Treatment Period 1, subjects will receive 2 subcutaneous (SC) injections of CHS-1420 or Humira on Week 0/Day 0 followed by of single SC injections of study drug every other week (QOW) from Week 1/Day 7 through Week 15/Day 105.

For Treatment Period 2, subjects that were taking Humira will either be switched to CHS-1420 at Week 16 or continue taking Humira, and will continue to receive single SC injections of study drug QOW from Week 15/Day 105 through Week 23/Day 161.

At the end of Treatment Period 2 (Week 24), all subjects who achieve at least a PASI-50 will be assigned CHS-1420 for Treatment Period 3 and continue QOW administration from Week 25/Day 175 through Week 47/Day 329.

Subjects should be encouraged not to miss study drug doses. Subjects who miss a dose of study drug, for whatever reason, should receive that dose of study drug as soon as it is realized that the dose was missed.

Subjects/caregivers should be instructed to inject study drug at approximately the same time and same day QOW. Injection sites should be rotated between abdomen and thighs.

4.6 Blinding

This is a double-blind study during Treatment Period 1 and 2. Blinding of the study will be achieved by the following measures:

- The Humira and CHS-1420 syringes will be matched in appearance.

- Designated study staff will be provided with instructions regarding how to unblind an individual subject treatment assignment; individual subject treatment assignments may be unblinded only in the case of an SAE or AE that requires knowledge of the study drug received by the subject in order to provide appropriate treatment or management of the SAE or AE or if required for regulatory reporting (Section 7.1.7). Whenever possible, the Sponsor will be consulted in the decision to unblind a subject; otherwise, the Sponsor will be notified as soon as possible in the event that unblinding of an individual subject's treatment assignment has occurred prior to study completion. Every effort is to be made to limit study site personnel unblinding to only those individuals providing direct care to that subject. Any intentional or unintentional breaking of the blind is to be reported immediately to the Sponsor.
- An independent, unblinded data monitoring committee (DMC) (Section 9) will review safety and efficacy data.

4.7 Study Drug Accountability and Retention

The study site will be supplied with a sufficient quantity of study drug to treat randomized subjects. Blinded study drug will be shipped under appropriate storage conditions to site personnel according to the regulations of the study country. Each delivery must be acknowledged by the addressee by confirming receipt of the study drug shipment in IxRS. Study drug cannot be assigned to a subject until the site confirms receipt in the IxRS. Using the IxRS, site personnel will dispense assigned study drug cartons to each subject.

A dispensing log will be kept by site personnel who will record the dates and quantity of the study drug dispensed to each subject. All unused syringes will be accounted for during the study using the subject's eDiary entries and the numbers of provided and returned unused syringes.

The subject/caregiver will be instructed to place used syringes into the sharps container provided and return the sharps container to the clinic once it is full. A new sharps container will then be provided to the subject/caregiver. Subjects/caregivers will also be provided with cool packs should they need to bring unused study drug to the clinic for any reason (e.g., further training with self-administration of study drug or issues with study drug). The study drug kit with any unused pre-filled syringes can be used for the next dose(s) of study drug and a new study drug kit with sufficient pre-filled syringes for dosing through the next study visit will be provided to the subject.

Once the site's study monitor has reviewed and confirmed study drug accountability, used and unused syringes may be destroyed on site, per each Institution's Standard Operating Procedure (SOP) or policy. The Sponsor may also request that the site return any unused syringes to the Sponsor or its designee once the site's monitor has reviewed and confirmed accountability.

4.8 Prior and Concomitant Medications

Concomitant medications (both prescription and non-prescription [including over the counter medicine, vitamins, supplements, and herbal supplements]), taken within 6 months before the Screening visit will be recorded in the Screening source documents and entered into the Electronic Case Report Form (eCRF). Doses of concomitant medications should remain stable, if possible, during the study. All concomitant medications taken throughout the course of the study, including any medications required to treat AEs or concomitant illnesses and any changes in concurrent medications, will also be recorded in study files and entered into the eCRF.

Allowed Medications

Low- to mid-potency (American Dermatology Association class 6 to 7) topical corticosteroids on scalp, face, axillae, groin, and genitalia are allowed except within 24 hours prior to PASI assessment at Screening and study visits.

Mild/bland moisturizers/lubricants are allowed at any time except within 24 hours prior to PASI assessment at Screening and study visits.

Single non-steroidal anti-inflammatory drug (NSAID) use is not prohibited in this protocol; however, the dose should not exceed the maximum dose recommended for that NSAID.

Insulin and hormone replacement therapy.

All medications required to adequately treat AEs or concurrent medical conditions are at the discretion of the Investigator.

Prohibited Medications

The following concomitant medications are prohibited during the study (and/or during the indicated time periods before the study):

- All TNF-inhibitor biologics (other than study drug, insulin and hormone replacement therapy) and biosimilars to TNF-inhibitors, including but not limited to: certolizumab pegol, infliximab, golimumab and etanercept.
- All biologics for PsO or indications other than PsO (including, but not limited to, tocilizumab, anakinra, abatacept, rituximab, and ustekinumab) during the study;
- Any kinase inhibitor for any reason (e.g., tofacitinib citrate) during the study;
- Any PDE4 inhibitor (e.g., apremilast [Otezla]) during the study and within 28 days prior to Randomization (Week 0/Day 0);
- Systemic psoriasis treatments such as oral retinoids, methotrexate, cyclosporine, vitamin A or D analog preparations, dithranole, psoralen plus ultraviolet A (PUVA),ultraviolet B (UVB) phototherapy and laser therapy during the study and within 28 days prior to Randomization (Week 0/Day 0);
- Systemic corticosteroids during the study and within 28 days prior to Randomization (Week 0/Day 0);
- American Dermatology Association class 1 to 5 topical corticosteroids during the study and within 15 days prior to Randomization (Week 0/Day 0);
- Drugs that may cause new onset or exacerbation of psoriasis (including, but not limited to, beta-blockers, lithium, and anti-malarials) within 6 months prior to Randomization (Week 0/Day 0) and during the study unless the subject has been on a stable dose for at least 6 months prior to Randomization (Week 0/Day 0) without exacerbation of psoriasis, and
- Live vaccines 4 weeks prior to Randomization, during the study and for 3 months after the last dose of study drug.

4.9 Treatment Compliance

Study drug will be dispensed in single-use pre-filled syringes. Subjects/caregivers will be instructed how to transport and store the study drug, to place used study drug syringes in the provided sharps containers, and to return all used study drug syringes when the sharps containers are full. If necessary, subjects/caregivers should transport any unused study drug syringes using the provided cold packs and insulated cooler.

Subjects/caregivers will be trained to utilize an eDiary to collect information about the bi-weekly injections and any possible ISRs. The study staff will help the subject/caregiver register into the eDiary system at the time of the first dosing visit.

Study staff and subjects will be notified if the subject/caregiver doesn't enter information into the eDiary system within 24 hours of the expected date/time of a dose. At each visit study staff will review the eDiary entries with the subject/caregiver and provide retraining as necessary.

Study drug compliance per protocol in this study will be assessed by the Investigator and study staff based on study drug usage recorded by the subject/caregiver in the eDiary. For subjects for whom there have been compliance issues (less than 90% or greater than 110%), subjects/caregivers will be re-educated by the Investigator or study staff on the importance of administering study drug per protocol.

5 MEASUREMENTS AND EVALUATIONS

5.1 Schedule of Procedures

The schedules of procedures performed at each clinic visit are presented in Table 1-3.

Table 1: Schedule of Procedures Screening through Week 16

		Treatment Period 1					
	Screening [a]	Baseline/ Randomi-zation/ Dosing [b]					
Day	**-28 to 0**	**0**	**Day 14**	**28, 56**	**42, 70**	**84**	**112**
Week	**-4 to 0**	**0**	**2**	**4, 8**	**6, 10**	**12**	**16**
Window			**± 1 day**	**± 3 days**	**± 3 days**	**± 3 days**	**± 3 days**
Informed consent	X						
Medical/surgical history and review CXR [c]	X						
Physical examination [d]	X	X	X	X	X	X	X
Injection site assessment [e]		X	X	X	X	X	X
Height [f] and weight	X						
BSA affected by chronic PsO	X						
Vital signs [g]	X	X	X	X	X	X	X
Prior/concomitant medications	X	X	X	X	X	X	X
12-lead ECG	X	X[h]					X
hs-CRP for subjects with PsA (only)		X				X	X
Hematology	X	X[h]		X		X	X
Chemistry	X	X[h]		X		X	X
Urinalysis[j]	X	X[h]		X		X	X
Viral screening (HBsAg, HBcAb, HCV, HIV)[k]	X						
QuantiFERON®-TB Gold[l]	X						
Serum sample for ADA testing		X	X	X		X	X
Serum sample (retention sample)[m]		X	X	X		X	X
Urine pregnancy test[n]	X	X	X	X		X	X
PASI assessment[o]	X	X	X	X	X	X	X
PSGA[p]	X	X	X	X	X	X	X
SGA of Psoriasis[p]	X	X	X	X	X	X	X
DLQI		X				X	
EQ-5D		X				X	
HAQ-DI for subjects with PsA (only)		X				X	X
Assess AEs		X	X	X	X	X	X
eDiary review and compliance evaluation			X	X	X	X	X

Table 1 (Continued):Schedule of Procedures Screening Through Week 16

		Treatment Period 1					
	Screening [a]	Baseline/ Randomi-zation/ Dosing [b]					
Day	**-28 to 0**	**0**	**Day 14**	**28, 56**	**42, 70**	**84**	**112**
Week	**-4 to 0**	**0**	**2**	**4, 8**	**6, 10**	**12**	**16**
Window			**± 1 day**	**± 3 days**	**± 3 days**	**± 3 days**	**± 3 days**
Contact IxRS	X	X		X (4 only)		X	X
Dispense study drug and/or collect unused study drug and/or Perform drug accountability [q]		X		X (4 only)		X	X
Perform injection training		X					
Perform eDiary registration and training		X					
Administer study drug [r]		X					

Table 2: Schedule of Procedures Week 17 through Week 24

	Treatment Period 2	
Day	**140**	**168**
Week	**20**	**24**
Window	**±3 days**	**±3 days**
Physical examination[d]	X	X
Injection site assessment[e]	X	X
Weight		X
Vital signs[g]	X	X
Prior/concomitant medications	X	X
12-lead ECG		X
hs-CRP for subjects with PsA (only)		X
Hematology	X	X
Chemistry	X	X
Urinalysis[j]	X	X
QuantiFERON®-TB Gold[l]		X
Serum sample for ADA testing	X	X
Serum sample (retention sample)[m]	X	X
Urine pregnancy test[n]	X	X
PASI assessment°	X	X
PSGA[p]	X	X
SGA of Psoriasis[p]	X	X
DLQI		X
EQ-5D		X
HAQ-DI for subjects with PsA (only)		X
Assess AEs	X	X
eDiary review and/or compliance evaluation	X	X
Contact IxRS		X
Dispense study drug and/or collect unused study drug and/or Perform drug accountability [q]		X

Table 3: Schedule of Procedures Week 25 through Week 48 and Follow-up or Early Termination Visits

	Treatment Period 3			**Follow-up (or ET Visit)**
Day	**224**	**280**	**336**	**392 (or 56 Days Post Last dose)**
Week	**32**	**40**	**48**	**55 (8 Weeks post last dose)**
Window	**±1 week**	**±1week**	**+/- 1 week**	**±1 week**
Physical examination[d]	X	X	X	X
Injection site assessment[e]	X	X	X	X
Weight	X	X	X	X[i]
Vital signs[g]	X	X	X	X
Prior/concomitant medications	X	X	X	X
12-lead ECG		X	X	X[i]
hs-CRP for subjects with PsA (only)		X	X	X[s]
Hematology	X	X	X	X[i]
Chemistry	X	X	X	X[i]
Urinalysis[j]	X	X	X	X[i]
QuantiFERON®-TB Gold[l]				X
Serum sample for ADA testing	X	X	X	X
Serum sample (retention sample)[m]	X	X	X	X
Urine pregnancy test[n]	X	X	X	X
PASI assessment°	X	X	X	X[s]
PSGA[p]	X	X	X	X[s]
SGA of Psoriasis[p]	X	X	X	X[s]
DLQI				X[s]
EQ-5D				X[s]
HAQ-DI for subjects with PsA (only)		X	X	X[s]
Assess AEs	X	X	X	X
eDiary review and/or compliance evaluation	X	X	X	X
Contact IxRS	X	X		X
Dispense study drug and/or collect unused study drug and/or Perform drug accountability [q]	X	X	X	X

