1.0 Title Page

AbbVie

REGISTRY PROTOCOL P10-023

A 10-Year, Post-marketing, Observational, Registry to Assess Long Term Safety of HUMIRA® (Adalimumab) in Adult Patients with Chronic Plaque Psoriasis (Ps)

Incorporating Amendments 1 and 2, Administrative Changes 1 and 2 and Amendment 3

Product Name:	HUMIRA® (adalimumab)
Type of Study:	A Post-marketing, Observational Registry
Date:	08 October 2013
Investigators:	Multicenter registry (investigator information on file at AbbVie)
Sponsor:	AbbVie Inc. (AbbVie)
Sponsor/Emergency Contact:	[redacted]
CRO:	

This registry will be conducted in compliance with this protocol.

1.1 Protocol Amendment: Summary of Changes

The purpose of this amendment is as follows:

- Section 3.1 Safety Information: Add new safety monitoring requirements.

  Rationale: To comply with an FDA requested, TNF-inhibitor class wide exploration of the rare appearance of malignancy in patients ≤ 30 years of age.
- Section 6.4 Registry Duration: Clarify the duration of follow-up for patients who develop an AESI or SAE.

  Rationale: Follow-up duration is based on post-marketing reporting requirements.
- Section 7.1.2 Adverse Events of Special Interest: Delete Kaposi's sarcoma from the list of serious and non-serious opportunistic infections.

  Rationale: Kaposi's sarcoma is a type of malignancy, and was removed from the list to more accurately represent examples of opportunistic infections.
- Section 7.3 Relationship to Pharmaceutical Product: Clarify language in regards to data collection requirements for Other cause of event for SAEs.

  Rationale: To align with standard Safety language.
- Section 7.4 Adverse Event Collection Period: Clarify the duration of follow-up for patients who develop an adverse event of interest or SAE.

  Rationale: Follow-up duration is based on post-marketing reporting requirements.
- Section 7.4 Adverse Event Collection Period: Revise language for ongoing events at the time of enrollment for roll-over patients.

  Rationale: All roll-over clinical studies have been completed and any updates for ongoing events at the time of enrollment will be collected within the registry database.

- Section 7.6 Pregnancy Reporting: The data collection period for pregnancy was updated to be from the date of first dose of Humira in registry through 150 days following the last dose of registry drug or end of registry (whichever is longer). The requirement to register for the AbbVie sponsored pregnancy registry for US, Puerto Rico and Canada was removed. In addition, the time period to report any event of pregnancy, spontaneous abortion, stillbirth, or congenital anomaly was updated to be within 24 hours.

  Rationale: Admission to the pregnancy registry is no longer available and the reporting time for pregnancy and pregnancy related events was updated to reflect current standard SAE reporting requirements.
- Section 8.1 Quality Assurance: Update language related to monitoring visits.

  Rationale: Specific details regarding site monitoring are identified in the Monitoring Plan.
- Section 10.1 Analyzable Populations: Clarify that the New Prescription Population is a subset of the All Treated Patient Population.
- Section 10.2 Demographics and Registry Enrollment Characteristics: Clarify the duration of observation and the calculation of exposure duration (distinguish total exposure and registry exposure and adapt calculation of exposure during treatment-interruptions).

  Rationale: Modify to ensure accuracy and reduction of bias in the statistical analyses: Align duration of observation, registry exposure and total exposure duration calculation with the definition of Observational, Registry Treatment-Emergent and All Treatment-Emergent Adverse Events, respectively. Use an approach for exposure calculation which is applicable for all subjects in the registry and is consistent with the approach in other registries.
- Section 10.3 Safety Analyses:
  - Clarify patients not covered by any of the analysis populations, who experience an Adverse Event will be reported in a separate listing.
  - Add clarification in the definitions of Observational Adverse Events and Treatment-Emergent Adverse Events.

    Rationale: Align observation/exposure duration calculation and definition of Observational/Treatment-Emergent Adverse Events, respectively.

- Section 10.3.4 Analysis of Observational AEs Excluding HCP Process: Correct the period for analysis of Observational Adverse Events.
- Section 10.5 Interim Analyses: Clarify requirements for submission of interim analyses reports to Regulatory Agencies.

  Rationale: Submission of interim analyses reports is based on requirements of applicable regulatory agencies.
- Correct minor typographical and grammatical errors throughout the document.
- Administrative Changes:
  - Incorporate Administrative Change 1:
    - Title page: Update contact information.
    - Section 7.1.2 Adverse Events of Special Interest: Correct two typos in a description of serious and non-serious opportunistic infections.
      - Paracoccidioides
      - Cytomagalovirus
  - Incorporate Administrative Change 2:
    - Change Sponsor from Abbott Laboratories (Abbott) to AbbVie in all instances found within the protocol and included new Sponsor address.

For an itemized list of all changes made to the protocol under this amendment, refer to Appendix O.

2.0 Table of Contents

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3.0 Introduction

Psoriasis (Ps) is a chronic immunologic disease characterized by marked inflammation and thickening of the epidermis, resulting in thick, scaly plaques involving the skin. It affects 1% to 3% of the general population, with North America and Europe having the highest disease prevalence.[1] Psoriasis equally affects men and women, with peak onset of symptoms during the teen years and again in the mid 50's. Many factors predispose a person to psoriasis, including genetic, endogenous and exogenous triggers such as trauma, medications and infection.

There are several types of psoriasis, classified according to cutaneous presentation: plaque psoriasis, guttate psoriasis, erythrodermic psoriasis, generalized pustular and localized pustular psoriasis, and inverse or intertriginous psoriasis. Plaque psoriasis is the most common type seen in 75% to 80% of psoriasis patients.[2] Nail involvement is sometimes associated and up to 30% of patients may have associated psoriatic arthritis (PsA).[3,4,6]

Treatment depends on the extent of disease. Topical corticosteroids are commonly used for mild to moderate cases. Keratolytic agents, anthralin, coal tar, vitamin D analogs, and retinoids are also used as topical medications.[7] For more widespread disease, phototherapy such as ultraviolet B (UVB) or ultraviolet A and psoralen (PUVA) is commonly used. Systemic therapy, including methotrexate (MTX), cyclosporine and synthetic retinoids may be effective in patients with severe disease.[8] Due to the toxicity of systemic agents, these medications are generally administered in rotation to avoid long-term or cumulative toxicities.[9]

Expression of tumor necrosis factor-alpha (TNF-α) and the presence of activated T lymphocytes in psoriatic plaques suggest their involvement in the pathogenesis of the disease.[10] Additionally, clinical trial data have shown that inhibitors of TNF-α are effective in treating psoriasis.[11,12]

HUMIRA® is a recombinant human immunoglobulin (IgG1) monoclonal antibody containing only human peptide sequences. HUMIRA® is produced by recombinant DNA technology in a mammalian cell expression system. It consists of 1330 amino acids and has a molecular weight of approximately 148 kilodaltons. HUMIRA® is comprised of fully human heavy and light chain variable regions, which confer specificity to human TNF, and human IgG1 heavy chain and kappa light chain sequences. HUMIRA® binds with high affinity and specificity to soluble TNF-α but not to lymphotoxin-α (TNF-β).

TNF is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. Elevated levels of TNF play an important role in pathologic inflammation. HUMIRA® binds specifically to TNF and neutralizes the biological function of TNF by blocking its interaction with the p55 and p75 cell surface TNF receptors.

HUMIRA® also modulates biological responses that are induced or regulated by TNF.

After treatment with HUMIRA® levels of acute phase reactants of inflammation (C-reactive protein [CRP] and erythrocyte sedimentation rate [ESR]) and serum cytokines rapidly decrease.

As of 06 November 2009 HUMIRA® has been evaluated in approximately 24,228 subjects with rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), Crohn's disease (CD), psoriasis (Ps), juvenile rheumatoid (idiopathic) arthritis (JRA/JIA) and ulcerative colitis (UC).

HUMIRA® is approved for the treatment of RA, AS, PsA, CD, Ps and JIA both in the European Union (EU) and in the United States (US) and in a number of countries worldwide.

Cumulative postmarketing exposure from the International Birth Date (31 December 2002, approval in USA) to 31 December 2009 has been estimated to be 1,054,068 Patient Treatment Years (PTY).

HUMIRA® has been granted a Marketing Authorization by both the European Commission and the US Food and Drug Administration (FDA) for treatment of adults with chronic plaque psoriasis. Approval was based on controlled clinical studies involving subjects with moderate to severe chronic plaque psoriasis. In these studies, HUMIRA® was well tolerated and the pattern and frequency of adverse events (AEs) were comparable to those seen in the other populations previously studied. Refer to the most current local product label for a summary of these studies and a comprehensive presentation of the safety information.

Fatalities, serious infections, and sepsis have been reported with the use of TNF antagonists. Many of the serious infections have occurred in subjects on concomitant immunosuppressive therapy that, in addition to their underlying immune disorder, could predispose them to infections. Tuberculosis (TB) has also been observed in subjects treated with TNF antagonists, including HUMIRA®. The event rate for TB in the Ps development program is consistent with the global HUMIRA® rate.

TNF antagonists including HUMIRA® have been associated with cases of demyelinating disease. Serious allergic adverse reactions have been reported in subjects following subcutaneous administration of HUMIRA®.

Patients with psoriasis have an increased risk of lymphoma, with the lymphoma risk being higher in patients with severe psoriasis (i.e., RR = 8.0 for patients requiring treatment with a systemic agent) than in patients with less severe psoriasis (i.e., RR = 2.1).[13] A more recent study also found a higher risk of lymphoma in psoriasis patients with severe psoriasis compared to mild psoriasis, with the suggestion of a strong association between psoriasis and cutaneous T-cell lymphoma.[5]

The risks of squamous cell carcinoma (SCC) and basal cell carcinoma (BCC) are known to be increased in patients with psoriasis. The standardized incidence ratio (SIR) has been reported to be 2.2 for BCC and 4.1 for SCC.[14] A meta-analysis confirmed the high risk of SCC in psoriasis patients treated with PUVA, as well as an increase in the ratio of SCC to BCC as the PUVA exposure level increased.[15] During the controlled portions of

HUMIRA® rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, and plaque psoriasis clinical trials, the rate of non-melanoma skin cancers was higher among HUMIRA®-treated subjects compared with control subjects. Accurate assessment of the magnitude of the difference in risk for non-melanoma skin cancer among HUMIRA®-treated psoriasis subjects compared with control subjects is complicated by the possibility of ascertainment bias, if established skin cancers have been obscured initially by coexisting psoriatic plaques.[19]

The risk of malignant melanoma has been reported to be increased in patients with a medical history of extensive immunosuppressant therapy or psoriasis patients with extensive PUVA exposure.[16] However other studies have not shown an increase in the risk of melanoma in patients with psoriasis.[17,18]

In the controlled portions of clinical trials of TNF-antagonists, more cases of malignancies including lymphoma and non-melanoma skin cancer have been observed among patients receiving a TNF-antagonist compared with control patients. The size of the control group and limited duration of the controlled portions of studies precludes the ability to draw firm conclusions. Furthermore, there is an increased background lymphoma risk in rheumatoid arthritis patients with long-standing, highly active, inflammatory disease, which complicates the risk estimation.[27-29]

Very rare postmarketing reports of hepatosplenic T-cell lymphoma (HSTCL), a rare aggressive lymphoma that is often fatal, have been identified in patients treated with HUMIRA®. Most of the patients had prior infliximab therapy as well as concomitant azathioprine or 6-mercaptopurine use for Crohn's disease. The causal association of HSTCL with HUMIRA® is not clear.

Malignancies, some fatal, have been reported among children and adolescents who received treatment with TNF-blocking agents. Most of the patients were receiving concomitant immunosuppressants. These cases were reported post-marketing and were derived from a variety of sources including registries and spontaneous postmarketing reports.

There have also been cases of acute and chronic leukemia reported in association with the use of TNF-antagonists including HUMIRA®. With the current knowledge, a possible risk for the development of lymphomas or other malignancies in patients treated with a TNF-antagonist cannot be excluded.

No studies have been conducted that include patients with a history of malignancy other than a successfully treated non-metastatic cutaneous squamous cell and/or basal cell carcinoma and/or localized carcinoma in situ of the cervix. Further, there are no data currently available on subjects who develop malignancy while receiving HUMIRA® and subsequently continue treatment. Thus additional caution should be exercised in considering HUMIRA® treatment in these patients.

3.1 Safety Information

Adalimumab therapy has a well established and well described safety profile based on extensive post-marketing experience and continued clinical trial patient exposure since the first approved indication in 2002 for rheumatoid arthritis. A detailed discussion of the clinical toxicology, metabolism, pharmacology and safety experience with adalimumab can be found in the current Package Insert. AbbVie is committed to continue to collect safety information including those events that may occur in this registry in order to confirm this established safety profile and to identify any unknown potential adverse reactions, rare events and those events with a long latency. AbbVie is participating in an FDA-requested, TNF inhibitor class wide exploration of the rare appearance of malignancy in patients who are 30 years of age or younger at the time of diagnosis. The risk of malignancy in this age group has not been established and is difficult to study due to its rarity. AbbVie appreciates your attention to the additional reporting requirements needed in this unlikely event, outlined in Section 7.5 under Serious Adverse Event Reporting.

4.0 Rationale

This protocol describes a post-marketing, observational registry that will evaluate the long-term safety and effectiveness of HUMIRA® as used in routine clinical practice in

adult patients with moderate to severe chronic plaque psoriasis, who are candidates for systemic therapy or phototherapy. This registry is part of a post-marketing commitment from AbbVie to the FDA and European Medicines Agency (EMA).

The participating physicians, with regard to countries and sites, will be representative of the dermatologists who prescribe HUMIRA® for patients with psoriasis in North America and Europe. Similarly, the patients selected for enrollment in the registry will be representative of the population for which HUMIRA® is used to treat psoriasis in the participating countries. The patients will receive commercial HUMIRA® that will be prescribed per their local prescribing information.

The data collected in this registry will be complementary to those from the pre-registration studies of HUMIRA® in psoriasis. The management of the patients in this registry will reflect the use of HUMIRA® in current clinical practice. The participating physician is free to determine the appropriate therapy for each patient and make treatment choices as deemed clinically necessary. Patients who consent to participate in the registry, will be followed for up to 10 years, providing important long term safety and effectiveness data on HUMIRA® in Ps patients. A follow-up procedure for patients who discontinue from the registry has been added to the protocol to maximize the safety information collected from all registry patients. The follow-up procedure will be referred to as the direct to Health Care Provider process (HCP) throughout the protocol.

5.0 Registry Objectives

The primary objective of this registry is to evaluate the long-term safety of HUMIRA® in adult Ps patients who are treated as recommended in the product label. The secondary objective is to evaluate long-term effectiveness of HUMIRA® in adult Ps patients in the United States who are treated as recommended in the product label.

