Title Page

Title	Real-World Outcome of Adalimumab on Rheumatoid Arthritis Patients in Taiwan
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Research Question and Objectives	The overall strategic objective of this non-interventional, observational study is to assess the effect of Adalimumab on health-related quality of life and work productivity in patients with Rheumatoid Arthritis (RA) in Taiwan.
Country(ies) of Study	Taiwan.
Author	Chun-jung Tsai, MD Medical Advisor AbbVie Biopharmaceuticals GmbH Taiwan Branch 15F, No.49, Min Sheng E. Road, Sec. 3, Taipei 104 Taiwan

This study will be conducted in compliance with this protocol.
Confidential Information
No use or disclosure outside AbbVie is permitted without prior written authorization from AbbVie.

Marketing Authorization Holder(s)

Marketing Authorization Holder(s)	AbbVie Biopharmaceuticals GmbH Taiwan Branch [redacted]
MAH Contact Person	Not applicable (Non-PASS PMOS)

1.0 Table of Contents

2.0 Abbreviations

ACR	American College of Rheumatology
AE	Adverse Events
ANOVA	Analysis of Variance
CRF	Case Report Form
CRP	C-Reactive Protein
CTCAE	Common Terminology Criteria for Adverse Events
DAS28	Disease Activity Score in 28 Joints
EQ-5D-3L	EuroQol 5 dimension, 3 level quality of life questionnaire
ESR	Erythrocyte Sedimentation Rate
EULAR	The European League Against Rheumatism
GP	General Practitioner
HAQ DI	Health Assessment Questionnaire Disability Index
HCRU	Healthcare Resource Utilization
ICF	Informed Consent Form
ICH-GCP	International Conference on Harmonization of Good Clinical Practice
NRS	Numeric Rating Scale
PGIC	Patient Global Impression of Change
PHI	Protected Health Information
PRO	Patient-Reported Outcome
QC	Quality Check
QoL	Quality of Life
RA	Rheumatoid Arthritis
SAP	Statistical Analysis Plan
SF-36	Short Form 36-Item Health Survey
SOC	System Organ Class
SOP	Standard Operating Procedure
TNF	Tumor Necrosis Factor
VAS	Visual Analogue Scale
WPAI	Work Productivity and Activity Impairment

3.0 Responsible Parties

Study-Designated Physician/ Sponsor:	[redacted]	
Affiliate Medical Director:	[redacted]	
Statistics Manager/ CRO(S):	[redacted]	
Principal Investigator:	Investigator information is on file at AbbVie	
Sponsor:	**AbbVie Biopharmaceuticals GmbH Taiwan Branch**	[redacted]
Clinical Project Manager:	[redacted]	[redacted]
Emergency Contacts- Affiliate Safety Representative	[redacted]	

PROTOCOL SIGNATURES

Investigator Signature:
I have read and agree to the Protocol Number (P15-778), "Real-World Outcome of Adalimumab on Rheumatoid Arthritis Patients in Taiwan". I am aware of my responsibilities as an investigator under the guidelines of Good Clinical Practices, local laws and regulations (as applicable) and the study protocol. I agree to conduct the study according to these laws and guidelines and to appropriately direct and assist the staff under my control, who will be involved in the study.

Principal (Site) Investigator:

Name (typed or printed): _____

Institution and Address: _____

_____

_____

_____

Telephone Number: _____

Signature: _____ Date: _____
(Day/ Month /Year)

Full investigational site contact details, including telephone numbers, will be documented in the Study Master File.

4.0 Abstract

Title: Real-World Outcome of Adalimumab on Rheumatoid Arthritis Patients in Taiwan.

Rationale and Background: Given the requirement to keep a balance between effectiveness and cost containment to ensure that the available health resources are used in a cost-effective manner, there is an increasing demand for real-world evidence (RWE) from policy makers, regulators, providers and payers in the region to optimize spending and patient outcomes.

So far, there are no data available regarding adalimumab's impact on patients' quality of life (QoL) and healthcare resource utilization (HCRU) in a realistic study design, which provides greater generalization in Taiwan.

The goal of this study is to determine the QoL, HCRU and costs of the patients care in subjects with RA who are treated with adalimumab in these three countries.

Results from study on the impact of adalimumab on Work Productivity and Activity Impairment (WPAI) scores and other Patient-Reported Outcomes (PROs) will be of interest to a variety of stakeholders in the healthcare system including patients, healthcare practitioners and payers in Taiwan.