FOOTNOTES TO TABLES 1-3

a All Screening assessments should be completed prior to randomization.
b The first dosing of study drug should occur at the Baseline/Randomization Visit (Week 0/Day 0).
c Obtain a medical/surgical history to include PsA, allergies (including drug, latex, food, and insect venom allergies), recent illnesses, prior illnesses of clinical significance, dates of procedures and of onsets and resolution of illnesses/conditions, and current statuses of illnesses/conditions and nicotine and alcohol use. Review findings from a CXR obtained in the previous 6 months and any viral tests performed within the previous 3 months.
d A complete physical examination will be conducted at Screening that will consist of general, head, eyes, ears, nose, throat, respiratory, gastrointestinal, extremity, musculoskeletal, cardiovascular, nervous system, lymph node, and dermatologic evaluations and height, weight, BSA, and any other physical conditions of note. At subsequent visits, abbreviated physical examinations will be performed by the Investigator or clinically trained designee that will include vital signs and evaluations of skin and joints and cardiovascular, respiratory, neurologic, and any other systems associated with the subject's complaints or AEs. The Week 0/Day 0 examination will be performed pre- randomization. Percentage of BSA affected by chronic PsO, PASI score, and PSGA may also be assessed during physical examinations at post-Screening visits.
e Injection site assessments will occur at the study site for 2 hours after the first dose of study drug. At each subsequent study visit, all injection sites (current and previous) should be assessed and findings recorded in the medical record and in the AE eCRF. For each injection site, the presence of pain/tenderness, erythema/redness, induration/swelling, pruritus/itching and hematoma/ecchymosis/bruising should be recorded.
f Measurement of height does not have to be repeated after Screening.
g Vital signs include blood pressure (use of arm or wrist cuff is acceptable), heart rate, respiratory rate, and temperature (use of oral, aural, or axillary thermometer is acceptable) and are to be performed after the subject has been seated for at least 5 minutes.
h The 12-lead ECG and chemistry, hematology, and urinalysis test collections are to be performed Week 0/Day 0 (pre- randomization) unless Screening tests were obtained within 2 weeks of starting study drug, in which case they do not have to be repeated, and Screening values may be used as Baseline values. ECGs and chemistry, hematology, and urinalysis tests are discussed in Sections 7.5, 7.2.7, 7.2.8, and 7.2.9, respectively.
i The following do not need to be repeated at the ET visit 56 days (8 weeks) after the last dose if obtained within 4 weeks of visit: weight, 12-lead ECG (and results were not abnormal and of clinical concern) and chemistry, hematology, and urinalysis tests (and results were within the normal reference ranges or within the specified allowed range for the protocol [e.g., liver function test results within 2 × ULN]).
j A urine microscopic examination will be performed when any of the following 3 dipstick results are abnormal: leukocyte esterase, blood, or nitrite.
k A subject's HIV and hepatitis screen test values that have been obtained by the investigational site within 3 months prior to Screening may be used as Screening values. In accordance with local regulations, an additional consent will be obtained for HIV testing.
l QuantiFERON-TB Gold test will be performed during Screening, at Week 24 and *if the subject discontinues study participation* at an ET visit 56 days (8 weeks) after the last dose of study drug (unless it has been reported in the previous 3 months). Additional monitoring may be performed as indicated in regions with high incidences of TB or to evaluate signs and symptoms that might be due to TB. If the test is positive for TB, perform a CXR to confirm diagnosis.
m Blood samples will be collected and serum retained at Week 0/Day 0 (pre- randomization); at Weeks 2,4,8,12,16,20, 24, 32, 40, 48 and at Follow Up Visit; and, if the subject discontinues study participation, at ET visit 56 days (8 weeks) after the last dose of study drug. Retained serum may be used for evaluation of AEs and adalimumab serum concentrations in conjunction with assessment of AEs, loss of response, or compliance; to correlate with ADA assay results; or to meet any other regulatory requirement. The exact date and time of each sample collection will be recorded.
n Urine pregnancy tests will be performed on women of childbearing potential at Screening; Week 0/Day 0 (pre-randomization); at Weeks 2, 4 ,8, 12,16, 20, 24, 32, 40, 48 and Follow Up Visit; and, *if the subject discontinues study participation*, at an ET visit 56 days (8 weeks) after the last dose.
o PASI assessments will be performed at Screening; Week 0/Day 0 (pre- randomization); at Weeks 2, 4, 6, 8, 10, 12, 16, 20, 24, 32, 40, 48 and*, if the subject discontinues study participation before Week 48*, at an ET visit 56 days (8 weeks) after the last dose of study drug.
p PSGA should be performed before the SGA and both should be performed at Randomization (Week 0/Day 0) and Weeks 2, 4, 6, 8, 10, 12, 16, 20, 24, 32, 40 48; and*, if the subject discontinues study participation* at an ET visit 56 days (8 weeks) after the last dose of study drug.
q Study drug will be dispensed at Week 0/Day 0 and at Weeks 4, 12, 16, 24, 32 and 40 all unused study drug will be collected at the end of Treatment Period 1, 2 and 3.Study Drug accountability will be performed at weeks 4, 12, 16, 24.32.40 and 48
r The first dose of study drug (2 injections) should be self-administered by the subject or administered by a caregiver at the investigative site and following training. Drug will be dispensed at Weeks 0, 4, 12, 16, 24, 32 and 40 only. Subsequent doses (single injections) will be self-administered or be administered by a caregiver at home every other week from Week 1 through Week 47 .Used syringes will be placed in the provided sharps container and brought to the clinic for replacement once the sharps container is full.
s Unless obtained at the Week 12 or 16 visit (for subjects discontinuing study participation during Treatment Period 1) or at the Week 24 visit (for subjects discontinuing study participation during Treatment Period: Obtain, blood sample for hs-CRP for subjects with PsA, Perform PASI, PGA and SPGA assessment; Administer HAQ-DI for subjects with PsA; Administer DLQI; Administer EQ-5D;

5.2 Study Schedules

See Table 1-3 for the schedules of procedures for Treatment Periods 1-3, respectively. These schedules include the allowed windows for study visits.

5.2.1 Screening Period (Up to 4 weeks prior to the Week 0/Day 0 Visit, Starting with the first screening procedure)

All subjects will be informed of the nature and purpose of the study and will be asked to sign the most current Institutional Review Board (IRB)/Ethics Committee (EC) approved version of the ICF prior to any study-related assessments or procedures.

After obtaining signed informed consent, conduct the following procedures:

- Obtain medical/surgical history (see Section 5.2.6; verify findings from previously obtained CXR) If a chest x-ray has not been obtained within the past 6 months one should be obtained during the Screening process) and review any viral tests performed within the last 3 months;
- Perform complete physical examination (see Section 7.2) including height and weight, and calculate BSA and percentage BSA affected by chronic PsO (see Section 7.2.3);
- Obtain vital signs (note: arm or wrist cuff for blood pressure and oral, aural, or axillary thermometer for temperature are acceptable) (see Section 7.4);
- Record prior medications;
- Perform 12-lead electrocardiogram (ECG);
- Obtain blood samples for chemistry and hematology testing and urine sample for urinalysis;
- Obtain blood samples for viral screening (HBsAg, HBcAb, HCV, and HIV) if test results not available from tests done within the last 3 months;

  Note: A subject's HIV and hepatitis screen test results that have been obtained by the investigational site within 3 months prior to Screening may be used. In accordance with local regulations, an additional consent may be obtained for HIV testing.
- Obtain blood sample for QuantiFERON-TB Gold test to rule out active disease process such as active or latent TB;
- Perform a urine pregnancy test for women of childbearing potential;
- Perform PASI assessment and determine PASI score;
- Perform PSGA (before Subject's Global Assessment [SGA]); and
- Perform SGA of PsO
- Contact IxRS to register subject in the study.

5.2.2 Treatment Period 1 (Week 0/Day 0 through Week 15)

Treatment Period 1 consists of 16 weeks of study treatment. At Randomization (Week 0/Day 0), subjects will be randomized in a 1:1 ratio and dosed with either Humira 80 mg or CHS-1420 80 mg by SC injection. Dosing should occur on the same day as Randomization (Week 0/Day 0). From Week 1/Day 7 through Week 15/Day 105, subjects will be dosed QOW with either Humira 40 mg or CHS-1420 40 mg by SC injection.

Week 0/Day 0 Visit

PRIOR TO RANDOMIZATION AND ADMINISTRATION OF FIRST DOSE OF STUDY DRUG:

- Perform abbreviated physical examination;
- Obtain vital signs (note: arm or wrist cuff for blood pressure and oral, aural, or axillary thermometer for temperature are acceptable);
- Record concomitant medications;
- Perform 12-lead ECG;

  Note: If ECG was taken within 2 weeks of starting study drug, it does not have to be repeated and the Screening value will be used as the Baseline value.
- Obtain blood samples for chemistry and hematology testing and urine sample for urinalysis;

  Note: If measurement was taken within 2 weeks of starting study drug, it does not have to be repeated and the Screening value will be used as the Baseline value.
- Obtain blood sample for highly sensitive C-reactive protein (hs-CRP) for subjects with PsA;
- Collect serum sample for ADA testing;
- Collect serum sample for retention;
- Perform a urine pregnancy test for women of childbearing potential;
- Perform PASI assessment and confirm PASI score meets inclusion criterion;
- Perform PSGA (before SGA);
- Perform SGA of PsO;
- For subjects with PsA, administer Health Assessment Questionnaire-Disability Index (HAQ-DI);
- Administer Dermatology Life Quality Index (DLQI);
- Administer EuroQol 5-Dimension Health Status Questionnaire (EQ-5D); and

- Assess and record any AEs occurring between the Screening and the Week 0/Day 0 visits.

ONCE ELIGIBILITY HAS BEEN CONFIRMED:

- Contact IxRS to confirm enrollment and assign study drug;
- Dispense study drug;
- Perform SC injection training with subject and/or caregiver;
- Each subject will receive the first dose of study drug at the site on the day of Randomization (Week 0/Day 0) visit (the first dose will be self-administered or administered by a caregiver);
- Train subject/caregiver on use of eDiary; register subject into the eDiary system and provide written instructions to subject; have subject perform test eDiary entry, and;
- Perform injection site assessment (for 2 hours following the injections). The ISRs observed during examination of injection sites should be recorded as AEs. The AE term "ISR" with grade of AE consistent with the worst grade for any 1 of the characteristics of the ISR (pain, swelling, erythema, etc.) should be reported.
- Dispense remaining syringes to subject/caregiver from first kit assigned.

Week 2/Day 14 Visit:

At the Week 2/Day 14 visit:

- Perform abbreviated physical examination, including injection site assessments of all current and previous injection sites. The ISRs observed during examination of injection sites should be recorded as AEs. The AE term "ISR" with grade of AE consistent with the worst grade for any 1 of the characteristics of the ISR (pain, swelling, erythema, etc.) should be reported;
- Obtain vital signs (note: arm or wrist cuff for blood pressure and oral, aural, or axillary thermometer for temperature are acceptable);
- Record concomitant medications;
- Collect serum sample for retention;
- Collect serum sample for ADA testing
- Perform a urine pregnancy test
- Perform PASI assessment;
- Perform PSGA (before SGA);
- Perform SGA of PsO;
- Assess and record AEs;

- Review subject's eDiary for any issues with compliance or with injecting study drug.

Week 4/Day 28, Week 6/Day 42, Week 8/Day 56, Week 10/Day 70 and Week 12/Day 84

At the Week 4/Day 28, Week 6/Day 42, Week 8/Day 56, Week 10/Day 70, Week 12/Day 84 visits (unless otherwise specified):

- Perform abbreviated physical examinations, including injection site assessments of all current and previous injection sites. The ISRs observed during examination of injection sites should be recorded as AEs. The AE term "ISR" with grade of AE consistent with the worst grade for any 1 of the characteristics of the ISR (pain, swelling, erythema, etc.) should be reported;
- Obtain vital signs (note: arm or wrist cuff for blood pressure and oral, aural, or axillary thermometer for temperature are acceptable);
- Record concomitant medications;
- At Weeks 4, 8, and 12 , obtain blood samples for chemistry and hematology testing and urine sample for urinalysis;
- At Weeks 4, 8, and 12 only, collect serum sample for retention;
- At Weeks 4, 8, and 12 only collect serum sample for ADA testing
- At Weeks 4, 8, and 12, perform a urine pregnancy test for women of childbearing potential;
- Week 12 Only: For subjects with PsA, obtain blood sample for hs-CRP
- Perform PASI assessment;
- Perform PSGA (before SGA);
- Perform SGA of psoriasis;
- Week 12 Only: For subjects with PsA, administer Health Assessment Questionnaire-Disability Index (HAQ-DI);
- Week 12 Only: Administer Dermatology Life Quality Index (DLQI);
- Week 12 Only: Administer EuroQol 5-Dimension Health Status Questionnaire (EQ-5D);
- Assess and record AEs;
- At Weeks 4 and 12 only, perform study drug accountability
- Review subject's eDiary for any issues with compliance or with injecting study drug.