6.0 Investigational Plan

Participating patients will agree to participate in the registry for up to 10 years, including patients who discontinue HUMIRA® before 10 years of participation in the registry.

This registry will assess the incidence and rate of HUMIRA® observational and treatment-emergent SAEs and AEs of Special Interest in Ps patients over a 10 year period.

6.1 Selection of Population

After a decision has been made between the physician and the patient to use HUMIRA® as part of usual care for chronic plaque psoriasis, sites will be encouraged to offer enrollment to all eligible patients. Patients from HUMIRA® clinical trials will be offered enrollment in the registry. Prior to collecting any registry related information, written patient informed consent must be obtained.

Patients who discontinue from the registry, but decide to participate in the direct to HCP Process for safety data collection, will be asked to sign a Patient Authorization for Use/Disclosure of Data form.

6.1.1 Inclusion Criteria

A patient will be eligible for participation in this registry if he/she meets all of the following criteria:

1. An adult patient (18 years of age or older) with chronic plaque psoriasis who has been prescribed HUMIRA® therapy according to the local product labeling and meets one of the following criteria:
    - Newly initiated (within 4 weeks of registry entry) on HUMIRA® therapy;
    - Initiated HUMIRA® therapy in the past and:
        - Has received continuous (no more than 70 consecutive days off drug) HUMIRA® therapy and the physician can provide source documentation of SAEs, AEs of Special Interest, and dosing information since initiation of therapy.

          OR

- Is entering after participation in an AbbVie HUMIRA (adalimumab) sponsored study and has received continuous (no more than 70 consecutive days off drug) HUMIRA® therapy after the completion of AbbVie sponsored study and the physician can provide source documentation of SAEs, AEs of Special Interest, and dosing information since initiation of commercial HUMIRA® (defined as a prescribed/non study drug).

2. Patient is willing to consent to data being collected and provided to AbbVie.
3. Patient is capable of and willing to give written informed consent and to comply with the requirements of the registry.

6.1.2 Exclusion Criteria

Patient should not be enrolled if he/she cannot be treated in accordance with the local product label.

6.1.3 Patient Follow-up Criteria – HCP Process

Patients who discontinue from the registry before Year 10 will be offered the option to participate in a direct to HCP Process, as applicable per local regulations. In order to participate in the follow-up process, the patient must sign a Patient Authorization for Use/Disclosure of Data form.

6.2 Number of Patients to be Enrolled

This is a multi-center, uncontrolled, observational registry of adult patients with chronic plaque Ps treated with HUMIRA® in a clinical practice setting. Approximately 5000 patients in the United States and Canada, and up to an additional 1000 patients in participating European countries will be enrolled. It is expected that approximately 5% to 10% of the patients enrolled in the registry will be continuing therapy started in a prior AbbVie HUMIRA® clinical study. The additional patients will be enrolled into the registry from the available psoriasis population within the physicians' practice.

6.3 Physician Selection Criteria

It is expected that approximately 300 physicians from the US and Canada and approximately 100 additional physicians from European countries will participate in this registry based on available eligible patient population. Qualified Physician Assistants and Nurse Practitioners from US sites who treat patients with HUMIRA® are allowed to enroll patients to the registry and will be referred to as physicians throughout the protocol. Approximately 100 sites will be included based on prior participation in HUMIRA® clinical development studies with subjects participating in clinical trials for HUMIRA®.

6.4 Registry Duration

The planned follow-up observation period is 10 years.

A patient may withdraw from the registry at any time without prejudice. If the physician, for any reason, decides it is in the best interest of the patient to discontinue HUMIRA®, treatment should be stopped. Physicians are encouraged to keep patients in the registry for a full 10-year observation period irrespective of future treatment decisions so that important and complete safety information can be obtained. Patients who develop an AESI or SAE while in the registry will be followed throughout the patient's participation in the registry or direct to HCP process until satisfactory resolution or until 70 days following the last registry dose (whichever is longer). Follow-up received on ongoing SAEs and/or AESIs at the time of registry conclusion should be reported using post-marketing reporting requirements. If a patient withdraws or is withdrawn from the registry, such should be noted, along with the reason for withdrawal on the electronic Study Completion eCRF). At the time of withdrawal, an assessment of the patient's current medical condition will be completed.

6.5 Registry Conduct

Physicians will be provided with a registry kit that includes a protocol, patient informed consent forms, access to electronic Case Report Forms (eCRFs), including SAE Report Forms, specially designed eCRFs to collect AEs of Special Interest and paper patient

questionnaires to collect Patient Reported Outcomes (PRO) (United States only). Physicians will determine the appropriate therapy for each patient in accordance with the locally approved label. The decision to prescribe HUMIRA® to the patients should be made separately from, and prior to the decision to enroll them into the registry.

The physician will follow the patient during regular office visits at intervals as determined by routine clinical practice or as recommended by national guidelines.

At the enrollment (baseline) visit, the physician will complete the Enrollment eCRFs by obtaining and recording all of the available required information. All SAEs and AEs of Special Interest (Table 2) that occurred since the first commercial dose of HUMIRA® will be collected on a specially designed questionnaire/source document for entry into EDC.

Information about medications taken for Psoriasis will be recorded on the eCRF at enrollment and during the regularly scheduled visits that are closest to Months 3, 6, 12, 18, 24, and every 6 months thereafter through Month 120. While the physician may deem it appropriate and necessary to have the patient return for additional visits during the observation period, data will be collected via electronic Case Report Forms (eCRFs) only at the intervals that most closely correspond to those described above. However, information related to safety should be captured at any time using the appropriate eCRFs.

Physicians should treat their patients as they would in their routine clinical practice. At any time, patients and physicians may choose to interrupt HUMIRA® therapy for any reason. Patients that intermittently stop treatment (Section 10.1) should continue to be monitored during their treatment interruption for safety (SAEs and AEs of Special Interest) and effectiveness, if applicable. These patients will be questioned for changes in their psoriasis medications and medical history at their regularly scheduled visits.

If treatment with HUMIRA® is permanently discontinued for any reason, patients will be encouraged to remain in the registry. If a patient discontinues the registry, the physician will offer the patient participation in the direct to HCP Process, as applicable per local regulations, regardless of HUMIRA® treatment. Patients that have affirmatively

withdrawn their authorization to have their personal health information used or disclosed in connection with the registry will not be asked to continue in the registry or asked to participate in the HCP Process.

For patients who discontinue the registry, physicians will be asked to obtain the patient's signature on a Patient Authorization for Use/Disclosure of Data form for the completion of a simplified Healthcare Provider (HCP) questionnaire on an annual basis, as applicable per local regulations. The first data collection period will capture data from the date of the patient's discontinuation visit or last contact in the registry through the completion of the first annual HCP questionnaire for the patient. The questionnaire focuses on the collection of surgeries, hospitalizations, deaths, and the events listed as AEs of Special Interest (Table 2), AEs of Special Interest that lead to permanent discontinuation of HUMIRA®, and psoriasis related medication use since registry discontinuation. The questionnaire may be completed by the registry physician or the patient's current HCP (if they are no longer under the care of a registry physician). Any other SAEs experienced should be reported according to standard spontaneous reporting procedures, and they are not subject to the requirements of this protocol.

Effectiveness measures will not be collected from patients participating in direct to HCP Process.

All patients that are unreachable after three consecutive documented attempts to contact the patient via phone, email, or certified letter, will be considered lost to follow-up.

AbbVie will take reasonable actions to ascertain vital status at the end of the patient's 10-year observational period. AbbVie will make every effort to work through investigational sites to match patients lost to follow-up against the National Death Index (NDI) in the US, national/regional cancer registries and vital registries as available in other countries and as allowed per local regulations.

The registry procedures to be conducted in the registry are outlined in the schematic presented in Table 1.

Table 1. Registry Activities

Activity	Registry Enrollment	Month[a] 3	Month[a] 6	Month[a] 12	Month[a] 18, 24, 30, 36, 42, 48, 54	Month[a] 60	Month[a] 66, 72, 78, 84, 90, 96, 102, 108, 114	Upon Completion Month[a] 120 or Premature Discontinuation	At Time of Reported Event
Inclusion/Exclusion Criteria	X								
Informed Consent	X								
Demographics	X								
Medical History and Treatment Modality	X								
Safety Data Collection (AEs of Special Interest/SAEs)	X	X	X	X	X	X	X	X	X
Prior and Concomitant Psoriasis Medications	X	X	X	X	X	X	X	X	X
Concomitant Medications at Time of Reported SAE or AE of Interest	X	X	X	X	X	X	X	X	X
Physician Global Assessment	X	X	X	X	X	X	X	X	
PROs[b]									
Patient Global Assessment	X	X	X	X	X	X	X	X	
DLQI	X		X	X	X[c]	X	X[c]	X	
PHQ-9	X		X	X	X[c]	X	X[c]	X	
Healthcare Resource Utilization (Unscheduled Outpatient Visits, Emergency Room Visits and Hospitalizations Questionnaire)	X		X	X	X[c]	X	X[c]	X	
WPAI	X		X	X	X[c]	X	X[c]	X	

Table 1. Registry Activities (Continued)

Activity	Registry Enrollment	Month[a] 3	Month[a] 6	Month[a] 12	Month[a] 18, 24, 30, 36, 42, 48, 54	Month[a] 60	Month[a] 66, 72, 78, 84, 90, 96, 102, 108, 114	Upon Completion Month[a] 120 or Premature Discontinuation	At Time of Reported Event
Rosenberg Self-Esteem Scale	X			X		X		X	
Census Socio-Demographic Questionnaire	X					X		X	
Medical Outcomes (MOS)-Social Activities Scale	X			X		X		X	
Psoriasis Impact and Experience	X			X		X		X	
Illness Cognition Questionnaire	X			X		X		X	
Insurance Status	X			X		X		X	
Case Report Form Completion	X	X	X	X	X	X	X	X	X

a. Data collection at regular visits that are closest to time points described. For patients participating in the direct to HCP process, follow-up is annually and AEs of Special Interest and AEs of Special Interest that lead to permanent discontinuation of HUMIRA®, surgeries, hospitalizations, deaths and medications taken for psoriasis will be collected.

b. Only sites in the US will conduct PRO assessments.

c. Data collected at annual visits only (i.e., Months 24, 36, 48, 60, 72, 84, 96, and 108).

The procedures outlined in Table 1 are discussed in detail in this section, with the exception of the collection of AE information, which is discussed in Section 7.0 and Patient Informed Consent, which is discussed in Section 8.0.

6.5.1 Inclusion/Exclusion

Patients will be screened to ensure they meet all inclusion criteria and do not meet the exclusion criteria prior to enrollment.

6.5.2 Demographics

Once the physician has determined that the patient is eligible for inclusion, and the patient has agreed to be included in the observational registry, the patient's demographic data, including date of birth, gender, race, ethnicity, and disease status will be recorded on the eCRFs at the Enrollment Visit.

6.5.3 Medical History

The physician will determine the patient's current health status and obtain a complete medical history including history of tobacco, alcohol and drug abuse at the enrollment visit.

After consent is obtained, patients will be asked to provide retrospective SAEs, AEs of Special Interest, and exposure to HUMIRA® data from the first dose of commercial HUMIRA®.

Patients rolling over from a prior HUMIRA® clinical trial will be asked to provide medical history only for previously unreported conditions and/or conditions not requested to be reported in the original study of participation.

6.5.4 Prior and Concomitant Medications

All prior and ongoing systemic therapy, biologic agent, and phototherapy to treat psoriasis since diagnosis should be documented. Prior systemic therapy for non-psoriasis medical conditions will be recorded for the prior 12 months. For all prior psoriasis therapies,

information on dosing, response to treatment, the year of last administration, length of time on the medication, and reason for stopping the psoriasis medication will be collected in the source documents and appropriate eCRF pages.

Any changes to ongoing psoriasis medications and new concomitant psoriasis medications should be recorded throughout the course of the registry. Medications used to treat AEs of Special Interest and/or SAEs will be recorded at the time of the event.

In addition, for patients age ≤ 30 with a reported malignancy adverse event, prior exposure to, or current use of, antineoplastics, or other drugs which have a risk of malignancy as stated in their label and other relevant dosing information to estimate total exposure will be collected in the source documents and appropriate eCRF pages. At the time of the reported malignancy adverse event, sites will be asked if any of the prior and concomitant medications contributed to the event. Any medications used prior to the registry will be captured on the appropriate eCRF. Information on the reason for use, date(s) of administration including start and end dates, highest maintained dose, dosage information including dose, route and frequency, and reason for stopping the medication will be collected in the source documents and appropriate eCRF pages.

Since this is an observational registry, the patient will be treated in accordance with the physician's usual and customary medical practice.

The administration of anakinra (Kineret®), abatacept (Orencia®) or other biologic agents may not be given concurrently while participating in the registry. Please refer to your local product label for the use of live vaccines while a patient is on HUMIRA®.

The AbbVie Study-Designated Physician (SDP) should be contacted if there any questions regarding prior or concomitant medications.

6.5.5 Physician's Global Assessment and Patient Reported Outcome Measurements

When applicable, information about the effectiveness of HUMIRA® therapy will be provided by the physicians and the patients. The Physician's Global Assessment (Appendix C) will be collected to assess the effectiveness of therapy at all registry visits at all sites. Effectiveness of therapy provided by the patient will be collected at US sites only utilizing patient reported outcomes (PROs) beginning at the enrollment visit and subsequently as outlined in Table 1. Effectiveness measures will be collected for patients participating in the registry regardless of HUMIRA® treatment. However effectiveness measures will not be collected as part of the HCP process. The PROs to be utilized include: Dermatology Life Quality Index (DLQI) (Appendix D), Patient Health Questionnaire PHQ-9 For Depression (PHQ-9) (Appendix E), Healthcare Resource Utilization (Unscheduled Outpatient Visits, Emergency Room Visits and Hospitalizations Questionnaire) (Appendix F), Work Productivity and Activity Impairment Questionnaire: Specific Health Problem V2.0 (WPAI:SHP) (Appendix G), Rosenberg Self-Esteem Scale (Appendix H, Census Socio-Demographic Questionnaire (Appendix I), Medical Outcomes (MOS)-Social Activities Scale (Appendix J), Psoriasis Impact and Experience (Appendix K), Illness Cognition Questionnaire (Appendix L), Insurance Status (Appendix M), and Patient Global Assessment (Appendix N).

6.5.6 Product Supply

HUMIRA® will be obtained through commercially available medication. AbbVie will not provide the medication for this registry.

6.6 Withdrawal of Patients from Registry

A patient may withdraw from the registry at any time without prejudice. If the physician, for any reason, decides it is in the best interest of the patient to permanently discontinue HUMIRA®, treatment should be stopped but the patient should be encouraged to continue in the registry as outlined in Section 6.0. If a patient withdraws or is lost to follow-up,

such should be noted, along with the reason for withdrawal on the Study Completion eCRF.

Patients who discontinue from the registry for any reason other than withdrawn consent, will be contacted to determine interest in participation in the direct to HCP Process, as applicable per local regulations.