FOLLOWING THE ABOVE PROCEDURES:

- At Weeks 4 and 12 only**,** contact IxRS and dispense study drug

Week 16/Day 112

At the Week 16/Day 112 visit:

- Perform abbreviated physical examination, including injection site assessments of all current and previous injection sites. The ISRs observed during examination of injection sites should be recorded as AEs. The AE term "ISR" with grade of AE consistent with the worst grade for any 1 of the characteristics of the ISR (pain, swelling, erythema, etc.) should be reported;
- Obtain vital signs (note: arm or wrist cuff for blood pressure and oral, aural, or axillary thermometer for temperature are acceptable);
- Record concomitant medications;
- Perform 12-lead ECG;
- Obtain blood samples for chemistry and hematology testing and urine sample for urinalysis;
- Collect serum sample for ADA testing;
- Collect serum sample for retention;
- Obtain blood sample for hs-CRP for subjects with PsA;
- Perform a urine pregnancy test for women of childbearing potential;
- Perform PASI assessment;
- Perform PSGA (before SGA);
- Perform SGA of psoriasis;
- For subjects with PsA, administer Health Assessment Questionnaire-Disability Index (HAQ-DI);
- Assess and record AEs;
- Perform study drug accountability; and
- Review subject's eDiary with subject/caregiver for issues with compliance or with injecting study drug. Collect Remaining Drug; and
- Contact IxRS and dispense study drug for Treatment Period 2.

5.2.3 Treatment Period 2 (Week 17 through Week 24)

Treatment Period 2 will start with the dispensing of study drug at Week 16.

Treatment Period 2 consists of 8 weeks of study treatment. For Treatment Period 2, subjects that were assigned to the switching arm will discontinue taking Humira, and, in Treatment Period 2, will start CHS-1420. Subjects will continue to receive single SC injections of study drug QOW from Week 17/Day 119 through Week 23/Day 161.

At the Week 20/Day 140, visit:

- Perform abbreviated physical examination, including injection site assessments of all current and previous injection sites. The ISRs observed during examination of injection sites should be recorded as AEs. The AE term "ISR" with grade of AE consistent with the worst grade for any 1 of the characteristics of the ISR (pain, swelling, erythema, etc.) should be reported;
- Obtain vital signs (note: arm or wrist cuff for blood pressure and oral, aural, or axillary thermometer for temperature are acceptable);
- Record concomitant medications;
- Obtain blood samples for chemistry and hematology testing and urine sample for urinalysis;
- Collect serum sample for ADA testing
- Collect serum sample for retention;
- Perform a urine pregnancy test for women of childbearing potential
- Perform PASI assessment;
- Perform PSGA (before SGA);
- Perform SGA of psoriasis;
- Assess and record AEs;
- Review subject's eDiary for any issues with compliance or with injecting study drug.

Week 24/Day 168 Visit

At the Week 24/Day 168 visit:

- Perform abbreviated physical examination and injection site assessments of all current and previous injection sites. The ISRs observed during examination of injection sites should be recorded as AEs. The AE term "ISR" with grade of AE consistent with the worst grade for any 1 of the characteristics of the ISR (pain, swelling, erythema, etc.) should be reported;

- Obtain vital signs (note: arm or wrist cuff for blood pressure and oral, aural, or axillary thermometer for temperature are acceptable);
- Obtain weight;
- Record concomitant medications;
- Perform 12-lead ECG;
- Obtain blood samples for chemistry and hematology testing and urine sample for urinalysis;
- Obtain blood sample for QuantiFERON-TB Gold test
- Obtain blood sample for hs-CRP for subjects with PsA
- Collect serum sample for ADA testing;
- Collect serum sample for retention;
- Perform urine pregnancy test for women of childbearing potential;
- Perform PASI assessment and calculate PASI-50;
- Perform PSGA (before SGA);
- Perform SGA of psoriasis;
- For subjects with PsA, administer HAQ-DI;
- Administer DLQI;
- Administer EQ-5D;
- Assess and record AEs;
- Perform study drug accountability; and
- Review subject's eDiary for any issues with compliance or with injecting study drug.
- If the subject has achieved at least a PASI-50 contact IxRS and dispense open label kit for Treatment Period 3

5.2.4 Treatment Period 3

Subjects that successfully complete 24 Weeks in Treatment Period 1 and 2 and achieve at least a PASI-50 score will be eligible to receive open label CHS-1420 for an additional 23 weeks.

Week 32/Day 224 and Week 40/Day 280 Visit

- Perform abbreviated physical examinations, including injection site assessments of all current and previous injection sites. The ISRs observed during examination of injection sites should be recorded as AEs. The AE term "ISR" with grade of AE consistent with the worst grade for any 1 of the characteristics of the ISR (pain, swelling, erythema, etc.) should be reported;
- Obtain weight
- Obtain vital signs (note: arm or wrist cuff for blood pressure and oral, aural, or axillary thermometer for temperature are acceptable);
- At Week 40 only: perform 12-lead ECG
- Record concomitant medications;
- Obtain blood samples for chemistry and hematology testing and urine sample for urinalysis;
- Collect serum sample for retention;
- Collect serum sample for ADA testing
- Perform a urine pregnancy test for women of childbearing potential;
- At Week 40 only: Obtain blood sample for hs-CRP for subjects with PsA
- Perform PASI assessment;
- Perform PSGA (before SGA);
- Perform SGA of psoriasis;
- At Week 40 only: For subjects with PsA, administer HAQ-DI;
- Assess and record AEs;
- Perform study drug accountability
- Review subject's eDiary for any issues with compliance or with injecting study drug.
- Contact IVRS and dispense study drug.

Week 48/Day 336 Visit

At the Week 48/Day 336 visit:

- Perform abbreviated physical examination, including injection site assessments of all current and previous injection sites. The ISRs observed during examination of injection sites should be recorded as AEs. The AE term "ISR" with grade of AE consistent with the worst grade for any 1 of the characteristics of the ISR (pain, swelling, erythema, etc.) should be reported;

- Obtain vital signs (note: arm or wrist cuff for blood pressure and oral, aural, or axillary thermometer for temperature are acceptable);
- Obtain weight;
- Record concomitant medications;
- Perform 12-lead ECG;
- Obtain blood samples for chemistry and hematology testing and urine sample for urinalysis;
- Obtain blood sample for hs-CRP for subjects with PsA
- Collect serum sample for ADA testing;
- Collect serum sample for retention;
- Perform urine pregnancy test for women of childbearing potential;
- Perform PASI assessment;
- Perform PSGA (before SGA);
- Perform SGA of psoriasis;
- For subjects with PsA, administer HAQ-DI;
- Assess and record AEs;
- Perform study drug accountability; and
- Review subject's eDiary for any issues with compliance or with injecting study drug.

5.2.5 Follow-up or ET Visit (56 Days [8 weeks] After the Last Dose of Study Drug

The study will conclude when the last subject completes evaluations at the Follow-up visit or ET visit 56 days (8 weeks) after the last dose of study drug.

Subjects who complete Week 48/Day 336 efficacy and safety evaluations will be seen for a Follow-up visit 8 weeks after their last scheduled dose of study drug; subjects who discontinue the study prior to Week 48 will be seen for an ET visit 8 weeks/56 days after the last dose of study drug.

8 Weeks/56 days after the subject's last dose of study drug:

- Perform abbreviated physical examination and injection site assessments of all previous injection sites. The ISRs observed during examination of injection sites should be recorded as AEs. The AE term "ISR" with grade of AE consistent with the worst grade for any 1 of the characteristics of the ISR (pain, swelling, erythema, etc.) should be reported;
- Obtain vital signs (note: arm or wrist cuff for blood pressure and oral, aural, or axillary thermometer for temperature are acceptable)

- For Early Termination Subjects: obtain the following if not obtained within 4 weeks of the visit:
    - Blood samples for chemistry and hematology testing, and urine sample for urinalysis (and results were within the normal reference range for the test or within the specified allowed range for the protocol, e.g., liver function test results within 2 × ULN);
    - Perform 12-lead ECG
    - Weight;
- For Early Termination Subjects: obtain the following if not completed at the Week 12 or 16 visit (for subjects discontinuing study participation during Treatment Period 1) or at the Week 24 visit (for subjects discontinuing study participation during Treatment Period 2)
    - Obtain blood sample for hs-CRP for subjects with PsA
    - Perform PASI assessment;
    - Administer HAQ-DI for subjects with PsA;
    - Administer DLQI;
    - Administer EQ-5D;
- Perform PSGA (before SGA);
- Perform SGA of psoriasis;
- Collect serum sample for ADA testing;
- Collect serum sample for retention;
- Obtain blood sample for QuantiFERON-TB Gold test if this test has not been drawn and reported in last 3 months;
- Perform a urine pregnancy test for women of childbearing potential;
- Assess and record AEs;
- Record concomitant medications;
- Perform study drug accountability for subjects discontinuing study participation early;
- Review subject's eDiary for any issues with compliance or with injecting study drug for subjects discontinuing study participation early;
- Collect any used and unused study drug if not previously collected, and assess compliance; and
- Contact IxRS to report subject's completion/discontinuation from study.

5.2.6 Medical and Surgical History

The Investigator or trained designee will obtain a medical and surgical history to include PsA, all allergies (including latex, drug, food, and insect venom allergies), recent illnesses, and prior illnesses of clinical significance, with date(s) of onset and current statuses of conditions; status of nicotine and alcohol use; and dates of any procedures.

6 EFFICACY MEASUREMENTS

6.1 Efficacy Variables

6.1.1 Primary Efficacy Variable

The primary efficacy endpoint is:

- 75% improvement in Psoriasis Area and Severity Index (PASI-75) at Week 12 relative to Baseline, where Baseline will be the last assessment prior to beginning study drug (scheduled for Week 0/day 0)

6.1.1.1 Psoriasis Area and Severity Index

The PsO lesions are scored on a scale of 0 to 4 for 3 characteristics: erythema, infiltration, and desquamation, weighted by the area of involvement (Fredriksson & Pettersson, 1978) (Feldman & Krueger, 2005). The lesions are scored within 4 anatomical regions: head, upper extremities, trunk, and lower extremities including buttocks. Within each of these regions, the area of involvement is scored on a scale of 0 to 6. The clinician will assess the subject's PsO lesions according to the PASI at Screening, Week 0/Day 0, and at the Week 2, 4, 6, 8, 10, 12, 16, 20, 24, 32, 40 and 48 visits, as well as at the ET and FU visit, as applicable. The Baseline value will be the last PASI assessment prior to receiving treatment at Week 0/Day 0. The clinician will determine PASI score at Screening and confirm that the PASI score still meets the inclusion criterion at Week 0/Day 0 (pre-randomization). Whenever possible, the same Investigator/Clinician or trained PASI assessor should conduct the PASI assessment for each subject at each visit.

6.1.2 Secondary Efficacy Variables

The secondary efficacy endpoints are

- PASI-75 at Weeks 2, 4, 6, 8, 10, 16, 20, 24, 32, 40 and 48;
- Percentage changes in PASI from Baseline at Weeks 2, 4, 6, 8, 10, 12, 16, 20, 24, 32, 40 and 48;
- 50% improvement in Psoriasis Area and Severity Index (PASI-50) at Weeks 2, 4, 6, 8, 10, 12, 16, 20, 24 32, 40 and 48;
- 90% improvement in Psoriasis Area and Severity Index (PASI-90) at Weeks 2, 4, 6, 8, 10, 12, 16, 20, 24 32, 40 and 48;
- Changes in PSGA of disease activity on a scale from 0 to 5 from Baseline to Weeks 2, 4, 6, 8, 10, 12, 16, 20, 24, 32, 40, 48 and, as applicable, the Follow-up or ET visit;
- Change in PSGA = 0 to 1, demonstrating clear or almost clear skin at Weeks 2, 4, 6, 8, 10, 12, 16, 20, 24, 32, 40 and 48 and, as applicable, the Follow-up or ET visit;

6.1.2.1 Physician's Static Global Assessment

The PSGA of PsO will be assessed on a scale of 0 to 5, with 0 indicating no psoriasis (clear of disease), 1 (almost clear), and 2 or higher scores indicating more severe disease (Appendix D).

The clinician's assessment should be made and recorded before attaining the subject's assessment at all visits. The PSGA will be performed at Screening; Randomization (Week 0/Day 0); and at the Week 2, 4, 6, 8, 10, 12, 16, 20, 24, 32, 40 and 48 visits; as well as at the Follow-up or ET visit, as applicable.

6.1.3 Other Efficacy Variables

The other efficacy endpoints are:

- Changes in SGA of Psoriasis on a scale from 0 to 5 from Baseline to Weeks 2, 4, 6, 8, 10, 12, 16, 20, 24, 32, 40 and 48 and, as applicable, the Follow-up or ET visit;
- Changes in DLQI from Baseline to Weeks 12 and 24;
- Changes in EQ-5D from Baseline to Weeks 12 and 24;
- Changes in HAQ-DI from Baseline to Weeks 12, 24, 40 and 48 for subjects with PsA only; and
- Changes in hs-CRP from Baseline to Weeks 12, 16, 24, 40 and 48 for subjects with PsA only.

6.1.3.1 Subject's Global Assessment

The SGA of PsO will be assessed on a scale ranging from 0 (good) to 5 (severe) (Leonardi, et al., 2003) (Appendix E). The SGA should be assessed at Randomization (Week 0/Day 0) and at the Week 2, 4, 6, 8, 10, 12, 16, 20, 24, 32, 40, 48 visits, as well as at the Follow-up or ET visit, as applicable.

6.1.3.2 Health Assessment Questionnaire-Disability Index

For subjects with PsA, the HAQ-DI will be performed at Randomization (Week 0/Day 0) and at the Week 12, 16, 24, 40 and 48 visits, as well as at the Follow-up or ET visit, as applicable. This is a validated 20-item assessment of a subject's functional abilities in 8 categories (Dressing and Grooming, Hygiene, Arising, Reach, Eating, Grip, Walking, and Common Daily Activities) (Appendix F). There are 4 response options ranging from "No Difficulty" to "Unable to Do," scored 0-3. The clinician will instruct the subject to rate each item on the questionnaire. The HAQ-DI was initially developed for evaluation of RA, but has been subsequently used in clinical trials in subjects with PsA (Mease, et al., 2011).

6.1.3.5 Dermatology Life Quality Index

The DLQI is a 10-question validated questionnaire to be performed at Randomization (Week 0/Day 0) and at the Week 12, Week 24 visits, as well as at the ET visit, as applicable. It is calculated by summing the score of each question resulting in a maximum of 30 and a minimum of 0. The higher the score, the more quality of life is impaired. The DLQI can also be expressed as a percentage of the maximum possible score of 30 (Finlay & Khan, 1994). See Appendix G.

6.1.3.6 EuroQol 5-Dimension Health Status Questionnaire

The EQ-5D will be performed at Randomization (Week 0/Day 0) and at the Week 12, Week 24 visits, as well as at the ET visit, as applicable. The EQ-5D is a generic (non-disease specific), preference-based health-related quality of life measure based on 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression (Brazier, Jones, & Kind, 1993). See Appendix H.

6.1.3.7 Highly Sensitive C-reactive Protein

For subjects with PsA, change in hs-CRP (mg/L) from Baseline to Weeks 12, 16, 24, 40 and 48 will be assessed, as well as at the ET visit, as applicable.

7 SAFETY MEASUREMENTS

Safety will be assessed by evaluating the incidence of and reasons for subject discontinuations, the incidence of treatment-emergent adverse events (TEAEs), ISRs, changes in safety laboratory parameters, vital signs, physical examinations, and ECG findings. In addition, subjects will be monitored for TB with regular QuantiFERON-TB Gold test (every 6 months or more frequently for regions with a high incidence of TB, or to evaluate signs and symptoms that might be due to TB).

Subjects who convert to a positive QuantiFERON-TB Gold test during the study will be withdrawn from study drug and evaluated for the presence of active TB and treated per the standard of care for treatment of reactivation or new onset TB as applicable. If the QuantiFERON-TB Gold test yields low positive results (defined as QuantiFERON TB Antigen minus Nil value = 0.35 - 2 IU/mL), a repeat test should be done. If the repeat test is negative, the patient can continue on the study, subject to the clinical judgment of the Investigator.

A list of the analytes to be measured for the safety evaluation is found below in Section 7.2.6. All laboratory test results must be evaluated by the Investigator as to their clinical significance. Any laboratory value considered by the Investigator to be clinically significant should be considered an AE and recorded on the eCRF.

7.1 Adverse Events

Adverse events will be collected, once the subject signs the ICF prior to undergoing Screening procedures, throughout the duration of the study. Treatment-emergent adverse events are those AEs starting after the subject receives the first dose of study drug. An AE is any unfavorable medical occurrence in a subject or clinical investigation subject administered a pharmaceutical product, which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not considered related to the medicinal (investigational) product. All AEs, including observed or suspected problems, complaints, or symptoms, are to be recorded on the appropriate eCRF. Documentation must be supported by an entry in the subject's source document. Each AE is to be evaluated for duration, severity, and causal relationship with the study drug or other factors.

Whenever possible, a specific disease or syndrome rather than individual associated signs and symptoms should be identified by the Investigator and recorded on the eCRF. However, if an observed or reported sign or symptom is not considered a component of a specific disease or syndrome by the Investigator, it should be recorded as a separate AE on the eCRF.

Any medical condition or signs or symptoms already present at Screening or Baseline should not be reported as an AE unless the medical condition or signs or symptoms present at Baseline worsen in severity or seriousness at any time during the study. In this case, it should be reported as an AE.

Clinically significant abnormal laboratory or other examination (e.g., ECG) findings that are detected during the study or are present at Baseline and significantly worsen during the study should be reported as AEs. The Investigator will exercise his or her medical and scientific judgment in deciding whether an abnormal laboratory finding or other abnormal assessment is clinically significant. Significant abnormal laboratory and other examination values occurring during the clinical study will be followed until repeat test results return to normal, stabilize, or are no longer clinically significant.

The ISRs observed during examination of injection sites by study staff should be recorded as AEs. The AE term "ISR" with grade of AE consistent with the worst grade for any 1 of the characteristics of the ISR (pain, swelling, erythema, etc.) should be reported.

ISRs observed by subjects will be reported in each subject's eDiary and will not be recorded as AEs unless also observed by study staff.

Unexpected Adverse Drug Reaction

An unexpected adverse drug reaction is defined as an adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g., Investigator's Brochure for an unapproved investigational product or package insert/summary of product characteristics for an approved product).

7.1.1 Grading and Intensity of Adverse Events

The Investigator will rate the intensity of each AE as mild, moderate, severe, or life threatening.

Severity or Toxicity Grading:

Grade 1: Mild – An event that is usually transient in nature and generally not interfering with normal activities.

Grade 2: Moderate – An event that is sufficiently discomforting to interfere with normal activities.

Grade 3: Severe – An event that is incapacitating with inability to work or perform normal daily activity.

7.1.2 Adverse Event Outcome

The Investigator will record the outcome of each adverse event as follows:

- Resolved
- Resolved with sequelae
- Not Resolved
- Death
- Unknown

7.1.3 Relationship to Study Drug

The assessment of the relationship of an AE to the administration of study drug (yes, no) is a clinical decision based on all available information at the time of the completion of the eCRF.

No (unrelated, not related, no relation, probably unrelated):
The time course between the administration of study drug and the occurrence or worsening of the AE rules out a causal relationship and another cause (concomitant drugs, therapies, complications, etc.) is suspected.

Yes (possibly related, related):
The time course between administration of study drug and the occurrence or worsening of the AE is consistent with a causal relationship and no other cause can be identified (concomitant drugs, therapies, complications, etc.).

The following factors should also be considered:

- Temporal sequence from drug administration;

  Event should occur after study drug is given. The length of time from drug exposure to event should be evaluated in the clinical context of the event.

- Underlying, concomitant, intercurrent diseases;

  Each report should be evaluated in the context of the natural history and course of the disease being treated and any other disease the subject may have.

- Concomitant medication;

  Other drugs the subject is taking or the treatment the subject receives should be examined to determine whether any of them might be recognized to cause the event in question.

- Known response pattern for this class of drug;

  Clinical and/or preclinical data may indicate whether a particular response is likely to be a class effect.

- Exposure to physical and/or mental stresses; and

  Exposure to stress might induce adverse changes in the recipient and provide a logical and better explanation for the event.

- Pharmacology and PK of the test drug.

  Known properties (absorption, distribution, metabolism, and excretion) of the test drug should be considered.

Unexpected AEs – An unexpected AE is an experience not previously reported or an AE that occurs with specificity, severity, or frequency that is not consistent with the current Investigator's Brochure.

7.1.4 Serious Adverse Event Reporting

An SAE is any untoward medical occurrence that, at any dose:

- Results in death;
- Is life-threatening;

  NOTE: An AE or adverse reaction is considered "life-threatening" if, in view of either the Investigator or Sponsor, its occurrence places the subject at immediate risk of death. It does not include an event that, had it occurred in a more severe form, might have caused death.

- Requires hospitalization or prolongation of an existing hospitalization;

  NOTE: Any hospital admission with at least 1 overnight stay will be considered an inpatient hospitalization. An emergency room visit without hospital admission will not be recorded as an SAE under this criterion, nor will hospitalization for a procedure planned or scheduled before signing of the ICF. However, unexpected complications and/or prolongation of hospitalization that occur during elective surgery should be recorded as AEs and assessed for seriousness.

  Admission to the hospital for social or situational reasons (i.e., no place to stay, live too far away to come for hospital visits) will not be considered inpatient hospitalizations.

- Results in a disability/incapacity;
- Is a congenital anomaly/birth defect; or
- Is an important medical event.

  Note: Medical or scientific judgment should be exercised in deciding whether reporting is appropriate in other situations, such as important medical events that may not be immediately life-threatening or result in death or hospitalization but may jeopardize the subject or may require medical or surgical intervention to prevent 1 of the other outcomes listed in the above definition. These should also be considered serious. Examples of such events are invasive or malignant cancers, intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalization, development of drug dependency, or drug abuse.

7.1.4 Serious Adverse Event Reporting—Procedure for Investigators

All SAEs occurring from Screening until 56 days (8 weeks) following the last administration of study drug must be reported to Worldwide Clinical Trials (WCT) Clinical Safety personnel within 24 hours of the knowledge of the occurrence. All SAEs occurring after the 56-day follow-up period, which the Investigator considers related to study drug, must also be reported to WCT Clinical Safety personnel.

To report the SAE, the Investigator is to complete the SAE form electronically in the electronic data capture (EDC) system for the study. When the form is completed, WCT Clinical Safety personnel will be notified electronically and will retrieve the form. If it is not possible to access the internet, a call should be made to the WCT SAE hotline (country specific phone numbers will be provided in the WCT Safety Plan and distributed to sites), and a completed paper SAE form should be faxed to WCT (fax number provided in the Study Manual) within 24 hours of awareness. When the EDC system becomes available, the SAE information must be entered within 24 hours of the system becoming available.

If the SAE is life-threatening or results in death, the Investigator is to telephone the Medical Monitor (telephone numbers are listed below).

The Investigator will be requested to supply detailed information regarding the event. All SAEs must also be reported to the reviewing IRB/EC according to IRB/EC policy, and a copy of that report must be retained at the investigative site and filed in the Investigator Site File in accordance with the requirements of that institution.

Safety Contact Information:

Worldwide Clinical Trials Clinical Safety
Isaac Newton Centre
Nottingham Science Park
Nottingham NG7 2RH
UK

Worldwide Clinical Trials SAE reporting – USA:
email: drugsafety@wwctrials.com
Fax: 1-866-387-5539 (eFAX)

Worldwide Clinical Trials SAE reporting – Europe:
email: drugsafety@wwctrials.com
Fax: +44 208 0434813 (eFAX)

Specific contact information for Medical Monitors will be distributed to investigative sites in the contact numbers provided.

Country specific numbers will be provided to the Investigators.