6.7 Registry Management

AbbVie, working in cooperation with United BioSource Corporation (UBC), will manage the registry, collect all registry information via eCRFs and PROs, if applicable, and complete all statistical analyses.

7.0 Adverse Events/Adverse Event Reporting

The physician will monitor each patient for SAEs and evidence of pre-defined AEs of Special Interest on a routine basis throughout the registry.

7.1 Definitions

7.1.1 Adverse Event

An AE is defined as any untoward medical occurrence that occurs during treatment in a patient, but does not necessarily have a causal relationship with their treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not the event is considered causally related to the use of the product.

Such an event can result from use of the drug as stipulated in the labeling, as well as from accidental or intentional overdose, drug abuse, or drug withdrawal. Any worsening of a pre-existing condition or illness is considered an AE.

An elective surgery/procedure scheduled to occur during a registry will not be considered an AE if the surgery/procedure is being performed for a pre-existing condition and the surgery/procedure has been planned prior to registry entry. However, if the pre-existing

condition deteriorates unexpectedly during the registry (e.g., surgery performed earlier than planned), then the deterioration of the condition for which the elective surgery/procedure is being done will be considered an AE.

7.1.2 Adverse Events of Special Interest

Table 2. AEs of Special Interest for This Registry

Serious and non-serious opportunistic infections, including the following bacterial, fungal, viral and parasitic infections: Aspergillus, Blastomyces, Candida, Coccidioides, Cryptococcal, Cytomegalovirus, Histoplasma, Listeria, Nocardia, Paracoccidioides, Pneumocystis, Toxoplasma, Tuberculosis, Herpes, Bacillary angiomatosis, Mucormycosis, Progressive Vaccinia, Zygomycosis, BK virus, and JC virus
Lymphoma
Hepatosplenic T-cell lymphoma
Leukemia
Non-melanoma skin cancer (NMSC)
Other malignancies (except lymphoma, leukemia and NMSC)
Immune reactions including lupus, lupus-like reactions, and severe allergic reactions
Congestive heart failure (CHF)
Cerebrovascular accident (CVA)
Myocardial infarction (MI)
CNS demyelinating disorders (including MS and Guillain-Barré syndrome)
Hepatic events that are serious or lead to permanent discontinuation of HUMIRA (e.g., persistent liver function test abnormalities, acute liver failure and other serious hepatic events)
Hematologic events that are serious or lead to permanent discontinuation of HUMIRA (e.g., aplastic anemia, Granulocytopenia, Granulocyte Maturation Arrest, Leukopenia, Neutropenia, Pancytopenia and Thrombocytopenia)
Worsening of Psoriasis
Vasculitis
Diverticulitis
Intestinal perforation

In addition, to the SAEs and AEs of Special Interest (Table 2), AEs that lead to permanent discontinuation of HUMIRA® will be collected.

For patients participating in the direct to HCP process in addition to surgeries, hospitalizations, deaths, and the events listed as AEs of Special Interest (Table 2), AEs of Special Interest that lead to permanent discontinuation of HUMIRA® will be collected.

During the course of the registry, additional AEs of Special Interest may be identified by AbbVie. Updates to the AEs of Special Interest will be maintained and collected through the eCRF system. Sites will be trained on all updates to the eCRF system.

The physician will assess and record any additional information on the AEs of Special Interest in detail on the AE of Special Interest eCRF.

The physician will assess all reported AEs for seriousness and follow the requirements/timelines for reporting any AE that fulfills the criteria of an SAE, as defined in Section 7.1.3.

7.1.3 Serious Adverse Events

If an AE (not limited to AEs of Special Interest) meets any of the following criteria, it is to be reported to AbbVie as a SAE within 24 hours of the site being made aware of the event.

Death of Patient	An event that results in the death of a patient.
Life-Threatening	An event that, in the opinion of the investigator, would have resulted in immediate fatality if medical intervention had not been taken. This does not include an event that would have been fatal if it had occurred in a more severe form.
Hospitalization	An event that results in an admission to the hospital for any length of time. This does not include an emergency room visit or admission to an outpatient facility.
Prolongation of Hospitalization	An event that occurs while the patient is hospitalized and prolongs the patient's hospital stay.
Congenital Anomaly	An anomaly detected at or after birth, or any anomaly that results in fetal loss.

Persistent or Significant Disability/Incapacity	An event that results in a condition that substantially interferes with the activities of daily living of a patient. Disability is not intended to include experiences of relatively minor medical significance such as headache, nausea, vomiting, diarrhea, influenza, and accidental trauma (e.g., sprained ankle).
Important Medical Event Requiring Medical or Surgical Intervention to Prevent Serious Outcome	An important medical event that may not be immediately life-threatening or result in death or hospitalization, but based on medical judgment may jeopardize the patient and may require medical or surgical intervention to prevent any of the outcomes listed above (i.e., death of patient, life-threatening, hospitalization, prolongation of hospitalization, congenital anomaly, or persistent or significant disability/incapacity). Examples of such events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.
Spontaneous Abortion	Miscarriage experienced by patient.
Elective Abortion	Elective abortion performed on patient.

The physician will assess and record any AE of Special Interest and/or SAE in detail on the Adverse Event eCRF, including the date and time of onset, description, severity, time course, duration and outcome, relationship of the AE to drug, information specific to the event, final diagnosis/syndrome (if known), and any action(s) taken. For all AEs of Special Interest, the physician must pursue and obtain all the above-mentioned information in order to adequately determine the outcome of the AE and to assess whether it meets the criteria for classification as an SAE as well as to determine a causal relationship. Follow-up safety queries will be issued to sites three times and considered closed after the next scheduled quarterly monitor contact per approval of the medical monitor listed in Section 1.0. In the event of a death, follow-up will include an autopsy report, if available, and a death certificate.

7.2 Severity

The physician will use the following definitions to rate the severity for any AE of Special Interest being collected as an endpoint/data point in the registry and for all SAEs.

Mild	The adverse event is transient and easily tolerated by the patient.
Moderate	The adverse event causes the patient discomfort and interrupts the patient's usual activities.
Severe	The adverse event causes considerable interference with the patient's usual activities and may be incapacitating or life-threatening.

7.3 Relationship to Pharmaceutical Product

The physician will use the following definitions for any AE of Special Interest being collected as an endpoint/datapoint in the registry and for all SAEs, to assess the relationship of the AE to the use of HUMIRA®. For all SAEs and AEs of Special Interest with a possible or probable causal relationship to HUMIRA® treatment, follow-up by the physician is required until the event or its sequelae resolve or stabilize at a level acceptable to the physician:

Probably Related	An adverse event has a strong temporal relationship to pharmaceutical product or recurs on re-challenge and another cause of event is unlikely or significantly less likely.
Possibly Related	An adverse event has a strong temporal relationship to the pharmaceutical product and another cause of event is equally or less likely compared to the potential relationship to drug.
Probably Not Related	An adverse event has little or no temporal relationship to the pharmaceutical product and/or a more likely other cause of event exists.
Not Related	An adverse event is due to an underlying or concurrent illness or effect of another drug and is not related to the pharmaceutical product (e.g., has no temporal relationship to drug or has a much more likely other cause of event).

If an Investigator's opinion of possibly, probably not, or not related to pharmaceutical product is given, an Other cause of event must be provided by the Investigator for the SAE.

7.4 Adverse Event Collection Period

SAEs, AEs of Special Interest, and AEs that lead to permanent registry HUMIRA® discontinuation will be reported to AbbVie starting from the first commercial dose of HUMIRA® or when the initial informed consent is signed, (whichever date is earlier), throughout the patient's participation in the registry, or direct to HCP process, until satisfactory resolution or for 70 days after their last dose of registry drug (whichever period is longer) to further evaluate safety.

Follow-up received on ongoing SAEs and/or AESIs post registry conclusion should be reported using standard Post-Marketing Reporting.

For patients participating in the direct to HCP process, surgeries, hospitalizations, deaths, events listed as AEs of Special Interest (Table 2), and AEs of Special Interest that lead to permanent discontinuation of HUMIRA® will be collected.

In the event HUMIRA® therapy is interrupted (Section 10.1), the patient will remain in the registry and continue to be monitored during the treatment interruption for SAEs and AEs of Special Interest and will be questioned for changes in their psoriasis medications and medical history of the event at their registry visits. If treatment with HUMIRA® is permanently discontinued for any reason, the reason will be recorded and the patient should be encouraged to remain in the registry for the full 10 years.

For patients enrolled from a prior AbbVie HUMIRA® study, ongoing events at the time of registry entry will be collected.

7.5 Serious Adverse Event Reporting

In the event of an SAE, and/or additionally, any non-serious event of malignancy in patients 30 years of age and younger, whether related to HUMIRA® or not, the physician

will notify the AbbVie Immunology Clinical Safety Management Team within 24 hours of the physician becoming aware of the event by entering the serious adverse event or non-serious event of malignancy in patients 30 years of age and younger data into the electronic data capture (EDC) system.

If the EDC system is unavailable, the completed Serious Adverse Event Form should be submitted via fax:

FAX to:	[redacted]

For SAE concerns, contact the Immunology Safety Team at:

[redacted]

For any emergent patient safety concerns, please contact the physician listed below:

AbbVie Safety and Medical Contact

7.6 Pregnancy Reporting

Pregnancy in a registry patient must be reported to AbbVie within 1 working day of the site becoming aware of the pregnancy. Pregnancies will be collected from the date of the first dose of HUMIRA® in registry through 150 days following the last dose of registry drug or the end of the patient's participation in registry (whichever is longer).

Physicians should refer to their local prescribing information when making treatment decisions for patients who become pregnant while being treated with HUMIRA® in the registry. Patients who become pregnant and interrupt their HUMIRA® therapy should remain in the registry and should continue to be monitored for new SAEs and AEs of Special Interest.

All female patients who become pregnant while enrolled in this registry will be followed from the time the pregnancy is reported until the outcome of the pregnancy is known. Information regarding a pregnancy occurrence in a registry patient and the outcome of the pregnancy will be collected.

Pregnancy in a registry patient is not considered an adverse event. However, the medical outcome of an elective or spontaneous abortion, stillbirth or congenital anomaly is considered a serious adverse event and must be reported to AbbVie within 24 hours of the site becoming aware of the event.

7.7 Data Collection Procedures for Patients Who Participate in the Direct to HCP Process

For patients participating in the direct to HCP Process, the registry physicians or the patient's current health care provider will document any hospitalizations, surgeries, deaths, and any Adverse Event of Special Interest as defined in Section 7.1.2 and AEs of Special Interest that lead to permanent discontinuation of HUMIRA® annually via a paper or electronic questionnaire. The registry physician or current health care provider will assess and record the date of onset (where known), event description, use of HUMIRA® and other psoriasis medications.

These events will be reported to AbbVie from the time of registry enrolment up to 10 years, irrespective of any treatment interruption, any changes in treatment, or discontinuation of HUMIRA®.

Effectiveness data will not be collected in the HCP Process.

8.0 Ethics and Quality

Prior to any registry-related data being collected, the informed consent statement will be reviewed and signed and dated by the patient and the person who administered the informed consent. A copy of the signed informed consent form will be given to the patient and the original will be placed in the patient's medical record. A patient informed consent template will be provided to the registry physician.

If a patient is willing to participate in the HCP process, a copy of the signed Patient Authorization for Use/Disclosure of Data form will be obtained prior to the participation.

8.1 Quality Assurance

Prior to the initiation of the registry, physician and site personnel will be trained on the registry. Training will include a detailed discussion of the protocol, performance of procedures, paper PRO completion, and eCRF completion. Sites will be given a paper PRO and eCRF completion workbook for reference.

Monitoring visits will be performed at a subset of the sites. At the visists a quality assurance check will be performed against entries on the paper and eCRF and a quality assurance check will be performed to ensure that the physician is complying with the protocol and local regulations. The monitoring plan will detail how sites will be selected for the on-site monitoring visits and what data will be source data verified during the visit. Throughout the registry, CRO and AbbVie will periodically follow-up with the sites to ensure that SAEs and AEs of Special Interest are being reported.

All registry data will be entered via the eCRF. Only PROs completed by the patients will be done via paper CRFs and these will be submitted to be entered into the database. All eCRF information will be imported directly into the electronic data capture system. Any necessary corrections will be made to the database and documented via addenda, queries, source data clarification forms or an audit trail. A manual review of selected line listings will also be performed at the end of the registry. All paper questionnaires (including direct to HCP questionnaire) will be entered into the database by the CRO data management group upon receipt.

9.0 Case Report Forms

All data associated with this registry will be collected and reported electronically (eCRF) via a web address and secure password. Patient self-administered questionnaires will be completed on paper forms and then submitted to be entered into the database.

At the Enrollment visit, the physician will complete the Enrollment eCRFs by obtaining and recording all available required information, as outlined in Section 6.5.

At subsequent visits corresponding to the schedule of assessment (Table 1), the physician will complete the appropriate eCRF by obtaining and recording all available information. Since this is an observational registry conforming to usual clinical practice, data from patient visits that most closely correspond to the recommended schedule of assessment at Months 3, 6, 12, 18, 24, and every 6 months through the end of registry participation will be collected.

Paper/electronic questionnaires will be generated for patients that have discontinued from the registry for any reason and signed the authorization for data release for the completion of the HCP questionnaire in the direct to HCP process.

Upon completion of or termination from the registry, all patients should have a Study Completion eCRF completed as well as an assessment of their current medical conditions.

10.0 Data Analysis Plan

10.1 Analyzable Populations

All Treated Patient Population is defined as patients who receive at least one dose of HUMIRA® in the registry.

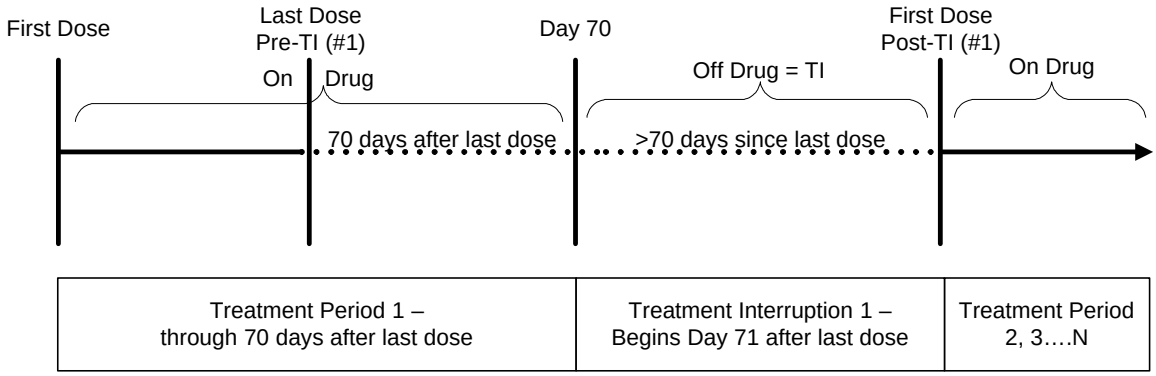
New Prescription Patient Population is defined as patients who have newly initiated HUMIRA® therapy within 4 weeks prior to the entry into the registry and who receive at least one dose of HUMIRA® in the registry (the New Prescription Population is a subset of the All Treated Patient Population).

The All Treated Patient Population and the New Prescription Patient Population will be used for safety and effectiveness analysis.

In addition, the Intermittent Treatment Population, defined as patients who have at least 2 treatment interruption periods with at least 3 treatment periods (Figure 1), will be used for the safety analysis. A treatment interruption period is defined as greater than 70 consecutive days during which the patient does not receive any HUMIRA® treatment. The treatment interruption period starts from 71 days after the last dose of HUMIRA® in

the preceding treatment period and up to the day prior to the first dose of HUMIRA® in the subsequent period. A treatment period is defined as at least one dose of HUMIRA® up to 70 days after the last dose of HUMIRA®.

Figure 1. Treatment Period and Treatment Interruption (TI) Period



10.2 Demographics and Registry Enrollment Characteristics

Demographics and baseline characteristics will be summarized for the All Treated Patient Population, the New Prescription Patient Population, and the Intermittent Treatment Population. Descriptive statistics will be presented. Number of patients with non-missing values, mean, and standard deviation will be provided for continuous variables. Counts and percentages will be provided for categorical variables. The number and percentage of patients that discontinue from the registry will be summarized, overall and by reason for discontinuation. Duration of observation in the registry and total duration of treatment will be summarized as follows:

- Duration of observation in the registry is defined from the first day in the registry (enrollment visit or date of informed consent, up to the end-of-registry (as defined in Section 12.0).
- The duration of treatment in the registry (registry exposure) is defined from the first dose of HUMIRA® in the registry to 14 days after the last dose of HUMIRA® excluding total days of any treatment interruptions.

- Total duration of treatment (total exposure) is defined from the first recorded dose of HUMIRA® (initial dose) to 14 days after the last dose of HUMIRA® excluding total days of any treatment interruptions.

Time to observational and treatment discontinuation will also be presented as Kaplan-Meier (KM) curves.

10.3 Safety Analyses

Five main safety analyses will be reported from this registry: four analyses will summarize data through the end-of-registry (as defined in Section 12.0) and one will exclude the HCP Process. The details of the analyses are in Section 10.3.1, Section 10.3.2, and Section 10.3.3. If a patient is not covered by any of the analysis populations, but experiences an AE, this AE will be reported in a separate listing.

- Observational AEs: SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® occurring from the first day in the registry (enrollment visit or date of informed consent, through the last contact (as defined in Section 10.3.1) irrespective of drug treatment duration.
- Registry Treatment-emergent AEs: SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® occurring from the first recorded dose of HUMIRA® in the registry through 70 days after the last dose excluding AEs occurring during treatment interruptions (as defined in Section 10.1).
- All Treatment Emergent AEs: SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® occurring from the first recorded dose of HUMIRA® (initial dose) through 70 days after the last dose excluding AEs occurring during treatment interruptions (as defined in Section 10.1.
- AEs for intermittent treatment: SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® in the Intermittent Treatment Population.

- Observational AEs excluding HCP process: SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® occurring from the first day in the registry through the last contact excluding the HCP process.

10.3.1 Analysis of Observational AEs

The number and percent of patients experiencing SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® during the registry, regardless of whether the AEs are reported during or after the HUMIRA® treatment, will be tabulated by body system and Medical Dictionary for Drug Regulatory Activities (MedDRA) preferred term. Rates (event per 100 patient-year of observation) of SAEs and AEs of Special Interest and the 95% confidence interval will be provided. The analysis will be performed using data from first day in the registry to the date of last contact for the All Treated Patient Population. The last contact date is defined as the last date of registry or direct to HCP process participation, whichever occurs later.

Standardized incidence ratios (SIRs) will be used to compare the rates of events in this registry to the general population.

10.3.2 Analysis of Treatment-Emergent AEs

Registry Treatment-emergent SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® and All Treatment-emergent SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® will be summarized.

Registry Treatment-emergent AEs includes AEs occurring from the first day in the registry to 70 days after the last dose of HUMIRA® excluding:

1. AEs occurring during TI which are more than 70 days after the last dose of HUMIRA® prior to the TI.
2. AEs occurring on or after the first day of the registry, but before the date of the first dose of HUMIRA®.

All Treatment-emergent AEs include AEs occurring from the first recorded dose of HUMIRA® (i.e., the initial dose) up to 70 days after the last dose of HUMIRA® (excluding AEs during TI which are more than 70 days after the last dose of HUMIRA® prior to TI). For patients enrolled from a prior HUMIRA® study or who initiated commercial HUMIRA® therapy before entering the registry, the summaries will include the events reported during their participation in the previous study, any events reported by retrospective data collection, and any events reported during this registry.

The number and percentage of patients experiencing treatment-emergent SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® will be tabulated by body system and MedDRA® preferred term. Rates (event per 100 patient-years of exposure to HUMIRA®, defined in Section 10.2) of SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® and the 95% confidence interval will be provided.

10.3.3 Analysis of AEs for Intermittent Treatment

The following analyses will be performed for the Intermittent Treatment:

1. Rates (event per 100 patient-years of exposure to HUMIRA®) of treatment-emergent SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® and the 95% confidence interval will be provided.
2. Rates (event per 100 patient-years) of SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® and the 95% confidence interval over the course of intermittent treatment strategy, defined as from the first day of HUMIRA® injection to the end of the last treatment period, will be provided.

To further evaluate the effect of intermittent treatment on the AE profile, rates of AEs per 100 patients-years of exposure to HUMIRA® will be analyzed for each treatment period for the subgroups of patients with at least 3, 4, and 5 or more TIs.

	Overall	1st Treatment Period	2nd Treatment Period	3rd Treatment Period	4th Treatment Period	5th Treatment Period	6th+ Treatment Period
> 2 TIs[a]	x.xx	x.xx	x.xx	x.xx			
> 3 TIs	x.xx	x.xx	x.xx	x.xx	x.xx		
> 4 TIs	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	
> 5 TIs	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx	x.xx

a. This is the Intermittent Treatment Population.

Summaries of AEs among patients not in the Intermittent Treatment Population will be provided as a reference.

10.3.4 Analysis of Observational AEs Excluding HCP Process

The analysis will be performed using data from first day in the registry through the last contact, excluding the HCP process. The number and percentage of patients experiencing SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® will be tabulated by body system and Medical Dictionary for Drug Regulatory Activities (MedDRA®) preferred term. Rates (event per 100 patient-year of observation) of SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® and the 95% confidence interval will be provided.

Summaries of SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® by severity and relationship to HUMIRA® will be provided.

10.3.5 Subgroup Analysis of Adverse Events

A summary of SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® will be provided by the following:

1. By geographic locations.
2. By types of physician practices.

3. For patients exposed to concomitant medications of interest. The categories of concomitant medications of interest that will be captured include phototherapy, systemic biologics, systemic non-biologics and PUVA.

In addition, the analysis of Observational AEs and the analyses of All Treatment-emergent AE will be performed for the New Prescription Patient Population.

10.4 Effectiveness Analyses

Effectiveness parameters measured in this registry for patients enrolled in the US include: Physician's Global Assessment (PGA), Dermatology Life Quality Index (DLQI), Patient Health Questionnaire PHQ-9 For Depression (PHQ-9), Healthcare Resource Utilization, Work Productivity and Activity Impairment (WPAI:SHP), Rosenberg Self-Esteem Scale, Census Socio-Demographic Questionnaire, Medical Outcomes (MOS)-Social Activities Scale, Psoriasis Impact and Experience, Illness Cognition Questionnaire, Insurance Status, and Patient Global Assessment.

Descriptive statistics will be provided for the following variables according to the collection schedule outlined in Table 1:

1. PGA:
   a. Proportion of patients achieving "clear."
   b. Proportion of patients achieving "clear or minimal."
2. DLQI:
   a. Proportion of patients achieving DLQI = 0.
   b. Proportion of patients achieving DLQI = 0 or 1.
   c. Change from baseline in DLQI.
3. PHQ9:
   a. Change from baseline in PHQ9 total score.
4. Health Resource Utilization

a. Proportion of subjects who had at least one event (e.g., hospitalization, ER, physician visits).
b. Average number of events occurred per subjective who had at least one event.

5. WPAI-SHP: Change from baseline in the four impairment percentages:
   a. Percent work time missed.
   b. Percent impairment while working.
   c. Percent impaired activity.
   d. Percent overall work impairment.
6. Rosenberg Self-Esteem Scale: change from baseline in total score.
7. Census Socio-Demographic Variables: proportion of subjects in each category.
8. Medical Outcomes (MOS)-Social Activities Scale: change from baseline.
9. Psoriasis Impact and Experience: proportion of subjects who strongly agree, agree, not sure but probably agree, not sure but probably disagree, disagree or strongly disagree with any of the statements.
10. Illness Cognition Questionnaire: change from baseline in helplessness sub-score, acceptance sub-score and total score.
11. Insurance Status: proportion of subjects uninsured, or insured in any of the plan types.
12. Patient Global Assessment:
    a. Proportion of patients achieving "Complete disease control."
    b. Proportion of patients achieving "Complete disease control or good disease control."

Effectiveness data will be analyzed as observed, as this is an observational registry. Number of patients with non-missing baseline and visit values, baseline mean, visit mean,

mean and standard deviation of change from baseline will be provided for continuous variables. Counts and percentages will be provided for categorical variables.

The effectiveness data will be summarized for the All Treated Patient Population (from the first dose in the registry) and the New Prescription Patient Population. For patients with TI, effectiveness summaries will combine data from all Treatment Periods, excluding the measurements from 14 days after the last dose during a treatment period up to the first dose in the subsequent Treatment Period.

10.5 Interim Analyses

Interim reports are prepared on an annual basis and began in February 2010. Interim reports are submitted to Regulatory Agencies, as required.

10.6 Determination of Sample Size

The proposed sample size for this registry of a minimum of 5,000 patients is based on the lowest frequency AE of Special Interest (i.e., lymphoma) seen in HUMIRA® clinical trials.

According to the latest US National Cancer Institute Surveillance Epidemiology and End Results (SEER) data, the age adjusted incidence rate of lymphoma in the general US population was 22.0 per 100,000 person-years during 2000-2004. Literature review has indicated a similar rate of 22.6/100,000 PY as reported by Gelfand and Margolis[5] in a control psoriasis population using the General Practice Research Database (GPRD) in the UK. However, the lymphoma rate was 47.7/100,000 PY in the psoriasis patient population that excluded mild cases (defined as those who had not previously received systemic therapy). Other studies have previously reported a higher rate of 56.0/100,000 PY in an older psoriasis patient population with an average age of 59, excluding cutaneous T cell lymphoma. Therefore, the data reported by Gelfand and Margolis were considered the most appropriate basis for calculation of the sample size for this registry.

Using the rate of 0.0477/100 PY from this reference as representative of patients that would be eligible for biological therapy for the treatment of psoriasis, a total of 21500 PY of observation time is needed to provide 80% power to rule out the doubling of 0.0477/100 PY with a 1-sided 95% CI, i.e., the upper bound of the one-sided confidence interval is < 0.0954/100 PY.

Using an expected patient year attrition rate of 40%, the ten-year registry of 5,000 patients will provide an expected 30,000 PY of observation. When considering the additional 1,000 patients who will be permitted to enter the registry from outside US and Canada, the ten-year registry of 6,000 patients will provide an expected 36,000 PY of observation. This will markedly exceed the number of patient-years of observation necessary to rule out the doubling of the lymphoma rate among moderate-to-severe psoriasis patients.

11.0 Final Report and Publications

At the end of the registry, a final registry report will be written. This report will contain a description of the objectives of the registry, the methodology of the registry and its results and conclusions. The completed eCRFs, questionnaires and the registry report must be treated as the confidential property of AbbVie and may not be released to unauthorized people in any form (publications or presentations) without express written approval from AbbVie. The results of this registry may be published by AbbVie or by any one of the participating physicians after agreement with AbbVie.

12.0 Completion of the Registry

The physician will conduct this registry in compliance with the protocol and all applicable regulatory and legal requirements. AbbVie may terminate this registry at any time, either in its entirety or at a site, for reasonable cause provided that written notice is submitted at a reasonable time in advance of the intended termination. The physician may also terminate the registry at their site for reasonable cause, after providing written notice to AbbVie a reasonable time in advance of the intended termination.

The end-of-registry is defined as the date of the last patient's visit in the registry or the HCP Process, whichever occurs later.

13.0 References

1. Greaves MW, Weinstein GD. Treatment of psoriasis. New Engl J Med. 1995;332(9):581-588.
2. Camp RDR. Psoriasis. In: Champion RH, Burton JL, Burns DA, Breathnach SM, eds. Textbook of Dermatology. 6th edition. 1998;2:1589-1649.
3. Brockbank JE, Schentag C, Rosen C, Gladman DD. Psoriatic arthritis (PsA) is common among patients with psoriasis and family medical clinic attendees. Arthritis Rheum. 2001;44 (suppl 9):S94.
4. Gladman DD. Psoriatic arthritis. Rheum Dis Clin North Am. 1998;24(4):829-844.
5. Gelfand JM, Shin DB, Neimann AL, Wang X, Margolis DJ, Troxel AB. The risk of lymphoma in patients with psoriasis. J Invest Dermatol. 2006;126:2194-2201.
6. Wallace K, et al. Presented at: Summer Academy Meeting of American Academy of Dermatology; July 28-August 4, 2013; New York, NY. M02-528, M02-529 24 Week data. Table revised with updated data – information on file at AbbVie. Available upon request.
7. Lebwohl M, Ali S. Treatment of psoriasis. Part 1. Topical therapy and phototherapy. J Am Acad Dermatol. 2001;45(4):487-498.
8. Lebwohl M, Ali S. Treatment of psoriasis. Part 2. Systemic therapies. J Am Acad Dermatol. 2001;45(5):649-661.
9. Menter MA, See JA, Amend WJ, Ellis CN, Krueger GG, Lebwohl M, et al. Proceedings of the psoriasis combination and rotation therapy conference. Deer Valley, Utah, Oct. 7-9, 1994. J Am Acad Dermatol. 1996;34(2 Pt 1):315-321.
10. Gottlieb AB. Psoriasis. Immunopathology and immunomodulation. Dermatol Clin. 2001;19(4):649-57.

11. Mease PJ, Goffe BS, Metz J, VanderStoep A, Finck B, Burge DJ. Etanercept in the treatment of psoriatic arthritis and psoriasis: Randomized trial. Lancet. 2000;356:385-390.