7.1.5 Serious Adverse Event Follow-up

The Investigator must continue to follow the subject until the SAE has subsided or until the condition becomes chronic in nature or stabilizes (in the case of persistent impairment) or the subject dies.

Within 24 hours of receipt of follow-up information, the Investigator must update the SAE form electronically in the EDC system for the study and submit any supporting documentation (e.g., subject discharge summary or autopsy reports) to WCT Clinical Safety personnel via fax or e-mail. If it is not possible to access the EDC system, refer to the procedures outlined above for initial reporting of SAEs.

7.1.6 Suspected Unexpected Serious Adverse Reactions

The Sponsor will send copies of expedited reports for all SAEs that are unexpected and suspected to be at least possibly related to the study treatment to all concerned regulatory authorities, active Investigator(s), and the IRBs/ECs in accordance with local and site-specific requirements. For all active Investigators located in Europe, the Sponsor or designee will be responsible for reporting suspected unexpected serious adverse reactions (SUSARs) and any other applicable SAEs to regulatory authorities including the European Medicines Agency (EMA), Investigators, and central or local ECs, as applicable, in accordance with national regulations in the countries where the study is conducted. SUSARs will be submitted within 7 days for fatal and life-threatening events and within 15 days for other serious events, unless otherwise required by national regulations.

7.1.7 Breaking Study Blind for Regulatory Reporting

If a SUSAR is reported and, if required by local regulatory authorities, the Sponsor or designee will ascertain the treatment assignment by unblinding the subject for the purposes of regulatory reporting ONLY. The treatment assignment will only be known by necessary Sponsor employees/consultants or designees in Pharmacovigilance and Regulatory Affairs. (The subject and study site personnel are to remain blinded). The subject's status is unchanged and continued participation in the study is unaffected. If necessary to treat the AE or SAE for which the subject is being unblinded, the Investigator may be informed of the unblinded treatment assignment (Section 4.6).

7.2 Protocol Assessments

7.2.1 Physical Examination

A complete physical examination will be conducted by the Investigator or clinically trained designee (i.e., MD, NP) at Screening and will consist of general, head, eyes, ears, nose, throat, respiratory, gastrointestinal, extremity, musculoskeletal, cardiovascular, nervous system, lymph node, and dermatologic evaluations and height, weight, BSA, and any other physical conditions of note (e.g., percentage of BSA affected by chronic PsO, PASI score, and PSGA). Body mass index will be calculated. At all visits after Screening, abbreviated physical examinations will be performed and should include vital signs and evaluations of skin and joints and cardiovascular, respiratory, neurologic, and any other systems associated with the subject's complaints or AEs.

7.2.2 Injection Site Assessments

Subjects will report any ISR to the eDiary. Subjects will describe the characteristics of the ISR (pain/tenderness, erythema/redness, induration/swelling, pruritus/itching, hematoma/ecchymosis/bruising) at the site of injection.

Study drug injection sites will be assessed by the site staff at each visit. Any findings (e.g., pain/tenderness, erythema/redness, induration/swelling,

pruritus/itching, hematoma/ecchymosis/bruising) will be recorded on the ISR worksheet and entered into the eCRF as an AE. The AE term "ISR" with the grade of AE consistent with the worst grade for any 1 of the findings should be reported. An additional eCRF will also be created to capture more detailed information regarding injection site reactions.

At the initial treatment visit (Week 0/Day 0), the subject will be asked to remain at the site for 2 hours after the initial injections in order to be monitored for ISRs and other AEs. At subsequent visits, all injection sites will be examined.

7.2.3 Weight, Height, Body Surface Area and Body Mass Index

Weight (kg) and height (cm) will be measured at Screening. Subjects should be weighed wearing indoor, daytime clothing with no shoes. Before being weighed, subjects should empty their bladders.

In addition, weight will also be measured at Week 24, 32, 40 and 48 and, if the subject discontinues study participation, at the ET visit 56 days (8 weeks) after the last dose of study drug.

Body Mass Index should be calculated at screening using the method below:

English Units: BMI = Weight (lb) / (Height (in) x Height (in)) x 703
Metric Units: BMI = Weight (kg) / (Height (m) x Height (m))

A web based calculator can be found at the following URL: http://www.nhlbi.nih.gov/health/educational/lose_wt/BMI/bmicalc.htm.

Body surface area (m^2) should be calculated at Screening using the Mosteller formula (Mosteller, 1987):

BSA (m^2) = $\sqrt{(Ht\ in\ cm\ x\ Wt\ in\ kg)/3600}$

A web-based calculator using the Mosteller formula may be found at the following URL: www.halls.md/body-surface-area/bsa.htm. Make sure that the Mosteller formula is used to calculate BSA as this website offers several formulas.

Percentage of BSA affected by chronic PsO should be roughly estimated by using the subject's palm size as roughly 1% of the total BSA and the BSA by body area used to assess PASI:

- Head and neck ~ 10%
- Upper extremities ~20%
- Trunk ~30%
- Lower extremities + buttocks ~40%

7.2.4 Vital Signs

Vital signs will be collected at every visit and include blood pressure (obtained using arm or wrist cuff), heart rate, respiratory rate, and oral, aural, or axillary temperature and will be obtained at all study visits using a standardized process:

- The subject should sit for 5 minutes with feet flat on the floor and his/her measurement arm supported so that the midpoint of the manometer cuff is at heart level.
- A mercury sphygmomanometer or automatic blood pressure device with an appropriately sized cuff with the bladder centered over the brachial artery should be used (note: a wrist cuff centered over the radial artery is also acceptable).
- Blood pressure and heart rate should then be measured and recorded.

Blood pressure should be recorded to the nearest 2 mmHg mark on the manometer or to the nearest whole number on an automatic device.

7.2.5 Electrocardiogram

A 12-lead ECG will be performed at Screening, Randomization (Week 0/Day 0) and at Weeks 12 24, 40 and 48 or, if the subject discontinues study participation before Week 48, at the ET visit 56 days (8 weeks) after the last dose of study drug. If the Screening ECG is obtained within 2 weeks before starting study drug, it does not have to be repeated at Randomization (Week 0/Day 0)and the Screening values will be used as Baseline values. If the 12-lead ECG was obtained within the 4 weeks prior to ET visit and the results were not abnormal and of clinical concern, it does not need to be repeated at that visit. The ECG will be performed after the subject has been in the supine position for at least 10 minutes, will include all 12 standard leads, and will be recorded at a paper speed of 25 mm/sec. Standard ECG parameters will be measured, including RR, PR, and corrected QT intervals, and QRS duration. All ECGs must be evaluated by a qualified physician (i.e., Investigator) for the presence of abnormalities. Any abnormalities of clinical concern to the qualified physician may be read by a consulting cardiologist, per the Investigator's decision.

7.2.6 Safety Laboratory Tests

Safety laboratory tests will be performed at Screening; Randomization (Week 0/Day 0); at Weeks 4, 8, 12, 16, 20, 24, 32, 40 and 48; and at the Follow-up visit or, if the subject discontinues study participation before Week 48, at the ET visit 56 days (8 weeks) after the last dose of study drug. If the Screening chemistry, hematology, and urinalysis are obtained within 2 weeks of starting study drug, they do not have to be repeated at Randomization (Week 0/Day 0), and the Screening values will be used as Baseline values. If the safety laboratory tests were obtained within the 4 weeks prior to the ET visit and the results were within the normal reference ranges or within the specified allowed range for the protocol (e.g., liver function test results within 2 × ULN), they do not need to be repeated at that visit.

7.2.7 Chemistry

Samples will be drawn for assessment of the following parameters: alkaline phosphatase; sodium; potassium; total protein; calcium; chloride; bicarbonate;

glucose; creatine phosphokinase; lactate dehydrogenase; alanine aminotransferase; aspartate aminotransferase; albumin; total, direct, and indirect bilirubin; blood urea nitrogen; creatinine; and uric acid.

7.2.8 Hematology

Samples will be drawn for assessment of the following parameters: hematocrit; hemoglobin, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, mean corpuscular volume, red blood cell count, white blood cell count with differential, and platelet count.

7.2.9 Urinalysis

Urine will be collected for urinalysis, which will include assessment of the following parameters: pH, specific gravity, protein, glucose, leukocyte esterase, bilirubin, blood, nitrite, and ketones. A urine microscopic examination will be performed when there are any abnormalities on any of the following 3 dipstick results: leukocyte esterase, blood, or nitrite.

7.2.10 Other Laboratory Tests

HIV and Hepatitis Screening

All subjects will be tested for HBsAg, HBcAb, HCV antibodies (and RNA as appropriate), and HIV at Screening. If screening for HIV and hepatitis was done within 3 months prior to Screening, these test results may be used as Screening values.

In accordance with local regulations, an additional consent will be obtained for HIV testing. Notification of state and federal authorities, as required by law, will be the responsibility of the Investigator.

Tuberculosis Screening

All patients will be tested for TB at Screening using the QuantiFERON-TB Gold test. Patients with a positive QuantiFERON-TB Gold test may not participate. The QuantiFERON® TB Gold test can be repeated once using a fresh sample in subjects with an indeterminate result or low positivity (defined as QuantiFERON TB Antigen minus Nil value = 0.35 - 2 IU/mL); if the repeat test result is negative, the subject may participate in the study (Raychaudhuri, Nguyen, Raychaudhuri, & Gershwin, 2009). Additional TB testing utilizing the QuantiFERON-TB Gold test will be performed at Week 24 and at the Follow-up or ET visit 56 days (8 weeks) after the last dose of study drug as applicable, if a test has not been performed within the previous 3 months. Monitoring may be performed more frequently for regions with high incidence of TB or to evaluate signs and symptoms that might be due to TB. At Screening, a CXR obtained within the last 6 months should not demonstrate evidence of active or latent TB or any other active disease process. If during the study or at follow up visits, if a patient has a positive QuantiFERON-TB Gold test, a CXR should be obtained to confirm the diagnosis of TB.

Pregnancy Test

Urine pregnancy tests will be performed on women of childbearing potential at Screening, Randomization (Week 0/Day 0); at Weeks 2, 4, 8, 12, 16, 20, 24, 32, 40, 48 ; and at the Follow-up visit or, if the subject discontinues study participation before Week 48, at the ET visit 56 days (8 weeks) after the last dose of study drug.

Pregnancy Reporting

If the subject participating in the study becomes pregnant during the study or within 56 days of last dose of study drug, the Investigator should report the pregnancy to WCT Clinical Safety personnel within 24 hours of being notified. WCT Clinical Safety personnel will then forward the Exposure In Utero form to the Investigator for completion.

A subject who becomes pregnant while on study drug will immediately be withdrawn from study treatment and ET visit study procedures will be performed.

The subject should be followed by the Investigator until completion of the pregnancy. If the pregnancy ends for any reason before the anticipated date, the Investigator should notify the Sponsor. At the completion of the pregnancy, the Investigator will document the outcome of the pregnancy. If the outcome of the pregnancy meets the criteria for immediate classification as an SAE (i.e., postpartum complication, spontaneous abortion, stillbirth, neonatal death, or congenital anomaly), the Investigator should follow the procedures for reporting an SAE.

7.2.11 Anti-Drug Antibody Assessment

Antibodies to adalimumab will be measured in the sera of subjects enrolled in this study to compare the immunogenicity of CHS-1420 to that of Humira. Immunogenicity will be evaluated over the course of the study. Comparison of immunogenicity will be made at Weeks 0/Day 0 (pre-dose), 2, 4, 8, 12, 16, 20, 24, 32, 40, 48 and at the ET or Follow Up visit 56 days/8 weeks after the last dose of study drug.

The immunogenicity testing will be performed using validated ECL ADA assays. Presence of ADA based on this confirmatory assay will be compared between groups. An assay to determine if ADAs are neutralizing may be used.

7.2.12 Highly Sensitive C-reactive Protein

Blood samples for measurement of hs-CRP will be collected for subjects with concurrent PsA at Randomization (Week 0/Day 0) and at Weeks 12, 16, 24, 40, 48 and the Follow Up Visit or, if the subject discontinues study participation before Week 48, at the ET visit 56 days (8 weeks) after the last dose of study drug. In this study, the hs-CRP (mg/L) is used as a marker of inflammation and not as a screening test for cardiovascular risk, and hs-CRP results will not be shared with the subject.