12. Chaudhari U, Romano P, Mulcahy LD, Dooley LT, Baker DG, Gottlieb AB. Efficacy and safety of infliximab monotherapy for plaque-type psoriasis: Randomized trial. Lancet. 2001;357:1842-1847.

13. Margolis D, Bilker W, Hennessy S, Vittorio C, Santana J, Strom BL. The risk of malignancy associated with psoriasis. Arch Dermatol. 2001;137:778-783.

14. Frentz G, Olsen JH. Malignant tumors and psoriasis: a follow-up study. Brit J Dermatol. 1999;140:237-242.

15. Stern RS, Lunder EJ. Risk of squamous cell carcinoma and methoxsalen (psoralen) and UV-A radiation (PUVA). Arch Dermatol. 1998;134:1582-1585.

16. Stern RS, Nichols KT, Väkevä LH. Malignant melanoma in patients treated for psoriasis with methoxsalen (psoralen) and ultraviolet A radiation (PUVA). New Engl J Med. 1997;336:1041-1045.

17. Boffetta P, Gridley G, Lindlöf B. Cancer risk in a population-based cohort of patients hospitalized for psoriasis in Sweden. J Invest Dermatol. 2001;117:1531-1537.

18. Lindelöf B, Sigurgeirsson B, Tegner E, Larkö O, Johannesson A, Berne B, et al. PUVA and cancer risk: the Swedish follow-up study. Brit J Dermatol. 1999;141:108-112.

19. Menter A, Tyring SK, Gordon K, Kimball AB, Leonardi CL, Langley RG, et al. Adalimumab therapy for moderate to severe psoriasis: A randomized, controlled phase III trial. J Am Acad Dermatol. 2008;58:106-15.

20. Spitzer R, Kroenke K, Williams J. Validation and utility of a self-report version of PRIME-MD: the PHQ Primary Care Study. Journal of the American Medical Association. 1999;282:1737-1744.

21. Kroenke K, Spitzer R L, Williams J B. The PHQ-9: validity of a brief depression severity measure. Journal of General Internal Medicine. 2001;16(9):606-613.

22. Rost K, Smith J. Retooling multiple levels to improve primary care depression treatment. Journal of General Internal Medicine. 2001;16:644-645.

23. Kroenke K, Spitzer RL. The PHQ-9: A new depression and diagnostic severity measure. Psychiatric Annals. 2002;32:509-521.

24. Williams JW, Noel PH, Cordes J A, Ramirez G, Pignone M. Is this patient clinically depressed? Journal of the American Medical Association. 2002;287:1160-1170.

25. Lowe B, Unutzer J, Callahan CM, Perkins AJ, Kroenke K. Monitoring depression treatment outcomes with the patient health questionnaire-9. Medical Care. 2004;42(12):1194-201.

26. Pinto-Meza A, Serrano-Blanco A, Peñarrubia MT, Blanco E, Haro JM. Assessing depression in primary care with the PHQ-9: can it be carried out over the telephone? J Genl Intern Med. 2005;20(8):738-42.

27. Gridley G, McLaughlin JK, Ekbom A, Klareskog L, Adami HO, Hacker DG, et al. Incidence of cancer among patients with rheumatoid arthritis. J Natl Cancer Inst. 1993;85:307-11.

28. Mellemkjaer L, Linet MS, Gridley G, Frisch M, Møller H, Olsen JH. Rheumatoid arthritis and cancer risk. Eur J Cancer. 1996;32A(10):1753-7.

29. Thomas E, Brewster DH, Black RJ, MacFarlane GJ. Risk of malignancy among patients with rheumatic conditions. Int J Cancer. 2000;88(3):497-502.

Appendix A. List of Abbreviations and Definition of Terms

Abbreviations

AE	Adverse event
AESI	Adverse event of special interest
AS	Ankylosing spondylitis
BCC	Basal cell carcinoma
CD	Crohn's disease
CHF	Congestive heart failure
CRO	Contract Research Organization
CVA	Cerebrovascular Accident
DLQI	Dermatology Life Quality Index
EC	Ethics Committee
eCRF	Electronic case report form
EDC	Electronic Data Capture
eSAE	Electronic serious adverse event
EU	European Union
FDA	US Food and Drug Administration
GPRD	General Practice Research Database
HCP	Health Care Provider
IgG1	Immunoglobulin
IRB	Institutional Review Board
KM	Kaplan Meier
MedDRA	Medical Dictionary for Regulatory Activities
MI	Myocardial Infarction
MTX	Methotrexate
NMSC	Non-melanoma skin cancer
PGA	Physician's Global Assessment
PRO	Patient reported outcome
Ps	Psoriasis
PsA	Psoriatic arthritis
PUVA	ultraviolet A and psoralen
PY	Patient-year
RA	Rheumatoid arthritis

SAE	Serious adverse event
SCC	Squamous cell carcinoma
SEER	Surveillance Epidemiology and End Results
SIR	Standardized incidence ratio
TB	Tuberculosis
TNF	Tumor necrosis factor
UBC	United BioSource Corporation
US	United States
UVB	Ultraviolet B
WPAI-SHP	Work Productivity and Activity Impairment-Specific Health Problem

Appendix B. List of Protocol Signatories

Name	Title	Functional Area
[redacted]		

Appendix C. Physician Global Assessment

The Physician's Global Assessment (PGA) is a 6-point scale used to measure the severity of disease at the time of the physician's evaluation of the patient. The degree of overall lesion severity will be evaluated using the following categories:

Score	Category	Category Description
0	Clear	Plaque elevation = 0 (no elevation over normal skin) Scaling = 0 (no scale) Erythema = ± (hyperpigmentation, pigmented macules, diffuse faint pink or red coloration)
1	Minimal	Plaque elevation = ± (possible but difficult to ascertain whether there is a slight elevation above normal skin) Scaling = ± (surface dryness with some white coloration) Erythema = up to moderate (up to definite red coloration)
2	Mild	Plaque elevation = slight (slight but definite elevation, typically edges are indistinct or sloped) Scaling = fine (fine scale partially or mostly covering lesions) Erythema = up to moderate (up to definite red coloration)
3	Moderate	Plaque elevation = moderate (moderate elevation with rough or sloped edges) Scaling = coarser (coarse scale covering most of all of the lesions) Erythema = moderate (definite red coloration)
4	Severe	Plaque elevation = marked (marked elevation typically with hard or sharp edges) Scaling = coarse (coarse, non tenacious scale predominates covering most or all of the lesions) Erythema = severe (very bright red coloration)
5	Very severe	Plaque elevation = very marked (very marked elevation typically with hard sharp edges) Scaling = very coarse (coarse, thick tenacious scale over most of all of the lesions; rough surface) Erythema = very severe (extreme red coloration; dusky to deep red coloration)

Note: Presented by Hon-Sum Ko, MD, Medical Officer, Division of Dermatologic and Dental Drug Products, Center for Drug Evaluation and Research, Food and Drug Administration. Bethesda (MD): Dermatologic and Ophthalmic Advisory Committee 49th Meeting; 20 March 1998.

Appendix D. Dermatology Life Quality Index

The aim of this questionnaire is to measure how much your skin problem has affected your life OVER THE LAST WEEK. Please check 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 **yard?**	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 E. Patient Health Questionnaire PHQ-9 For Depression

PATIENT HEALTH QUESTIONNAIRE-9 72883

THIS SECTION FOR USE BY STUDY PERSONNEL ONLY.

Were data collected? **No** ☐ *(provide reason in comments)*

If **Yes**, data collected on visit date ☐ **or** specify date: _____ (DD-Mon-YYYY)

Comments:

Only the patient (subject) should enter information onto this questionnaire.

Over the last 2 weeks, how often have you been bothered by any of the following problems?	**Not at all**	**Several days**	**More than half the days**	**Nearly every day**
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

SCORING FOR USE BY STUDY PERSONNEL ONLY

0 + _____ + _____ + _____

=Total Score: _____

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all	**Somewhat difficult**	**Very difficult**	**Extremely difficult**
☐	☐	☐	☐

Developed by Drs. Robert L. Spitzer, Janet B.W. Williams, Kurt Kroenke and colleagues, with an educational grant from Pfizer Inc.

 EPI0905.PHQ9P

I confirm this information is accurate.	Patient's/Subject's initials:	Date:

Appendix F. Health Care Resource Utilization (Unscheduled Outpatient Visits, Emergency Room Visits and Hospitalizations)

1. Since the last study visit has the subject had any physician/health care visits for their Chronic Plaque Psoriasis other than the protocol visits?

☐ No ☐ Yes (if yes provide the following)

If yes provide the following:

I. Since the last visit, has the subject been seen by a physician for his/her Psoriasis?

YES: _____
NO: _____
If YES, how many times: _____

II. Since the last visit, has the subject been seen in the Emergency Room for his/her Psoriasis?

YES: _____
NO: _____
If YES, how many times: _____

III. Since the last visit, has the subject been admitted to the hospital due to his/her Psoriasis?

YES: _____
NO: _____
If YES, how many times: _____
IF YES, please indicate the total number of days in the hospital: _____

Appendix G. Work Productivity and Activity Impairment Questionnaire: Specific Health Problem V2.0 (WPAI:SHP)

The following questions ask about the effect of your PSORIASIS on your ability to work and perform regular activities. *Please fill in the blanks or circle a number, as indicated.*

1. Are you currently employed (working for pay)? _____ NO ___ YES
   If NO, check "NO" and skip to question 6.

The next questions are about the **past seven days**, not including today.

2. During the past seven days, how many hours did you miss from work because of problems associated with your PSORIASIS? *Include hours you missed on sick days, times you went in late, left early, etc., because of your PSORIASIS. Do not include time you missed to participate in this study.*

   _____ HOURS

3. During the past seven days, how many hours did you miss from work because of any other reason, such as vacation, holidays, time off to participate in this study?

   _____HOURS

4. During the past seven days, how many hours did you actually work?

   _____HOURS *(If "0," skip to question 6.)*

5. During the past seven days, how much did your PSORIASIS affect your productivity while you were working?

   Think about days you were limited in the amount or kind of work you could do, days you accomplished less than you would like, or days you could not do your work as carefully as usual. If PSORIASIS affected your work only a little, choose a low number. Choose a high number if PSORIASIS affected your work a great deal.

   Consider only how much PSORIASIS affected productivity while you were working.

PSORIASIS had no effect on my work	0	1	2	3	4	5	6	7	8	9	10	PSORIASIS completely prevented me from working

CIRCLE A NUMBER

6. During the past seven days, how much did your PSORIASIS affect your ability to do your regular daily activities, other than work at a job?

By regular activities, we mean the usual activities you do, such as work around the house, shopping, childcare, exercising, studying, etc. Think about times you were limited in the amount or kind of activities you could do and times you accomplished less than you would like. If PSORIASIS affected your activities only a little, choose a low number. Choose a high number if PSORIASIS affected your activities a great deal.

Consider only how much PSORIASIS affected your ability to do your regular daily activities, other than work at a job.

PSORIASIS had no effect on my daily activities	0	1	2	3	4	5	6	7	8	9	10	PSORIASIS completely prevented me from doing my daily activities

CIRCLE A NUMBER

WPAI:SHP V2.0 (US English)

Appendix H. Rosenberg Self-Esteem Scale

Instructions: Below is a list of statements dealing with your general feelings about yourself. If you strongly agree, circle **SA**. If you agree with the statement, circle **A**. If you disagree, circle **D**. If you strongly disagree, circle **SD**.

1.	On the whole, I am satisfied with myself.	**SA**	**A**	**D**	**SD**
2.	At times, I think I am no good at all.	**SA**	**A**	**D**	**SD**
3.	I feel that I have a number of good qualities.	**SA**	**A**	**D**	**SD**
4.	I am able to do things as well as most other people.	**SA**	**A**	**D**	**SD**
5.	I feel I do not have much to be proud of.	**SA**	**A**	**D**	**SD**
6.	I certainly feel useless at times.	**SA**	**A**	**D**	**SD**
7.	I feel that I'm a person of worth, at least on an equal plane with others.	**SA**	**A**	**D**	**SD**
8.	I wish I could have more respect for myself.	**SA**	**A**	**D**	**SD**
9.	All in all, I am inclined to feel that I am a failure.	**SA**	**A**	**D**	**SD**
10.	I take a positive attitude toward myself.	**SA**	**A**	**D**	**SD**

Rosenberg M. *Society and the adolescent self-image.* Princeton, NJ: Princeton University Press; 1965.

Appendix I. Census Socio-Demographic Questionnaire

1. Are you from a Spanish/Hispanic/Latino background?
   - ☐ Yes
   - ☐ No, not Spanish/Hispanic/Latino

2. What is the highest level of education you have completed? *(check one answer)*
   - ☐ Less than high school
   - ☐ High school
   - ☐ Associate degree, technical, or trade school
   - ☐ College
   - ☐ Graduate school
   - ☐ Other

3. What is your marital status?
   - ☐ Now married *(if checked, proceed to question 4)*
   - ☐ Widowed
   - ☐ Divorced *(if checked, proceed to question 5)*
   - ☐ Separated
   - ☐ Never married

   If you checked "now married" or "divorced" above, please answer questions 4 and 5.

4. If you are currently married, is this your:
   - ☐ First marriage
   - ☐ Second marriage
   - ☐ Third marriage
   - ☐ Greater than third marriage

5. If you are divorced, is this your:
   - ☐ First divorce
   - ☐ Second divorce
   - ☐ Greater than second divorce

6. What is your current work status?

- ☐ Working for pay at a job or business
- ☐ Unemployed
- ☐ Working, but not for pay, at a family-owned job or business

If you currently have a job or business, proceed to question 7.
If you currently do not have a job or business, proceed to question 8.

7. What category below best describes your current job or business?

- ☐ Administrator, Manager
- ☐ Teacher
- ☐ Professional
- ☐ Administrative support, including clerical
- ☐ Sales, retail
- ☐ Sales, business goods and services
- ☐ Technician
- ☐ Protective service
- ☐ Private household service
- ☐ Other service
- ☐ Machine operator, assembler, inspector
- ☐ Transportation operator
- ☐ Handler, helper, laborer
- ☐ Mechanic, repairer, precision production
- ☐ Construction, mining
- ☐ Farming
- ☐ Forestry, fishing, groundskeeping
- ☐ Armed forces

8. What is the main reason you do not have a job or business?

- ☐ Taking care of house or family
- ☐ Going to school
- ☐ Retired
- ☐ On family or maternity leave
- ☐ Disabled

9. What was your overall income last year (from wages or salary, tips, commissions, bonuses and other sources)?

- ☐ < $5,000
- ☐ $5,001 – $10,000
- ☐ $10,001 – $20,000
- ☐ $20,001 – $30,000
- ☐ $30,001 – $40,000
- ☐ $40,001 – $50,000
- ☐ $50,001 – $75,000
- ☐ $75,001 – $100,000
- ☐ $100,000 or more

Census's American Community Survey (ACS) (www.census.gov), Bureau of Labor Statistics surveys (www.bls.gov), and the Medical Expenditure Panel Survey (MEPS) (www.meps.ahrq.gov)

Appendix J. Medical Outcomes (MOS)-Social Activities Scale

The next questions ask about your social activities.

1. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

(Circle One)

All of the time 1
Most of the time 2
A good bit of the time 3
Some of the time 4
A little of the time 5
None of the time 6

---

2. Compared to your usual level of social activity, has your social activity during the past 6 months decreased, stayed the same, or increased because of a change in your physical or emotional condition?

(Circle One)

Much less socially active than before 1
Somewhat less socially active than before 2
About as socially active as before 3
Somewhat more socially active than before 4
Much more socially active than before 5

3. Compared to others your age, are your social activities more or less limited because of your physical health or emotional problems?

(Circle One)

Much more limited than others 1
Somewhat more limited than others 2
About the same as others 3
Somewhat less limited than others 4
Much less limited than others 5

Stewart AL, Ware JE. *Measuring functioning and well-being: the medical outcomes study approach.* Durham: Duke University Press; 1992.

Appendix K. Psoriasis Impact and Experience

Instructions: The following lists several statements by people with psoriasis. Please indicate the extent to which you agree or disagree with each of the statements.

		Strongly Agree	Agree	Not Sure but Probably Agree	Not Sure but Probably Disagree	Disagree	Strongly Disagree
1	I sometimes avoid social situations because of psoriasis.	☐	☐	☐	☐	☐	☐
2	If I thought an employer might discriminate against someone because of psoriasis, I would not apply for the job.	☐	☐	☐	☐	☐	☐
3	An employer who knows a person has a history of psoriasis will probably pass over the application and give the job to someone else.	☐	☐	☐	☐	☐	☐
4	People do not want to be my friend when they learn I have psoriasis.	☐	☐	☐	☐	☐	☐
5	I would not apply or get training for a job that involved dealing with the public because of my psoriasis.	☐	☐	☐	☐	☐	☐
6	I feel the need to hide the fact that I have psoriasis.	☐	☐	☐	☐	☐	☐
7	I feel embarrassed because of my psoriasis.	☐	☐	☐	☐	☐	☐
8	I sometimes think that I am rejected or treated with caution because of my psoriasis.	☐	☐	☐	☐	☐	☐
9	I have the feeling that I am worth less than others.	☐	☐	☐	☐	☐	☐
10	When skin has broken out badly, there are times when I think that life is not worth living.	☐	☐	☐	☐	☐	☐
11	I try to dress in a way that makes my psoriasis as unnoticeable as possible.	☐	☐	☐	☐	☐	☐

Items 1–5 from the Feelings of Stigmatization Questionnaire (Ginsburg & Link 1989)

Items 6–11 from the Questionnaire for the Experience of Skin Complaints (QES) (Schmid-Ott et al. 1996)

Appendix L. Illness Cognition Questionnaire

To what extent do you agree with the following statements?	not at all	some-what	to a large extent	completely
1. Because of my illness I miss the things I like to do most.	1	2	3	4
2. I can handle the problems related to my illness.	1	2	3	4
3. I have learned to live with my illness.	1	2	3	4
4. Dealing with my illness has made me a stronger person.	1	2	3	4
5. My illness controls my life.	1	2	3	4
6. I have learned a great deal from my illness.	1	2	3	4
7. My illness makes me feel useless at times.	1	2	3	4
8. My illness had made life more precious to me.	1	2	3	4
9. My illness prevents me from doing what I would really like to do.	1	2	3	4
10. I have learned to accept the limitations imposed by my illness.	1	2	3	4
11. Looking back, I can see that my illness has also brought about some positive changes in my life.	1	2	3	4
12. My illness limits me in everything that is important to me.	1	2	3	4
13. I can accept my illness well.	1	2	3	4
14. I think I can handle the problems related to my illness, even if the illness gets worse.	1	2	3	4
15. My illness frequently makes me feel helpless.	1	2	3	4
16. My illness has helped me realize what's important in life.	1	2	3	4
17. I can cope effectively with my illness.	1	2	3	4
18. My illness has taught me to enjoy the moment more.	1	2	3	4

Appendix M. Insurance Status

1.	Do you currently have insurance coverage?	☐ Yes	☐ No
	If yes, are you covered by:		
a.	A health insurance plan provided through your or your family member's current or former employer or union?	☐ Yes	☐ No
b.	A health insurance plan that you or your member(s) purchased directly from an insurance company (i.e., not related to current or past employment)?	☐ Yes	☐ No
c.	Medicare?	☐ Yes	☐ No
d.	Medicaid?	☐ Yes	☐ No
e.	TRICARE, CHAMPUS, CHAMPVA, VA, military health care, or Indian Health Service?	☐ Yes	☐ No

Current Population Survey (www.census.gov/cps/)

Appendix N. Patient Global Assessment

Patients will rank the severity of their psoriasis at the time of their registry visit.

Please check the box corresponding to the description which best describes your psoriasis today.

☐ 0 = complete disease control

☐ 1 = good disease control

☐ 2 = limited disease control

☐ 3 = uncontrolled disease

Appendix O. Protocol Amendment: List of Changes

The summary of changes is listed in Section 1.1.

Global Protocol Change

Changed all instances of "DRF" and eDRF" to "eCRF."

Specific Protocol Changes

Section 1.0 Title Page
"Sponsor/Emergency Contact:"
Previously read:

Sponsor/Emergency Contact:	[redacted]

Has been changed to read:

Sponsor/Emergency Contact:	[redacted]

Section 3.0 Introduction
Sixteenth paragraph previously read:

The risks of squamous cell carcinoma (SCC) and basal cell carcinoma (BCC) are known to be increased in patients with psoriasis. The standardized incidence ratio (SIR) has been

reported to be 2.2 for BCC and 4.1 for SCC.[14] A meta-analysis confirmed the high risk of SCC in psoriasis patients treated with PUVA, as well as an increase in the ratio SCC to BCC as the PUVA exposure level increased.[15] During the controlled portions of HUMIRA® rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, and plaque psoriasis trials, the rate of non-melanoma skin cancers was higher among HUMIRA®-treated subjects compared with control subjects. Accurate assessment of the magnitude of the difference in risk for non-melanoma skin cancer among HUMIRA®-treated psoriasis subjects compared with control subjects is complicated by the possibility of ascertainment bias, if established skin cancers have been obscured initially by coexisting psoriatic plaques.[19]

Has been changed to read:

The risks of squamous cell carcinoma (SCC) and basal cell carcinoma (BCC) are known to be increased in patients with psoriasis. The standardized incidence ratio (SIR) has been reported to be 2.2 for BCC and 4.1 for SCC.[14] A meta-analysis confirmed the high risk of SCC in psoriasis patients treated with PUVA, as well as an increase in the ratio of SCC to BCC as the PUVA exposure level increased.[15] During the controlled portions of HUMIRA® rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, and plaque psoriasis clinical trials, the rate of non-melanoma skin cancers was higher among HUMIRA®-treated subjects compared with control subjects. Accurate assessment of the magnitude of the difference in risk for non-melanoma skin cancer among HUMIRA®-treated psoriasis subjects compared with control subjects is complicated by the possibility of ascertainment bias, if established skin cancers have been obscured initially by coexisting psoriatic plaques.[19]

Section 3.1 Safety Information
Add: new section

3.1 Safety Information

Adalimumab therapy has a well established and well described safety profile based on extensive post-marketing experience and continued clinical trial patient exposure since the

first approved indication in 2002 for rheumatoid arthritis. A detailed discussion of the clinical toxicology, metabolism, pharmacology and safety experience with adalimumab can be found in the current Package Insert. AbbVie is committed to continue to collect safety information including those events that may occur in this registry in order to confirm this established safety profile and to identify any unknown potential adverse reactions, rare events and those events with a long latency. AbbVie is participating in an FDA-requested, TNF inhibitor class wide exploration of the rare appearance of malignancy in patients who are 30 years of age or younger at the time of diagnosis. The risk of malignancy in this age group has not been established and is difficult to study due to its rarity. AbbVie appreciates your attention to the additional reporting requirements needed in this unlikely event, outlined in Section 7.5 under Serious Adverse Event Reporting.

Section 6.1 Selection of Population
First paragraph previously read:

Once a decision has been made between the physician and the patient to use HUMIRA® as part of usual care for chronic plaque psoriasis, sites will be encouraged to offer enrollment to all eligible patients. Patients from HUMIRA® clinical trials will be offered enrollment in the registry. Prior to collecting any registry related information, written patient informed consent must be obtained.

Has been changed to read:

After a decision has been made between the physician and the patient to use HUMIRA® as part of usual care for chronic plaque psoriasis, sites will be encouraged to offer enrollment to all eligible patients. Patients from HUMIRA® clinical trials will be offered enrollment in the registry. Prior to collecting any registry related information, written patient informed consent must be obtained.

Section 6.1.3 Patient Follow-up Criteria - HCP Process
Previously read:

Patients who discontinue from the registry before Year 10 will be offered the option to participate in a direct to HCP Process. In order to participate in the follow-up process, the patient must sign a Patient Authorization for Use/Disclosure of Data form.

Has been changed to read:

Patients who discontinue from the registry before Year 10 will be offered the option to participate in a direct to HCP Process, as applicable per local regulations. In order to participate in the follow-up process, the patient must sign a Patient Authorization for Use/Disclosure of Data form.

Section 6.2 Number of Patients to be Enrolled
Previously read:

This is a multi-center, uncontrolled, observational registry of adult patients with chronic plaque Ps treated with HUMIRA® in a clinical practice setting. Approximately 5000 patients in the United States and Canada, and up to an additional 1000 patients in participating European countries will be enrolled. It is expected that approximately 5% to 10% of the patients enrolled in the registry will be continuing therapy started in a prior Abbott HUMIRA® Psoriasis clinical study. The additional patients will be enrolled into the registry from the available psoriasis population within the physicians' practice.

Has been changed to read:

This is a multi-center, uncontrolled, observational registry of adult patients with chronic plaque Ps treated with HUMIRA® in a clinical practice setting. Approximately 5000 patients in the United States and Canada, and up to an additional 1000 patients in participating European countries will be enrolled. It is expected that approximately 5% to 10% of the patients enrolled in the registry will be continuing therapy started in a prior AbbVie HUMIRA® clinical study. The additional patients will be enrolled into the registry from the available psoriasis population within the physicians' practice.

Section 6.3 Physician Selection Criteria
Previously read:

It is expected that approximately 300 physicians from the US and Canada and approximately 100 additional physicians from European countries will participate in this registry based on available eligible patient population. Qualified Physician Assistants and Nurse Practitioners from US sites who treat patients with HUMIRA® are allowed to enroll patients to the registry and will be referred as physicians throughout the protocol. Approximately 100 sites will be included based on participation in HUMIRA® clinical development studies with subjects participating in clinical trials for psoriasis.

Has been changed to read:

It is expected that approximately 300 physicians from the US and Canada and approximately 100 additional physicians from European countries will participate in this registry based on available eligible patient population. Qualified Physician Assistants and Nurse Practitioners from US sites who treat patients with HUMIRA® are allowed to enroll patients to the registry and will be referred to as physicians throughout the protocol. Approximately 100 sites will be included based on prior participation in HUMIRA® clinical development studies with subjects participating in clinical trials for HUMIRA®.

Section 6.4 Registry Duration
Second paragraph previously read:

A patient may withdraw from the registry at any time without prejudice. If the physician, for any reason, decides it is in the best interest of the patient to discontinue HUMIRA®, treatment should be stopped. Physicians are encouraged to keep patients in the registry for a full 10-year observation period irrespective of future treatment decisions so important and complete safety information can be obtained. Patients who develop an AE of Special Interest or SAE while in the registry will be followed until event resolution. For patients who develop an AE of Special Interest or SAE in the final year of the registry will be followed maximally for one year following the onset of the event. If a patient withdraws or is withdrawn from the registry, such should be noted, along with the reason

for withdrawal on the electronic Termination Data Report Form (eTDRF). At the time of withdrawal, an assessment of the patient's current medical condition will be completed.

Has been changed to read:

A patient may withdraw from the registry at any time without prejudice. If the physician, for any reason, decides it is in the best interest of the patient to discontinue HUMIRA®, treatment should be stopped. Physicians are encouraged to keep patients in the registry for a full 10-year observation period irrespective of future treatment decisions so that important and complete safety information can be obtained. Patients who develop an AESI or SAE while in the registry will be followed throughout the patient's participation in the registry or direct to HCP process until satisfactory resolution or until 70 days following the last registry dose (whichever is longer). Follow-up received on ongoing SAEs and/or AESIs at the time of registry conclusion should be reported using post-marketing reporting requirements. If a patient withdraws or is withdrawn from the registry, such should be noted, along with the reason for withdrawal on the electronic Study Completion eCRF). At the time of withdrawal, an assessment of the patient's current medical condition will be completed.

Section 6.5 Registry Conduct
First through ninth paragraphs previously read:

Physicians will be provided with a registry kit that includes a protocol, patient informed consent forms, access to electronic Data Report Forms (eDRFs), including SAE Report Forms, specially designed eDRFs to collect AEs of Special Interest and paper patient questionnaires to collect Patient Reported Outcomes (PRO) (United States only). Physicians will determine the appropriate therapy for each patient in accordance with the locally approved label. The decision to prescribe HUMIRA® to the patients should be made separately from, and prior to the decision to enroll them into the registry.

The physician will follow the patient during regular office visits at intervals as determined by routine clinical practice or as recommended by national guidelines.

At the enrollment (baseline) visit, the physician will complete the Enrollment eDRFs by obtaining and recording all of the available required information. All SAEs and AEs of Special Interest (Table 2) that occurred since the first commercial dose of HUMIRA® will be collected on a specially designed questionnaire/source document for entry into EDC.

Information about medications taken for Ps will be recorded on the eDRF at enrollment and during the regularly scheduled visits that are closest to Months 3, 6, 12, 18, 24, and every 6 months thereafter through Month 120. While the physician may deem it appropriate and necessary to have the patient return for additional visits during the observation period, data will be collected via Data Report Forms (DRFs) only at the intervals that most closely correspond to those described above. However, information related to safety should be captured at any time using the appropriate DRFs.

Physicians should treat their patients as they would in their routine clinical practice. At any time, patients and physicians may choose to interrupt HUMIRA® therapy for any reason. Patients that intermittently stop treatment (Section 10.1) should continue to be monitored during their treatment interruption for safety (SAEs and AEs of Special Interest) and effectiveness. These patients will be questioned for changes in their psoriasis medications and medical history at their regularly scheduled visits.

If treatment with HUMIRA® is permanently discontinued for any reason, patients will be encouraged to remain in the registry. If a patient discontinues the registry, the physician will offer the patient participation in the direct to HCP Process regardless of HUMIRA® treatment. Patients that have affirmatively withdrawn their authorization to have their personal health information used or disclosed in connection with the registry will not be asked to continue in the registry or asked to participate in the HCP Process.

For patients who discontinue the registry, physicians will be asked to obtain the patient's signature on a Patient Authorization for Use/Disclosure of Data form for the completion of a simplified Healthcare Provider (HCP) questionnaire on an annual basis. The first data collection period will capture data from the date of the patient's discontinuation visit or last contact in the registry through the completion of the first annual HCP

questionnaire for the patient. The questionnaire focuses on the collection of surgeries, hospitalizations, deaths, and the events listed as AEs of Special Interest (Table 2), AEs of Special Interest that lead to permanent discontinuation of HUMIRA®, and psoriasis related medication use since registry discontinuation. The questionnaire may be completed by the registry physician or the patient's current HCP (if they are no longer under the care of a registry physician). Any other SAEs experienced should be reported according to standard spontaneous reporting procedures, and they are not subject to the requirements of this protocol.

Effectiveness measures will not be collected from patients participating in direct to HCP Process.

All patients that are unreachable after three documented attempts to contact the patient via phone, email, or certified letter, will be considered lost to follow-up.

Has been changed to read:

Physicians will be provided with a registry kit that includes a protocol, patient informed consent forms, access to electronic Case Report Forms (eCRFs), including SAE Report Forms, specially designed eCRFs to collect AEs of Special Interest and paper patient questionnaires to collect Patient Reported Outcomes (PRO) (United States only). Physicians will determine the appropriate therapy for each patient in accordance with the locally approved label. The decision to prescribe HUMIRA® to the patients should be made separately from, and prior to the decision to enroll them into the registry.

The physician will follow the patient during regular office visits at intervals as determined by routine clinical practice or as recommended by national guidelines.

At the enrollment (baseline) visit, the physician will complete the Enrollment eCRFs by obtaining and recording all of the available required information. All SAEs and AEs of Special Interest (Table 2) that occurred since the first commercial dose of HUMIRA® will be collected on a specially designed questionnaire/source document for entry into EDC.

Information about medications taken for Psoriasis will be recorded on the eCRF at enrollment and during the regularly scheduled visits that are closest to Months 3, 6, 12, 18, 24, and every 6 months thereafter through Month 120. While the physician may deem it appropriate and necessary to have the patient return for additional visits during the observation period, data will be collected via electronic Case Report Forms (eCRFs) only at the intervals that most closely correspond to those described above. However, information related to safety should be captured at any time using the appropriate eCRFs.

Physicians should treat their patients as they would in their routine clinical practice. At any time, patients and physicians may choose to interrupt HUMIRA® therapy for any reason. Patients that intermittently stop treatment (Section 10.1) should continue to be monitored during their treatment interruption for safety (SAEs and AEs of Special Interest) and effectiveness, if applicable. These patients will be questioned for changes in their psoriasis medications and medical history at their regularly scheduled visits.

If treatment with HUMIRA® is permanently discontinued for any reason, patients will be encouraged to remain in the registry. If a patient discontinues the registry, the physician will offer the patient participation in the direct to HCP Process, as applicable per local regulations, regardless of HUMIRA® treatment. Patients that have affirmatively withdrawn their authorization to have their personal health information used or disclosed in connection with the registry will not be asked to continue in the registry or asked to participate in the HCP Process.

For patients who discontinue the registry, physicians will be asked to obtain the patient's signature on a Patient Authorization for Use/Disclosure of Data form for the completion of a simplified Healthcare Provider (HCP) questionnaire on an annual basis, as applicable per local regulations. The first data collection period will capture data from the date of the patient's discontinuation visit or last contact in the registry through the completion of the first annual HCP questionnaire for the patient. The questionnaire focuses on the collection of surgeries, hospitalizations, deaths, and the events listed as AEs of Special Interest (Table 2), AEs of Special Interest that lead to permanent discontinuation of HUMIRA®, and psoriasis related medication use since registry discontinuation. The

questionnaire may be completed by the registry physician or the patient's current HCP (if they are no longer under the care of a registry physician). Any other SAEs experienced should be reported according to standard spontaneous reporting procedures, and they are not subject to the requirements of this protocol.

Effectiveness measures will not be collected from patients participating in direct to HCP Process.

All patients that are unreachable after three consecutive documented attempts to contact the patient via phone, email, or certified letter, will be considered lost to follow-up.

Table 1. Registry Activities
Previously read:

Activity	Registry Enrollment	Month[a] 3	Month[a] 6	Month[a] 12	Month[a] 18, 24, 30, 36, 42, 48, 54	Month[a] 60	Month[a] 66, 72, 78, 84, 90, 96, 102, 108, 114	Upon Completion Month[a] 120 or Premature Discontinuation	At Time of Reported Event
Inclusion/Exclusion Criteria	X								
Informed Consent	X								
Demographics	X								
Medical History and Treatment Modality	X								
Safety Data Collection (AEs of Special Interest/SAEs)	X	X	X	X	X	X	X	X	X
Concomitant Ps Medications	X	X	X	X	X	X	X	X	X
Concomitant Medications used to treat AE of Special Interest/SAE	X	X	X	X	X	X	X	X	X
Physician Global Assessment	X	X	X	X	X	X	X	X	
PROs[b]									
Patient Global Assessment	X	X	X	X	X	X	X	X	
DLQI	X		X	X	X[c]	X	X[c]	X	
PHQ-9	X		X	X	X[c]	X	X[c]	X	
Healthcare Resource Utilization (Unscheduled Outpatient Visits, Emergency Room Visits and Hospitalizations Questionnaire)	X		X	X	X[c]	X	X[c]	X	
WPAI	X		X	X	X[c]	X	X[c]	X	

Table 1. Registry Activities (Continued)

Activity	Registry Enrollment	Month[a] 3	Month[a] 6	Month[a] 12	Month[a] 18, 24, 30, 36, 42, 48, 54	Month[a] 60	Month[a] 66, 72, 78, 84, 90, 96, 102, 108, 114	Upon Completion Month[a] 120 or Premature Discontinuation	At Time of Reported Event
Rosenberg Self-Esteem Scale	X			X		X		X	
Census Socio-Demographic Questionnaire	X					X		X	
Medical Outcomes (MOS)-Social Activities Scale	X			X		X		X	
Psoriasis Impact and Experience	X			X		X		X	
Illness Cognition Questionnaire	X			X		X		X	
Insurance Status	X			X		X		X	
Data Report Form Completion	X	X	X	X	X	X	X	X	X

Has been changed to read:

Activity	Registry Enrollment	Month[a] 3	Month[a] 6	Month[a] 12	Month[a] 18, 24, 30, 36, 42, 48, 54	Month[a] 60	Month[a] 66, 72, 78, 84, 90, 96, 102, 108, 114	Upon Completion Month[a] 120 or Premature Discontinuation	At Time of Reported Event
Inclusion/Exclusion Criteria	X								
Informed Consent	X								
Demographics	X								
Medical History and Treatment Modality	X								
Safety Data Collection (AEs of Special Interest/SAEs)	X	X	X	X	X	X	X	X	X
Prior and Concomitant Psoriasis Medications	X	X	X	X	X	X	X	X	X
Concomitant Medications at Time of Reported SAE or AE of Interest	X	X	X	X	X	X	X	X	X
Physician Global Assessment	X	X	X	X	X	X	X	X	
PROs[b]									
Patient Global Assessment	X	X	X	X	X	X	X	X	
DLQI	X		X	X	X[c]	X	X[c]	X	
PHQ-9	X		X	X	X[c]	X	X[c]	X	
Healthcare Resource Utilization (Unscheduled Outpatient Visits, Emergency Room Visits and Hospitalizations Questionnaire)	X		X	X	X[c]	X	X[c]	X	
WPAI	X		X	X	X[c]	X	X[c]	X	

Table 1. Registry Activities (Continued)

Activity	Registry Enrollment	Month[a] 3	Month[a] 6	Month[a] 12	Month[a] 18, 24, 30, 36, 42, 48, 54	Month[a] 60	Month[a] 66, 72, 78, 84, 90, 96, 102, 108, 114	Upon Completion Month[a] 120 or Premature Discontinuation	At Time of Reported Event
Rosenberg Self-Esteem Scale	X			X		X		X	
Census Socio-Demographic Questionnaire	X					X		X	
Medical Outcomes (MOS)-Social Activities Scale	X			X		X		X	
Psoriasis Impact and Experience	X			X		X		X	
Illness Cognition Questionnaire	X			X		X		X	
Insurance Status	X			X		X		X	
Case Report Form Completion	X	X	X	X	X	X	X	X	X

Section 6.5.3 Medical History
Third paragraph previously read:

Patients rolling over from a prior psoriasis clinical trial will be asked to provide medical history only for previously unreported conditions and/or conditions not requested to be reported in the original study of participation.

Has been changed to read:

Patients rolling over from a prior HUMIRA® clinical trial will be asked to provide medical history only for previously unreported conditions and/or conditions not requested to be reported in the original study of participation.

Section 6.5.4 Prior and Concomitant Medications
Add: new third paragraph

In addition, for patients age ≤ 30 with a reported malignancy adverse event, prior exposure to, or current use of, antineoplastics, or other drugs which have a risk of malignancy as stated in their label and other relevant dosing information to estimate total exposure will be collected in the source documents and appropriate eCRF pages. At the time of the reported malignancy adverse event, sites will be asked if any of the prior and concomitant medications contributed to the event. Any medications used prior to the registry will be captured on the appropriate eCRF. Information on the reason for use, date(s) of administration including start and end dates, highest maintained dose, dosage information including dose, route and frequency, and reason for stopping the medication will be collected in the source documents and appropriate eCRF pages.

Section 6.5.4 Prior and Concomitant Medications
Add: new last paragraph

The AbbVie Study-Designated Physician (SDP) should be contacted if there any questions regarding prior or concomitant medications.

Section 6.6 Withdrawal of Patients from Registry
Previously read:

A patient may withdraw from the registry at any time without prejudice. If the physician, for any reason, decides it is in the best interest of the patient to permanently discontinue HUMIRA®, treatment should be stopped but the patient should be encouraged to continue in the registry as outlined in Section 6.0. If a patient withdraws or is lost to follow-up, such should be noted, along with the reason for withdrawal on the eTDRF.

Patients who discontinue from the registry for any reason other than withdrawn consent, will be contacted to determine interest in participation in the direct to HCP Process.

Has been changed to read:

A patient may withdraw from the registry at any time without prejudice. If the physician, for any reason, decides it is in the best interest of the patient to permanently discontinue HUMIRA®, treatment should be stopped but the patient should be encouraged to continue in the registry as outlined in Section 6.0. If a patient withdraws or is lost to follow-up, such should be noted, along with the reason for withdrawal on the Study Completion eCRF.

Patients who discontinue from the registry for any reason other than withdrawn consent, will be contacted to determine interest in participation in the direct to HCP Process, as applicable per local regulations.

Table 2. AEs of Special Interest for This Registry
Previously read:

Serious and non-serious opportunistic infections, including the following bacterial, fungal, viral and parasitic infections: Aspergillus, Blastomyces, Candida, Coccidioides, Cryptococcal, Cytomegaloviral, Histoplasma, Listeria, Nocardia, Paracoccidiodes, Pneumocystis, Toxoplasma, Tuberculosis, Herpes, Kaposi's sarcoma, Bacillary angiomatosis, Mucormycosis, Progressive Vaccinia, Zygomycosis, BK virus, and JC virus
Lymphoma
Hepatosplenic T-cell lymphoma
Leukemia
Non-melanoma skin cancer (NMSC)
Other malignancies (except lymphoma, leukemia and NMSC)
Immune reactions including lupus, lupus-like reactions, and severe allergic reactions
Congestive heart failure (CHF)
Cerebrovascular accident (CVA)
Myocardial infarction (MI)
CNS demyelinating disorders (including MS and Guillain-Barré syndrome)
Hepatic events that are serious or lead to permanent discontinuation of HUMIRA (e.g., persistent liver function test abnormalities, acute liver failure and other serious hepatic events).
Hematologic events that are serious or lead to permanent discontinuation of HUMIRA (e.g., aplastic anemia, Granulocytopenia, Granulocyte Maturation Arrest, Leukopenia, Neutropenia, Pancytopenia and Thrombocytopenia)
Worsening of Psoriasis
Vasculitis
Diverticulitis
Intestinal perforation

Has been changed to read:

Serious and non-serious opportunistic infections, including the following bacterial, fungal, viral and parasitic infections: Aspergillus, Blastomyces, Candida, Coccidioides, Cryptococcal, Cytomegalovirus, Histoplasma, Listeria, Nocardia, Paracoccidioides, Pneumocystis, Toxoplasma, Tuberculosis, Herpes, Bacillary angiomatosis, Mucormycosis, Progressive Vaccinia, Zygomycosis, BK virus, and JC virus
Lymphoma
Hepatosplenic T-cell lymphoma
Leukemia
Non-melanoma skin cancer (NMSC)
Other malignancies (except lymphoma, leukemia and NMSC)
Immune reactions including lupus, lupus-like reactions, and severe allergic reactions
Congestive heart failure (CHF)
Cerebrovascular accident (CVA)
Myocardial infarction (MI)
CNS demyelinating disorders (including MS and Guillain-Barré syndrome)
Hepatic events that are serious or lead to permanent discontinuation of HUMIRA (e.g., persistent liver function test abnormalities, acute liver failure and other serious hepatic events)
Hematologic events that are serious or lead to permanent discontinuation of HUMIRA (e.g., aplastic anemia, Granulocytopenia, Granulocyte Maturation Arrest, Leukopenia, Neutropenia, Pancytopenia and Thrombocytopenia)
Worsening of Psoriasis
Vasculitis
Diverticulitis
Intestinal perforation

Section 7.3 Relationship to Pharmaceutical Product
Add: second paragraph

If an Investigator's opinion of possibly, probably not, or not related to pharmaceutical product is given, an Other cause of event must be provided by the Investigator for the SAE.

Section 7.4 Adverse Event Collection Period
Previously read:

SAEs and AE of Special Interest will be reported to Abbott starting from the first commercial dose of HUMIRA or when the initial informed consent is signed, (whichever date is earlier), throughout the patient's participation in the registry, up to 10 years. AEs that lead to permanent HUMIRA® discontinuation will be reported to Abbott following enrollment throughout the patient's participation in the registry, up to 10 years. If an SAE or AE of Special Interest begins in the 10th year, the patient will be followed to a satisfactory clinical resolution for up to one-year after the onset of the AE. Events that are ongoing at the end of the 10-year observational period will be reported via standard post-marketing reporting practices.

SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® will be recorded throughout the patient's participation in the registry. For patients participating in the direct to HCP process in addition to surgeries, hospitalizations, deaths, and the events listed as AEs of Special Interest (Table 2), AEs of Special Interest that lead to permanent discontinuation of HUMIRA® will be collected.