7.2.13 Serum Retention Samples

Serum samples will be collected from all subjects at Randomization (Week 0/Day 0) (pre-dose); at Weeks 2, 4, 8, 12, 16, 20, 24, 32, 40, 48 ; and at the Follow-up visit or, if the subject discontinues study participation before Week 48, at the ET visit 56 days (8 weeks) after the last dose of study drug. These serum samples may be used to evaluate AEs and serum adalimumab levels in conjunction with assessment of AEs, loss of response, or compliance; to correlate with ADA assay results; or to meet any other regulatory requirement. No other biomarkers or genetic testing will be performed on these samples. Samples will be retained at the Medpace Reference Laboratory until testing and unused samples and remnants or used samples will be destroyed 2 years after the study is completed (final database lock).

7.2.13.1 Sample Collection Procedures and Bioanalytical Methods

Instructions for sample collection and handling are included in the laboratory manual. All clinical laboratory evaluations should be performed at the same central laboratory. In the event that immediate laboratory analyses are required to assess an AE, a local laboratory may be used; however, a duplicate blood sample should also be sent to the central laboratory.

8 PLANNED ANALYSES

8.1 Analysis Populations

8.1.1 Randomized Population

The Randomized Population will include all randomized subjects. Subjects will be allocated to the treatment arm they are randomized to for a particular Treatment Period of analysis.

8.1.2 Full Analysis Population

The Full Analysis Population (FAP) will include all randomized subjects who receive 1 or more doses of study drug. The FAP is the primary efficacy analysis population. Subjects will be allocated to the treatment arm they are randomized to for a particular Treatment Period of analysis.

8.1.3 Safety Population

The Safety Population, like the FAP, will include all randomized subjects who receive 1 or more doses of study drug, but subjects will be allocated to the treatment arm based upon actual treatment received for a particular Treatment Period of analysis.

8.1.4 Per Protocol Population

The Per Protocol Population is defined as those subjects in the FAP completing at least 12 weeks of treatment and follow-up with respect to the PASI and have no protocol violations that may affect the interpretation of the primary efficacy endpoint. These violations will be identified by the Sponsor prior to study unblinding.

Subjects will be allocated to the treatment arm they are randomized to for a particular Treatment Period of analysis.

8.1.5 Open Label Extension Population:

The Open Label Extension Population is defined as those subjects receiving at least 1 dose of open label treatment. Subjects will be allocated to the treatment arm they received in Treatment Period 2.

8.2 Statistical Methods

8.2.1 Demographic and Baseline Characteristics

Descriptive summaries of demographic and Baseline characteristics at the time of randomization will be presented by treatment group. A detailed description of subject disposition will also be provided.

8.2.2 Efficacy Analysis

The primary statistical analyses will be based on:

- The difference between the percentages of subjects in the CHS-1420 and Humira groups achieving PASI-75 at Week 12.

Equivalence will be based upon the 95% (2-sided) confidence interval for the difference in PASI-75 rates. If both the lower and upper bounds of the 95% confidence interval exclude ±15% (inclusive), equivalence will be established. The mean percent change in PASI from Baseline to Week 12 between the CHS-1420 and Humira (US) groups will be assessed as a supporting secondary endpoint.

Subjects who lack a PASI assessment at Week 12 will be considered non-responders in the primary analyses. As a sensitivity analysis, the last available score will be used.

For PASI-75 at Week 12 (as well as for other binary outcomes where formal evaluations are made, if applicable), Cochran-Mantel-Haenszel weights will be used to combine the stratum specific differences (LaVange, Durham, & Koch, 2005) formed by the randomization strata.

For the percent change in PASI from Baseline (as well as for other continuous outcomes where formal evaluations are made, if applicable), the stratum-specific differences will be combined using an analysis of variance approach with weights proportionate to the stratum sizes.

Other secondary continuous variables will be summarized using descriptive statistics (N, mean, standard deviation, 95% confidence interval, median, minimum, and maximum) and discrete variables will be summarized using frequency counts and percentages.

For data collected after the start of Treatment Period 2, data summaries for efficacy will be presented by the particular treatment sequence received in Treatment Periods 1 and 2: CHS-1420/CHS-1420, Humira/Humira and Humira/CHS-1420.

For data collected during the open label extension, only descriptive data summaries will be presented. These summaries will be presented by the particular treatment received in Treatment Period 2, regardless of treatment received in Treatment Period 1.

8.2.3 Safety Analysis

Safety data will be summarized and listed. No inferential statistical analyses of the safety data are planned. All safety summaries and listings will be generated using the Safety Population based upon treatment received for the Treatment Period of interest.

Safety data through Week 16 will be presented by the treatment received (CHS-1420 or Humira). Safety data for the study as a whole will be presented for subjects receiving CHS-1420 during Treatment Period 1 and those receiving

Humira during Treatment Period 1. Separate summaries will also be presented for Treatment Period 2 based upon the particular treatment sequence received in Treatment Periods 1 and 2: CHS-1420/CHS-1420, Humira/Humira and Humira/CHS-1420.

Safety data for the open label extension will be summarized separately. The primary focus of these summaries will be events that are recorded after beginning open-label treatment and events that began in Treatment Period 1 or 2 and worsen in severity in Treatment Period 3. The events will be summarized by treatment received in Treatment Period 2 and overall.

Adverse events will be coded and classified by system organ class and preferred term using the Medical Dictionary for Regulatory Activities (MedDRA). Data summaries will be based on TEAEs. All TEAEs will be listed and summarized by the subjects' treatment group (Treatment Period specific) when the events were reported. A summary of all drug-related AEs will also be generated. If there are any SAEs or any AEs leading to the discontinuation of study drug, a separate data listing will be generated.

Clinical laboratory data will be summarized descriptively and listed by treatment (Treatment Period specific) group. The change from pre-dose to the end of the study will also be summarized. For selected laboratory assessments, the frequency of abnormal values will be tabulated where abnormal ranges are available.

Prior and concomitant medications will be coded with the World Health Organization Drug Dictionary (WHO-DD) and listed. All concomitant medication taken after first dosing of study drug will be summarized.

Vital sign and ECG data will be summarized and listed by dose group and visit.

8.2.4 Immunogenicity Analysis

The immunogenicity of CHS-1420 will be evaluated using ECL assay that uses an incubation of acid-dissociated serum samples with biotinylated and SULFO-TAB CHS-1420 reagents and subsequent excitation of the SULFO-TAG via an electrochemical reaction and the luminescent readout that correlates with the level of human anti-CHS-1420 or anti-adalimumab antibodies present in the serum. These data will be summarized descriptively by treatment received.

8.2.5 Pharmacokinetic Analysis

No overall PK analysis is planned in this study. However, serum samples will be collected at Week 0/Day 0 (pre-dose); at Weeks 2, 4, 8, 12, 16, 20, 24, 32, 40, 48 and at the Follow-up or ET visit 56 days (8 weeks) after the last dose of study drug. These samples will be stored and may be used to evaluate serum adalimumab levels in conjunction with assessment of AEs, loss of response, or compliance or to correlate with ADA assay results. The PK data will be summarized descriptively for any subject for whom these samples were assayed. These samples will not be used to assess biomarkers genetic markers. These serum samples will be destroyed 2 years after the completion of the study (database lock).

8.3 Determination of Sample Size

Approximately 500 subjects will be randomized and treated for this trial (approximately 250 per arm in Treatment Period 1).

The sample size was determined to show comparable efficacy for the following endpoint based upon the PASI at Week 12:

- The percentages of subjects in each group, CHS-1420 and Humira, achieving PASI-75 at Week 12

For the proportion of subjects achieving a PASI-75, it has been assumed that 70% of subjects will be responders in both the reference group, Humira, and the CHS-1420 group. The sample size will produce 90% power to establish equivalence at the 5% alpha level (2-sided) with an equivalence margin of 15% (absolute). Subjects who lack a PASI assessment at Week 12 will be considered non-responders in the primary analyses.

The margin for equivalence has been based statistically on the study results from Menter (2008) and to a lesser extent Gordon (2006). At 12 weeks, Menter had PASI-75 responses of 68% (554/814) for Humira and 5% (20/398) for control. This results in a treatment effect of approximately 63% (absolute). A lower 95% confidence bound (2-sided) for the difference in response rates can be calculated to be 59%. The proposed 15% margin for demonstrating equivalence is much smaller than the demonstrated benefit associated with Humira.

Though Gordon (2006) was a considerably smaller study, at 12 weeks this study had similar PASI-75 responses of 71% (70/99) for Humira and 19% (9/48) for control. This results in a treatment effect of approximately 52% (absolute). Pooling Gordon and Menter using the method of Der Simonian and Laird, yields a lower bound on the treatment effect of at least 50% which also supports the use of a 15% equivalence margin.

9 DATA MONITORING COMMITTEE

An independent data monitoring committee (DMC) will be convened under a separate charter to review accumulating data and monitor the safety of subjects over the course of the study. In addition to periodic reviews of the accumulating safety data, after the last subject completes the evaluations at the Week 12 visit (or a an earlier time if adequate Week 12 data are available), the DMC may review the unblinded database for safety and efficacy as well as whether or not equivalence is likely to be shown. The sponsor will remain blinded to individual subject treatment assignments and will be informed only of the group level results for public announcement. The DMC will not be requested to close the trial early for equivalence, only to recommend if the study is unlikely to achieve its objective. As such, no statistical adjustment is proposed.

10 DATA MANAGEMENT

10.1 Data Handling

Data will be recorded at the site in the subject's medical records and/or study documents and reviewed by the Clinical Research Associate (CRA) during monitoring visits. The CRA will verify data recorded in the eCRF system with source documents. All corrections or changes made to any study data must be appropriately tracked in an audit trail in the eCRF system. The eCRFs will be considered complete when all missing, incorrect, and/or inconsistent data have been accounted for.

10.2 Computer Systems

Data will be processed using a validated computer system conforming to regulatory requirements.

10.3 Data Entry

Data must be recorded using the eCRF system as the study is in progress. All study site personnel must log into the system using their secure usernames and passwords in order to enter, review, or correct study data. These procedures will comply with Title 21 of the FDA CFR (21 CFR Part 11). All passwords will be strictly confidential.

10.4 Medical Information Coding

For medical information, the following thesauri will be used:

- MedDRA for AEs and
- WHO-DD for concomitant medications.

10.5 Data Validation

Validation checks programmed within the eCRF system, as well as supplemental validation performed via review of the downloaded data, will be applied to the data in order to ensure accurate, consistent, and reliable data. Data identified as erroneous, or data that are missing, will be referred to the investigative site for resolution through data queries.

Once all data have been monitored, queried, cleaned, and considered ready for final database lock, the Investigator will electronically sign the eCRF for each subject at the completion of the study.

11 STUDY ADMINISTRATION

11.1 Regulatory and Ethical Considerations

11.1.1 Regulatory Authority Approval

This study will be conducted in accordance with International Conference on Harmonisation (ICH), Good Clinical Practice (GCP), an international ethical and scientific quality standard for designing, conducting, recording, and reporting studies that involve human subjects. Compliance with this standard provides public assurance that the rights, safety, and well-being of study subjects are protected, consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical study data are credible.

11.1.2 Ethics Approval

It is the responsibility of the Investigator to ensure that the appropriate IRB or EC has reviewed and approved this protocol prior to initiating the study.

The IRB/EC must also review and approve the investigative site's ICF, other written information provided to the subject, and all advertisements that may be used for subject recruitment.

If the protocol or the ICF are amended during the study, the Investigator is responsible for ensuring that the IRB/EC has reviewed and approved these amended documents. In addition, IRB/EC approval of the amended documents must be obtained before implementation and before new subjects are consented to participate in the study using the amended version of the ICF. The Investigator must provide the CRA with the dated IRB/EC approval of the amended documents as soon as it is available.

11.1.3 Subject Informed Consent

Prior to study entry, the Investigator, or a qualified person designated by the Investigator, will explain the nature, purpose, benefits, and risks of participation in the study to each subject, subject's legally acceptable representative, or impartial witness. Written informed consent must be obtained prior to the subject entering the study (before initiation of any study-related procedure and administration of the study medication). Sufficient time will be allowed to discuss any questions raised by the subject. If the consenting process is conducted by an Investigator designee, then the subject is offered the opportunity to discuss any of his/her questions or concerns regarding the ICF or the study with an Investigator. The Investigator or designated staff will document this process in the subject's medical record An ICF must be signed by all subjects. The process of obtaining informed consent will be in compliance with all federal regulations, ICH GCP, and local laws.

If the ICF is amended during the study, the Investigator must follow all applicable regulatory requirements pertaining to approval of the amended ICF by the IRB/EC. The investigative site must use the amended ICF for all new subjects and repeat the consent process with the amended ICF for any ongoing subjects, as applicable.