In the event HUMIRA® therapy is interrupted (Section 10.1), the patient will remain in the registry and continue to be monitored during the treatment interruption for SAEs and AEs of Special Interest and will be questioned for changes in their psoriasis medications and medical history of the event at their registry visits. If treatment with HUMIRA® is permanently discontinued for any reason, the reason will be recorded and the patient should be encouraged to remain in the registry for the full 10 years.

For patients enrolled from a prior Abbott psoriasis study, ongoing events at the time of registry entry will be collected and resolved within the primary clinical trial.

Has been changed to read:

SAEs, AEs of Special Interest, and AEs that lead to permanent registry HUMIRA® discontinuation will be reported to AbbVie starting from the first commercial dose of

HUMIRA® or when the initial informed consent is signed, (whichever date is earlier), throughout the patient's participation in the registry, or direct to HCP process, until satisfactory resolution or for 70 days after their last dose of registry drug (whichever period is longer) to further evaluate safety.

Follow-up received on ongoing SAEs and/or AESIs post registry conclusion should be reported using standard Post-Marketing Reporting.

For patients participating in the direct to HCP process, surgeries, hospitalizations, deaths, events listed as AEs of Special Interest (Table 2), and AEs of Special Interest that lead to permanent discontinuation of HUMIRA® will be collected.

In the event HUMIRA® therapy is interrupted (Section 10.1), the patient will remain in the registry and continue to be monitored during the treatment interruption for SAEs and AEs of Special Interest and will be questioned for changes in their psoriasis medications and medical history of the event at their registry visits. If treatment with HUMIRA® is permanently discontinued for any reason, the reason will be recorded and the patient should be encouraged to remain in the registry for the full 10 years.

For patients enrolled from a prior AbbVie HUMIRA® study, ongoing events at the time of registry entry will be collected.

Section 7.5 Serious Adverse Event Reporting
Previously read:

In the event of a SAE, whether related to HUMIRA® or not, the physician will complete and submit the Serious Adverse Event (SAE) information into the electronic data capture system (EDC) within 24 hours of being made aware of the SAE. If the EDC system is unavailable, the completed Serious Adverse Event Form should be submitted via fax or email to:

[redacted]

For any emergent patient safety concerns, please contact the appropriate medical monitor listed in Section 1.0.

Has been changed to read:

In the event of an SAE, and/or additionally, any non-serious event of malignancy in patients 30 years of age and younger, whether related to HUMIRA® or not, the physician will notify the AbbVie Immunology Clinical Safety Management Team within 24 hours of the physician becoming aware of the event by entering the serious adverse event or non-serious event of malignancy in patients 30 years of age and younger data into the electronic data capture (EDC) system.

If the EDC system is unavailable, the completed Serious Adverse Event Form should be submitted via fax:

FAX to:	[redacted]

For SAE concerns, contact the Immunology Safety Team at:

[redacted]

For any emergent patient safety concerns, please contact the physician listed below:

AbbVie Safety and Medical Contact

[redacted]

Section 7.6 Pregnancy Reporting
Previously read:

Pregnancy in a registry patient must be reported to Abbott within 24 hours of the site becoming aware of the pregnancy. Physicians should refer to their local prescribing information when making treatment decisions for patients who become pregnant while being treated with HUMIRA® in the registry. Patients who become pregnant and interrupt their HUMIRA® therapy should remain in the registry and should continue to be monitored for new SAEs and AEs of Special Interest.

All female patients who become pregnant while enrolled in this registry will be followed from the time the pregnancy is reported until the outcome of the pregnancy is known. Information regarding a pregnancy occurrence in a registry patient and the outcome of the pregnancy will be collected. See Appendix O for additional information.

To monitor the outcomes of pregnant women exposed to HUMIRA®, a pregnancy registry has been established in the United States and Canada (http://www.otispregnancy.org). Patients in the United States and Canada are encouraged to register by calling [redacted]

Pregnancy is not considered an AE. However, the medical outcome of an elective or spontaneous abortion, stillbirth or congenital anomaly is considered a SAE and must be reported within 24 hours of the site becoming aware of the event.

Has been changed to read:

Pregnancy in a registry patient must be reported to AbbVie within 1 working day of the site becoming aware of the pregnancy. Pregnancies will be collected from the date of the first dose of HUMIRA® in registry through 150 days following the last dose of registry drug or the end of the patient's participation in registry (whichever is longer).

Physicians should refer to their local prescribing information when making treatment decisions for patients who become pregnant while being treated with HUMIRA® in the registry. Patients who become pregnant and interrupt their HUMIRA® therapy should remain in the registry and should continue to be monitored for new SAEs and AEs of Special Interest.

All female patients who become pregnant while enrolled in this registry will be followed from the time the pregnancy is reported until the outcome of the pregnancy is known. Information regarding a pregnancy occurrence in a registry patient and the outcome of the pregnancy will be collected.

Pregnancy in a registry patient is not considered an adverse event. However, the medical outcome of an elective or spontaneous abortion, stillbirth or congenital anomaly is considered a serious adverse event and must be reported to AbbVie within 24 hours of the site becoming aware of the event.

Section 8.0 Ethics and Quality
Second paragraph previously read:

If a patient has not withdrawn the registry consent, a copy of the signed Patient Authorization for Use/Disclosure of Data form will be obtained prior to participation in the HCP process.

Has been changed to read:

If a patient is willing to participate in the HCP process, a copy of the signed Patient Authorization for Use/Disclosure of Data form will be obtained prior to the participation.

Section 8.1 Quality Assurance
Second paragraph previously read:

Ten percent (10%) of the sites will be monitored on-site during the course of registry participation. At each site selected for a visit, one hundred percent (100%) source document review for SAEs, AEs of Special Interest and dose interruption data will be performed against entries on the eCRF and a quality assurance check will be performed to ensure that the physician is complying with the protocol and local regulations. The monitoring plan will detail how sites will be selected for the on-site monitoring visits. Throughout the registry, CRO and AbbVie will periodically follow-up with the sites to ensure that SAEs and AEs of Special Interest are being reported.

Has been changed to read:

Monitoring visits will be performed at a subset of the sites. At the visists a quality assurance check will be performed against entries on the paper and eCRF and a quality assurance check will be performed to ensure that the physician is complying with the protocol and local regulations. The monitoring plan will detail how sites will be selected for the on-site monitoring visits and what data will be source data verified during the visit. Throughout the registry, CRO and AbbVie will periodically follow-up with the sites to ensure that SAEs and AEs of Special Interest are being reported.

Section 9.0 Case Report Forms
Fifth paragraph previously read:

Upon completion of or termination from the registry, all patients who should have a Termination Data Report Form (eTDRF) completed as well as an assessment of their current medical conditions.

Has been changed to read:

Upon completion of or termination from the registry, all patients should have a Study Completion eCRF completed as well as an assessment of their current medical conditions.

Section 10.1 Analyzable Populations
Second paragraph previously read:

New Prescription Patient Population is defined as patients who have newly initiated HUMIRA® therapy in or within 4 weeks of entry into the registry.

Has been changed to read:

New Prescription Patient Population is defined as patients who have newly initiated HUMIRA® therapy within 4 weeks prior to the entry into the registry and who receive at least one dose of HUMIRA® in the registry (the New Prescription Population is a subset of the All Treated Patient Population).

Section 10.2 Demographics and Registry Enrollment Characteristics
First paragraph and bullets previously read:

Demographics and baseline characteristics will be summarized for the All Treated Patient Population, the New Prescription Patient Population, and the Intermittent Treatment Population. Descriptive statistics will be presented. Number of patients with non-missing values, mean, and standard deviation will be provided for continuous variables. Counts and percentages will be provided for categorical variables. The number and percentage of patients that discontinue from the registry will be summarized, overall and by reason for discontinuation. Duration of observation in the registry and total duration of treatment will be summarized as follows:

- Duration of observation in the registry is defined from the first dose of HUMIRA® in the registry up to the end-of-registry (as defined in Section 12.0).
- Total duration of treatment is defined from the first recorded dose of HUMIRA® to 14 days after the last dose of HUMIRA® excluding that portion

of the treatment interruption period which is more than 14 days after the last dose prior to each treatment interruption.

Has been changed to read:

Demographics and baseline characteristics will be summarized for the All Treated Patient Population, the New Prescription Patient Population, and the Intermittent Treatment Population. Descriptive statistics will be presented. Number of patients with non-missing values, mean, and standard deviation will be provided for continuous variables. Counts and percentages will be provided for categorical variables. The number and percentage of patients that discontinue from the registry will be summarized, overall and by reason for discontinuation. Duration of observation in the registry and total duration of treatment will be summarized as follows:

- Duration of observation in the registry is defined from the first day in the registry (enrollment visit or date of informed consent, up to the end-of-registry (as defined in Section 12.0).
- The duration of treatment in the registry (registry exposure) is defined from the first dose of HUMIRA® in the registry to 14 days after the last dose of HUMIRA® excluding total days of any treatment interruptions.
- Total duration of treatment (total exposure) is defined from the first recorded dose of HUMIRA® (initial dose) to 14 days after the last dose of HUMIRA® excluding total days of any treatment interruptions.

Section 10.3 Safety Analyses
Previously read:

Five main safety analyses will be reported from this registry: four analyses will summarize data through the end-of-registry (as defined in Section 12.0) and one will exclude the HCP Process. The details of the analyses are in Section 10.3.1, Section 10.3.2, and Section 10.3.3.

- Observational AEs: SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® occurring from the first day in the registry through the last contact irrespective of drug treatment duration.
- Registry Treatment-emergent AEs: SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® occurring from the first day in the registry through 70 days after the last dose. For patients who are not taking HUMIRA on the first day in the registry, analysis will begin from the first dose in the registry.
- All Treatment Emergent AEs: SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® occurring from the first recorded dose of HUMIRA® through 70 days after the last dose.
- AEs for intermittent treatment: SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® in the Intermittent Treatment Population.
- Observational AEs excluding HCP process: SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® occurring from the first day in the registry through the last contact excluding the HCP process.

Has been changed to read:

Five main safety analyses will be reported from this registry: four analyses will summarize data through the end-of-registry (as defined in Section 12.0) and one will exclude the HCP Process. The details of the analyses are in Section 10.3.1, Section 10.3.2, and Section 10.3.3. If a patient is not covered by any of the analysis populations, but experiences an AE, this AE will be reported in a separate listing.

- Observational AEs: SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® occurring from the first day in the registry (enrollment visit or date of informed consent, through the last contact (as defined in Section 10.3.1) irrespective of drug treatment duration.
- Registry Treatment-emergent AEs: SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® occurring from the first recorded dose of HUMIRA® in the registry through 70 days after the last

dose excluding AEs occurring during treatment interruptions (as defined in Section 10.1).

- All Treatment Emergent AEs: SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® occurring from the first recorded dose of HUMIRA® (initial dose) through 70 days after the last dose excluding AEs occurring during treatment interruptions (as defined in Section 10.1.
- AEs for intermittent treatment: SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® in the Intermittent Treatment Population.
- Observational AEs excluding HCP process: SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® occurring from the first day in the registry through the last contact excluding the HCP process.

Section 10.3.2 Analysis of Treatment-emergent AEs
Third paragraph previously read:

All Treatment-emergent AEs includes AEs occurring from the first recorded dose of HUMIRA®, up to 70 days after the last dose of HUMIRA® (excluding AEs during TI which are more than 70 days after the last dose of HUMIRA® prior to TI). For patients enrolled from a prior HUMIRA® study or who initiated commercial HUMIRA® therapy before entering the registry, the summaries will include the events reported during their participation in the previous study, any events reported by retrospective data collection, and any events reported during this registry.

Has been changed to read:

All Treatment-emergent AEs include AEs occurring from the first recorded dose of HUMIRA® (i.e., the initial dose) up to 70 days after the last dose of HUMIRA® (excluding AEs during TI which are more than 70 days after the last dose of HUMIRA® prior to TI). For patients enrolled from a prior HUMIRA® study or who initiated commercial HUMIRA® therapy before entering the registry, the summaries will include

the events reported during their participation in the previous study, any events reported by retrospective data collection, and any events reported during this registry.

Section 10.3.4 Analysis of Observational AEs Excluding HCP Process
First paragraph previously read:

The analysis will be performed using data from first recorded dose of HUMIRA® through the last contact, excluding the HCP process. The number and percentage of patients experiencing SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® will be tabulated by body system and Medical Dictionary for Drug Regulatory Activities (MedDRA®) preferred term. Rates (event per 100 patient-year of observation) of SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® and the 95% confidence interval will be provided.

Has been changed to read:

The analysis will be performed using data from first day in the registry through the last contact, excluding the HCP process. The number and percentage of patients experiencing SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® will be tabulated by body system and Medical Dictionary for Drug Regulatory Activities (MedDRA®) preferred term. Rates (event per 100 patient-year of observation) of SAEs, AEs of Special Interest and AEs that lead to permanent discontinuation of HUMIRA® and the 95% confidence interval will be provided.

Section 10.5 Interim Analyses
Previously read:

Interim reports are prepared on an annual basis and began in February 2010. Biennial interim analyses beginning in February 2010 will be based on requirements from Regulatory Agencies.

Has been changed to read:

Interim reports are prepared on an annual basis and began in February 2010. Interim reports are submitted to Regulatory Agencies, as required.

Appendix A. List of Abbreviations and Definition of Terms
Subsection Abbreviations
Add: two abbreviations

AESI Adverse event of special interest
EDC Electronic Data Capture

Appendix A. List of Abbreviations and Definition of Terms
Subsection Abbreviations
"eDRF" previously read:

eDRF Electronic data report form

Has been changed to read:

eCRF Electronic case report form

Appendix A. List of Abbreviations and Definition of Terms
Subsection Abbreviations
Delete: one abbreviation

eTDRF Electronic termination data report form

Appendix B. List of Protocol Signatories
Previously read:

Name	Title	Functional Area
[redacted]		

Has been changed to read:

Name	Title	Functional Area
[redacted]		

Appendix O. Pregnancy Reporting
Delete: appendix

Appendix O. Pregnancy Reporting

Contact the Medical Monitor listed in Section 1.0 to report a patient that is pregnant. A pregnancy reporting form will be supplied separately and should be completed and faxed to the Abbott Medical Monitor within 5 working days of positive test result.

A second form will also be sent approximately 9 months from the date of notification to collect information on the outcome of the pregnancy. This form will also need to be completed and sent back to Abbott.

To monitor outcomes of pregnant women exposed to HUMIRA®, a pregnancy registry has been established for the United States. Physicians in the United States are encouraged to register patients by calling [redacted] and/or provide this information to the patient.

Document Approval

Study P10023 - A 10-Year, Post-marketing, Observational, Registry to Assess Long Term Safety of HUMIRA (Adalimumab) in Adult Patients with Chronic Plaque Psoriasis (Ps) - Amendment 3 - 08Oct2013

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Signed by:	Date:	Meaning Of Signature:
[redacted]		