11.1.4 Investigator Reporting Requirements

In accordance with applicable regulatory requirements, the Investigator is solely obligated to inform the IRB/EC of progress of the study and notify the IRB/EC of study closure. The Investigator must also provide the Sponsor with copies of all IRB/EC correspondence that relates to study approvals, updates, or changes. The Investigator must also forward all IRB/EC renewals to the Sponsor or Sponsor's representative.

11.2 Study Monitoring

In accordance with applicable regulations, ICH GCP, and the procedures of the Sponsor and its designees, the CRA will periodically contact the investigative sites, including conducting on-site visits.

During these contacts, the monitoring activities will include:

- Checking and assessing the progress of the study;
- Reviewing study data collected to date for completeness and accuracy;
- Conducting source document verifications by reviewing each subject's eCRF against source documents; and
- Identifying any issues and addressing resolutions.

These activities will be done in order to verify that the:

- Data are authentic, accurate, and complete;
- Safety and rights of the subject are being protected; and
- Study is conducted in accordance with the currently approved protocol (and any amendments), GCP, and all applicable regulatory requirements.

In addition to contacts during the study, the CRA will visit the investigative site prior to the start of the study to discuss the protocol and data collection procedures with site personnel.

11.3 Quality Control

Quality assurance checks will be performed by Coherus or designee of all clinical studies that it sponsors. Before the enrollment of any subject in this study, Coherus or its designee will review and provide training as needed to the site Investigator and site personnel regarding the following: protocol, Investigator's Brochure, eCRFs and procedures for their completion, informed consent process, procedures for reporting SAEs, and subject randomization and drug tracking requirements. Site visits will be performed by the Sponsor and/or designees CRAs periodically throughout the study. During these visits, information recorded on the eCRFs will be verified against source documents, and requests for clarification or correction may be made. The eCRFs will be reviewed by the CRA for safety information, legibility, completeness, accuracy, and logical consistency. Computer programs that identify data inconsistencies may be used to help monitor the clinical study. If necessary, requests for clarification or correction will be sent to Investigators via data queries.

11.4 Study Initiation

Before the start of this study at each investigative site, the following documents must be on file with Sponsor or a Sponsor representative:

- All regulatory documentation (including FDA Form 1572 and financial disclosure forms) as required by local and national regulations (completed by the Investigator with the assistance of the Sponsor);
- Current curricula vitae and medical licenses (or medical registration numbers) of the Principal Investigator and all Sub-investigators;
- IRB/EC membership list and/or Department of Health and Human Services number, where applicable;
- Written documentation of IRB/EC approval of protocol (identified by the Sponsor protocol number or title and date of approval) and ICF(s) (identified by Sponsor protocol number or title and date of approval);
- A copy of the IRB/EC-approved ICF;
- Written documentation of IRB/EC review and approval of any advertising or other materials to be used for study recruitment, if applicable. Such materials must be reviewed and approved by the Sponsor prior to submission to the IRB/EC;
- Current laboratory certification of the laboratories performing the analyses (if other than a Sponsor-approved central laboratory), as well as current normal laboratory ranges for all laboratory tests; and
- A signed Clinical Site Agreement.

11.5 Study Completion

Upon completion of the study, the following activities, when applicable, must be conducted by the CRA and the Investigator:

- Return of all study data to the Sponsor;
- Data clarifications and/or resolutions;
- Accounting, reconciliation, and final disposition of used and unused study drug; and
- Review of site study records for completeness.

In addition, Coherus reserves the right to temporarily suspend or prematurely terminate this study for any reason as referenced in section 3.3.3.

If the study is suspended or terminated for safety reasons, Coherus or its designee will promptly inform the Investigator and the regulatory authorities of the suspension or termination of the study and the reasons for the action. The Investigator is responsible for promptly informing the IRB/EC and providing the reasons for the suspension or termination of the study.

If the study is prematurely terminated, all study data must be returned to Coherus. In addition, the investigative site must conduct the final disposition of all unused study drugs in accordance with Coherus' procedures for the study.

11.6 Site Termination

The Sponsor has the right to terminate a study site at any time for any reason. Study termination can occur due to last reason specified in 3.3.3 and subject follow-up will be performed in compliance with the conditions set forth in 21 CFR Parts 312.50 and 312.56.

11.7 Records Retention

Records of subjects, source documents, monitoring visit logs, inventory of study product, regulatory documents, and other Coherus correspondence pertaining to the study must be kept in the appropriate study files at the site. Source documents include all recordings and observations or notations of clinical activities and all reports and records necessary for the evaluation and reconstruction of the clinical study. These records will be retained in a secure file for the period required by the institution or site policy. Prior to the transfer or destruction of these records, Coherus must be notified in writing and be given the opportunity to continue to store such records.

11.8 Confidentiality of Information

Subjects' names will remain confidential and will not be included in the database. All study findings will be stored in electronic databases. The Investigator will maintain a subject identification list (subject and treatment numbers with the corresponding subject names) to enable records to be identified.

11.9 Publication Policy

Coherus is responsible for the final clinical study report prepared according to the ICH guideline on structure and contents of clinical study reports. A final clinical study report will be prepared and include any subject who has signed an ICF, regardless of whether the study is completed or prematurely terminated. If appropriate, an abbreviated report may be prepared. The clinical study report will be in compliance with any applicable regulatory requirements and national laws and will be in English.

All unpublished information given to the Investigator by Coherus shall not be published or disclosed to a third party without the prior written consent of Coherus.

When the Sponsor or designee generate reports from the data collected in this study for presentation to regulatory authorities, drafts may be circulated to the Investigator for comments and suggestions. An endorsement of the final report will be sought from the Investigator when required by local regulatory agencies.

No patent application(s) based on the results of the study may be made by the Investigator nor may assistance be given to any third party to make such an application without the written authorization of Coherus.

The Principal Investigator or anyone else working on the study may not submit any publications, papers, abstracts, or other written materials or oral presentations related to the study without the written consent of Coherus.

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APPENDIX A: ADALIMUMAB PRESCRIBING INFORMATION

The US-sourced Humira (adalimumab) prescribing information can be viewed electronically at the following web link: http://www.rxabbvie.com/pdf/humira.pdf.

APPENDIX B: PSORIASIS AREA AND SEVERITY INDEX

PASI Scoring System: Component 1

Body Region	Body Surface Area (%)
Head	10
Upper Extremities	20
Trunk	30
Lower Extremities (includes buttocks)	40

PASI Scoring System: Component 2

Rating of Individual Parameter	0 = Nil, 4 = Severe
Erythema	0-4
Infiltration	0-4
Desquamation	0-4

PASI Scoring System: Component 3

Percentage of Body Region Affected (%)	Extent Indicator
No involvement	0
<10	1
10 to <30	2
30 to <50	3
50 to <70	4
70 to <90	5
90 to 100	6

$PASI = 0.1 (E_h+I_h+D_h) A_h +$
$0.2 (E_u+I_u+D_u) A_u +$
$0.3 (E_t+I_t+D_t) A_t +$
$0.4 (E_l+I_l+D_l) A_l$

Key:
E = erythema
I = infiltration
D = desquamation
A = area of psoriatic involvement

h = head
t = trunk
u = upper extremities
l = lower extremities

Fredriksson T, Pettersson U. Severe psoriasis-oral therapy with a new retinoid. *Dermatologica* 1978; 157:238-244 (Fredriksson & Pettersson, 1978)

Psoriasis Activity and Severity Index Worksheet

		Head	Upper Extremities	Trunk	Lower Extremities + Buttock
1	Redness 0-4				
2	Thickness 0-4				
3	Scaliness 0-4				
4	Sum of rows 1,2,3				
5	Affected area %				
6	Area Score 0-6 (see below)				
7	Area Weights	0.1	0.2	0.3	0.4
8	Row 4 X Row 6 X Row 7				
9	**PASI Sum of Row 8**				**Total =**

Table 1 Elements of the Psoriasis Area and Severity Index (PASI)*

		Head	Upper extremities	Trunk	Lower extremities
1	Redness†				
2	Thickness†				
3	Scale†				
4	Sum of rows 1, 2, and 3				
5	Area score‡				
6	Score of row 4×row 5×the area multiplier	row 4×row 5×0.1	row 4×row 5×0.2	row 4×row 5×0.3	row 4×row 5×0.4
7	**Sum row 6 for each column for PASI score**				

**Steps in generating PASI score*
(*a*) Divide body into four areas: head, arms, trunk to groin, and legs to top of buttocks.
(*b*) Generate an average score for the erythema, thickness, and scale for each of the 4 areas (0=clear; 1–4=increasing severity)†.
(*c*) Sum scores of erythema, thickness, and scale for each area.
(*d*) Generate a percentage for skin covered with psoriasis for each area and convert that to a 0–6 scale (0=0%; 1=<10%; 2=10–<30%; 3=30–<50%; 4=50–<70%; 5=70–<90%; 6=90–100%).
(*e*) Multiply score of item (*c*) above times item (*d*) above for each area and multiply that by 0.1, 0.2, 0.3, and 0.4 for head, arms, trunk, and legs, respectively.
(*f*) Add these scores to get the PASI score.
†Erythema, induration and scale are measured on a 0–4 scale (none, slight, mild, moderate, severe)
‡*Area scoring criteria* (score: % involvement)
0: 0 (clear)
1: <10%
2: 10–<30%
3: 30–<50%
4: 50–<70%
5: 70–<90%
6: 90–<100%

Adapted from Feldman & Krueger, 2005 (Feldman & Krueger, 2005)

APPENDIX D: PHYSICIAN'S STATIC GLOBAL ASSESSMENT

Physician's Static Global Assessment

Induration (I) (averaged over all lesions): _____

0=no evidence of plaque elevation
1=minimal plaque elevation, =0.25 mm
2=mild plaque elevation, =0.5 mm
3=moderate plaque elevation, =0.75 mm
4= severe plaque elevation, =1 mm
5=very severe plaque elevation, =1.25 mm or more

Erythema (E) (averaged over all lesions): _____

0=no evidence of erythema, hyperpigmentation may be present
1=faint erythema
2=light red coloration
3=moderate red coloration
4=bright red coloration
5=dusky to deep red coloration

Scaling (S) (averaged over all lesions): _____

0=no evidence of scaling
1=minimal; occasional fine scale over less than 5% of the lesion
2=mild; fine scale dominates
3=moderate; coarse scale predominates
4=severe; thick, non-tenacious scale dominates
5=very severe; very thick tenacious scale predominates

Add I+E+S= _____ / 3= _____ (Total Average)

Physician's Static Global Assessment based upon the Total Average

0=Clear, except for residual discoloration
1=Minimal-majority of lesions have individual scores for I+E+S / 3 that averages 1
2=Mild-majority of lesions have individual scores for I+E+S / 3 that averages 2
3=Moderate-majority of lesions have individual scores for I+E+S / 3 that averages 3
4=Severe-majority of lesions have individual scores for I+E+S / 3 that averages 4
5=Very Severe-majority of lesions have individual scores for I+E+S / 3 that averages 5

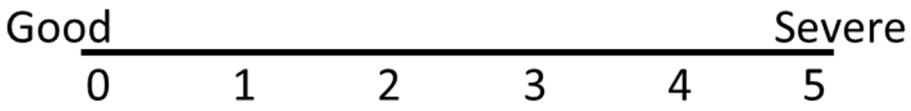
Note: Scores should be rounded to the nearest whole number.

Investigator's signature: _____Date: _____

Adapted from Leondardi et al., 2003 (Leonardi, et al., 2003)

APPENDIX E: SUBJECT'S GLOBAL ASSESSMENT

Considering all of the ways your psoriasis has affected you, how do you feel your psoriasis is today on a scale from 0 (good) to 5 (severe)?



Adapted from Leonardi et al., 2003 (Leonardi, et al., 2003)

APPENDIX F: HEALTH ASSESSMENT QUESTIONNAIRE – DISABILITY INDEX

HAQ1-5

Subject Initial: ___ ___ ___ Subject Number: ___ ___ ___-___ ___ ___ Visit Date: ___ ___/___ ___/ ___ ___ ___ ___
(mm/dd/yyyy)

*I **confirm** that the information on this module is accurate.*	Patient's initials

HEALTH ASSESSMENT QUESTIONNAIRE

In this section we are interested in learning how your illness affects your ability to function in daily life.

Please check the response which best describes your usual abilities OVER THE PAST WEEK:

	Without ANY Difficulty	With SOME Difficulty	With MUCH Difficulty	UNABLE To Do
DRESSING & GROOMING **Are you able to:**				
- Dress yourself, including tying shoelaces and doing buttons?	❑	❑	❑	❑
- Shampoo your hair?	❑	❑	❑	❑
ARISING **Are you able to:**				
- Stand up from a straight chair?	❑	❑	❑	❑
- Get in and out of bed?	❑	❑	❑	❑
EATING **Are you able to:**				
- Cut your meat?	❑	❑	❑	❑
- Lift a full cup or glass to your mouth?	❑	❑	❑	❑
- Open a new milk carton?	❑	❑	❑	❑

English for USA_V13

HAQ2-5

Subject Initial: ___ ___ ___ Subject Number: ___ ___ ___-___ ___ ___ Visit Date: ___ ___/___ ___/___ ___ ___ ___
(mm/dd/yyyy)

*I **confirm** that the information on this module is accurate.*	Patient's initials

HEALTH ASSESSMENT QUESTIONNAIRE

Please check the response which best describes your usual abilities OVER THE PAST WEEK:

WALKING Are you able to:	**Without ANY Difficulty**	**With SOME Difficulty**	**With MUCH Difficulty**	**UNABLE To Do**
- Walk outdoors on flat ground?	❑	❑	❑	❑
- Climb up five steps?	❑	❑	❑	❑

Please check any AIDS or DEVICES that you usually use for any of the activities on pages 1 and 2:

❑ Cane ❑ Crutches ❑ Built up or special utensils
❑ Walker ❑ Wheelchair ❑ Special or built up chair
❑ Devices used for dressing

Please check any categories for which you usually need HELP FROM ANOTHER PERSON:

❑ Dressing and Grooming ❑ Arising ❑ Eating ❑ Walking

English for USA_V13

HAQ3-5

Subject Initial: ___ ___ ___ Subject Number: ___ ___ ___-___ ___ ___ Visit Date:___ ___/___ ___/___ ___ ___ ___
(mm/dd/yyyy)

*I **confirm** that the information on this module is accurate.*	Patient's initials

HEALTH ASSESSMENT QUESTIONNAIRE

Please check the response which best describes your usual abilities OVER THE PAST WEEK:

HYGIENE **Are you able to:**	**Without ANY Difficulty**	**With SOME Difficulty**	**With MUCH Difficulty**	**UNABLE To Do**
- Wash and dry your body?	❑	❑	❑	❑
- Take a tub bath?	❑	❑	❑	❑
- Get on and off the toilet?	❑	❑	❑	❑
REACH **Are you able to:**				
- Reach and get down a 5 pound object (such as a bag of sugar) from just above your head?	❑	❑	❑	❑
- Bend down to pick up clothing from the floor?	❑	❑	❑	❑
GRIP **Are you able to:**				
- Open car doors?	❑	❑	❑	❑
- Open jars which have been previously opened?	❑	❑	❑	❑
- Turn faucets on and off?	❑	❑	❑	❑

English for USA_V13

HAQ4-5

Subject Initial: ___ ___ ___ Subject Number: ___ ___ ___-___ ___ ___ Visit Date: ___ ___/___ ___/___ ___ ___ ___
(mm/dd/yyyy)

*I **confirm** that the information on this module is accurate.*	Patient's initials

HEALTH ASSESSMENT QUESTIONNAIRE

Please check the response which best describes your usual abilities OVER THE PAST WEEK:

ACTIVITIES **Are you able to:**	**Without ANY Difficulty**	**With SOME Difficulty**	**With MUCH Difficulty**	**UNABLE To Do**
- Run errands and shop?	❑	❑	❑	❑
- Get in and out of a car?	❑	❑	❑	❑
- Do chores such as vacuuming or yardwork?	❑	❑	❑	❑

Please check any AIDS or DEVICES that you usually use for any of the activities on pages 3 and 4:

❑ Raised toilet seat
❑ Bathtub seat
❑ Jar opener *(for jars previously opened)*
❑ Bathtub bar
❑ Long-handled appliances for reach
❑ Long-handled appliances in bathroom

Please check any categories for which you usually need HELP FROM ANOTHER PERSON:

❑ Hygiene ❑ Reach ❑ Gripping and opening things ❑ Errands and chores

English for USA_V13

HAQ5-5

Subject Initial: ___ ___ ___ Subject Number: ___ ___ ___-___ ___ ___ Visit Date: ___ ___/___ ___/___ ___ ___ ___
(mm/dd/yyyy)

*I **confirm** that the information on this module is accurate.*	Patient's initials

Your ACTIVITIES: To what extent are you able to carry out your everyday physical activities such as walking, climbing stairs, carrying groceries, or moving a chair?:

COMPLETELY	MOSTLY	MODERATELY	A LITTLE	NOT AT ALL
❑	❑	❑	❑	❑

We are also interested in learning whether or not you are affected by pain because of your illness.

How much pain have you had because of your illness IN THE PAST WEEK?

PLACE A VERICAL (|) MARK ON THE LINE TO INDICATE THE SEVERITY OF THE PAIN

Considering all the ways your illness affects you, mark an "X" through the line for how well you are doing.

English for USA_V13

Scoring

Score the number circled for each item. If more than one consecutive number is circled for one item, code the higher number (more difficulty). If responses are not consecutive, code as blank.

There are eight categories; first score within each category:

- Dressing and Grooming, includes items 1 and 2
- Arising, includes items 3 and 4
- Eating, includes items 5, 6, and 7
- Walking, includes items 8 and 9
- Hygiene, includes items 10, 11, and 12
- Reach, includes items 13 and 14
- Grip, includes items 15, 16, and 17
- Activities, includes items 18, 19, and 20

Each of the items has a companion aids-devices variable that is used to record what type(s) of assistance, if any, the subject uses for his/her usual activities. These variables are coded as follows:

- 0 = No assistance is needed
- 1 = A special device is used by the subject in his/her usual activities
- 2 = The subject usually needs help from another person
- 3 = The subject usually needs BOTH a special device AND help from another person

Assignment of devices to particular disability categories assumes that the devices are used only for the purpose for which they are designed. For example, if an individual indicates that he/she uses a cane, it is presumed that they use the cane as an aid in walking. However, it is possible for that subject to use that cane as an aid in performing other activities. For example, the subject may check off the cane listed at the bottom of the page 1 (or write “cane” under the “other” slot) and then write a note in the margin stating that the cane is also used on a regular basis as an aid in helping them rise out of a chair and to rise off of the toilet. In such a case, the variables should be coded as “1” to reflect the subject's use of a cane in these three areas of daily functioning. Devices written in the “Other” sections or notes written next to any component questions are considered if they would be used for any of the stated categories. Permanent adaptations of the person's environment (e.g., changing faucets in the bathroom or kitchen, using Velcro closures on clothing) should also be counted as aids and devices.

The score for each category is the single response within the category with the highest score (greatest difficulty). For example, in the "Eating" category, there are two answers (one for each item). If "Cut your food with a knife or fork" is marked as "3" and "Lift a full cup or glass to your mouth" is marked as "0", then the score for the "Eating" category would be "3" (the response indicating the greatest difficulty within the category). If a component question is left blank or the response is too ambiguous to assign a score, then the score that that category is determined by the remaining completed question(s). However, if any "aids or devices" and/or "help from another person" items at the bottom of each page are checked, the category to which they apply is adjusted upward to "2". If the basic score is already "2" or "3", the score remains unchanged. "Aids or devices" and "help from another person" can only change a category's score to "2"; they do not change the score to a "1" or a "3".

The score for the disability index is the mean of the eight category scores. If more than two of the categories, or 25%, are missing, do not score the scale. If fewer than 2 of the categories are missing, divide the sum of the categories by the number of answered categories. Alternately, you can score the index without using the aids and devices questions (leaving the aids and devices off the questionnaire). The higher score indicates greater disability.

Characteristics

Tested on 1,079 subjects with arthritis.

No. of items	Observed Range	Mean	Standard Deviation	Internal Consistency Reliability	Test-Retest Reliability
20	0-3	1.06	0.753		

Source of Psychometric Data

Stanford ARAMIS/Arthritis Self-Management Study. Psychometrics unpublished.

Comments

This is the Stanford Health Assessment Questionnaire disability scale. It should be noted that the items have been chosen as they represent use of every major joint in the body. While closely related to an ADL scale this is not an ADL scale but rather a disability scale. The Disability Index is sensitive to change and is a good predictor of future disability and costs. Test-retest correlations have ranged from 0.87 to 0.99. Correlations between interview and questionnaire format have ranged from 0.85 to 0.95. Validity has been demonstrated in literally hundreds of studies. There is consensus that the HAQ Disability Index possesses face and content validity. Correlations between questionnaire or interview scores and task performance have ranged from 0.71 to 0.95 demonstrating criterion validity. The construct/convergent validity, predictive validity and sensitivity to change have also been established in numerous observational studies and clinical trials. The HAQ Disability Index has also demonstrated a high level of convergent validity based on the pattern of correlations with other clinical and laboratory measures.

We use the 8-item scale in our studies now, as it is less burdensome for our participants.

Reprinted with permission. This scale available in Spanish.

References: (Fries, Spitz, Kraines, & Holman, 1980)

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Downloaded from Stanford.edu website.
http://patienteducation.stanford.edu/research/haq20.html. Accessed February 13, 2013.

APPENDIX G: DERMATOLOGY LIFE QUALITY INDEX

DERMATOLOGY LIFE QUALITY INDEX

DLQI

Hospital No: Date:
Name: Score:
Address: Diagnosis:

The aim of this questionnaire is to measure how much your skin problem has affected your life OVER THE LAST WEEK. Please tick one box for each question.

1.	Over the last week, how **itchy**, **sore**, **painful** or **stinging** has your skin been?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	
2.	Over the last week, how **embarrassed** or **self conscious** have you been because of your skin?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	
3.	Over the last week, how much has your skin interfered with you going **shopping** or looking after your **home** or **garden**?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	 Not relevant ❒
4.	Over the last week, how much has your skin influenced the **clothes** you wear?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	 Not relevant ❒
5.	Over the last week, how much has your skin affected any **social** or **leisure** activities?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	 Not relevant ❒
6.	Over the last week, how much has your skin made it difficult for you to do any **sport**?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	 Not relevant ❒
7.	Over the last week, has your skin prevented you from **working** or **studying**?	Yes No	❒ ❒	 Not relevant ❒
	If "No", over the last week how much has your skin been a problem at **work** or **studying**?	A lot A little Not at all	❒ ❒ ❒	
8.	Over the last week, how much has your skin created problems with your **partner** or any of your **close friends** or **relatives**?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	 Not relevant ❒
9.	Over the last week, how much has your skin caused any **sexual difficulties**?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	 Not relevant ❒
10.	Over the last week, how much of a problem has the **treatment** for your skin been, for example by making your home messy, or by taking up time?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	 Not relevant ❒

Please check you have answered EVERY question. Thank you.

APPENDIX H: EUROQOL 5-DIMENSION HEALTH STATUS QUESTIONNAIRE

Under each heading, please tick the ONE box that best describes your hea

MOBILITY

I have no problems in walking about ❑
I have slight problems in walking about ❑
I have moderate problems in walking about ❑
I have severe problems in walking about ❑
I am unable to walk about ❑

SELF-CARE

I have no problems washing or dressing myself ❑
I have slight problems washing or dressing myself ❑
I have moderate problems washing or dressing myself ❑
I have severe problems washing or dressing myself ❑
I am unable to wash or dress myself ❑

USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure activities)*

I have no problems doing my usual activities ❑
I have slight problems doing my usual activities ❑
I have moderate problems doing my usual activities ❑
I have severe problems doing my usual activities ❑
I am unable to do my usual activities ❑

PAIN / DISCOMFORT

I have no pain or discomfort ❑
I have slight pain or discomfort ❑
I have moderate pain or discomfort ❑
I have severe pain or discomfort ❑
I have extreme pain or discomfort ❑

ANXIETY / DEPRESSION

I am not anxious or depressed ❑
I am slightly anxious or depressed ❑
I am moderately anxious or depressed ❑
I am severely anxious or depressed ❑
I am extremely anxious or depressed ❑

- We would like to know how good or bad your health is TODAY.
- This scale is numbered from 0 to 100.
- 100 means the best health you can imagine.
  0 means the worst health you can imagine.
- Mark an X on the scale on the scale to indicate how your health is TODAY.
- Now, please write the number you marked on the scale in the box below.

YOUR HEALTH TODAY = ☐