Research Question and Objectives: The objective of this non-interventional, observational study is to assess the impact of adalimumab on health-related QoL and work productivity in patients with Rheumatoid Arthritis (RA) in Taiwan. Specifically, to achieve the above objective the following concrete steps will be taken:

1. Recruit investigators who are willing and able to recruit and follow new adalimumab users for 6 months follow-up
2. Collect the patients' clinical profile, patient-reported QoL, functioning, work productivity, treatment satisfaction and HCRU of RA patients at adalimumab initiation
3. Follow the patients initiating adalimumab for 24 weeks and identify the changes in clinical, economic, and PROs associated with adalimumab

Study Design: The study is designed as a prospective, observational study to assess the effect of adalimumab on health-related QoL and work productivity in patients with RA in Taiwan.
Note: This study is non-interventional and the subjects/investigators will follow the current clinical practice in each site and also the routine clinical follow up as determine by the treating physician.

RA patients, for whom adalimumab treatment has already been decided, will be recruited from within the clinical settings of each rheumatologist participating in the study. Approximately 100 patients diagnosed with RA that meet the inclusion and exclusion criteria will be enrolled at approximately 7 sites in Taiwan.

To assess health and disability outcomes, the HAQ DI at baseline, Week 12 and Week 24 after treatment initiation with adalimumab will be collected. In addition, other PROs of work activity and well-being, including the WPAI, EQ-5D, and SF-36, will also be collected.

In addition, the health care resource utilization will be collected. This includes surgical procedures, hospitalizations, bed days in hospital, physician consultations etc. Costs will be assigned based on the health care resource utilization using standardized costs for each participating centers.

Population: Subjects will be males and/or females who are attending a routine clinical visit and meet all of the inclusion criteria and none of the exclusion criteria. Approximately 100 patients diagnosed with RA will be recruited.

Inclusion Criteria:
Patients meeting all of the following inclusion criteria at baseline will be included:

1. Subject has a diagnosis of RA as defined by the 1987 revised American College of Rheumatology (ACR) classification criteria and/or the ACR/the European League against Rheumatism (EULAR) 2010 classification criteria (any duration since diagnosis).
2. Male or female subjects ≥ 18 years of age (local definition according to adalimumab label) who is in compliance with eligibility for adalimumab based on the local label.
3. Patients with moderate to severe RA defined as Disease Activity Score in 28 Joints (DAS28) (ESR) or DAS28 (CRP) >3.2
4. Biologically treatment naïve and initiated adalimumab at baseline visit
5. Availability of clinical data of the previous 12 weeks prior to baseline
6. Ability to self-complete patient questionnaires
7. Subject must be able and willing to provide written informed consent and comply with the requirements of this study protocol.

Exclusion Criteria:
Patients meeting any of the following exclusion criteria at baseline will be excluded:

1. Patients who are pregnant or breast feeding at enrolment or wish to become pregnant in the next 24 weeks.
2. Participation in any RA-related clinical trial at the time of enrolment, at baseline or at any point during the past 24 weeks prior to baseline
3. Patients, who in the clinician's view, may not be able to accurately report their QoL or prior resource utilization
4. Patients, who in the clinician's view, may not be able to adhere to adalimumab therapy over 24 weeks.

Variables:

Primary Variable

- Change in HAQ DI score at week 24 from baseline

Secondary Variable

- Change in other PROs (SF-36 domain scales, EQ-5D Index, Work Productivity and Activity Impairment Questionnaire [WPAI]) from baseline to weeks 12 and 24
- Change in HAQ DI score at week 12 from baseline
- Number and percent of patients achieving a clinically meaningful improvement on the HAQ DI, from baseline to weeks 12 and 24
- Healthcare Resource Utilization (HCRU) at baseline, 12 and 24 weeks

Exploratory Variable

- Difference of the change in HAQ DI score from baseline to 24 weeks between as observed population and withdrawal population
- Change in patient satisfaction questions from baseline to weeks 12 and 24
- Patient's impression of change at weeks 12 and 24 from baseline
- Association between disease severity and PROs
- Association between change in disease severity and change in PROs

Data Sources: Case Report Forms (CRFs) and patient questionnaires. Collection of data includes but not limited to subject demographics, clinical history, comorbidities, spontaneous adverse events, and concomitant medications. The following questionnaires will be utilized to collect data directly from participating subjects:

- EQ-5D
- SF-36
- HAQ DI
- WPAI
- HCRU
- Patient Global Impression of Change (PGIC)
- Patient Treatment Satisfaction Questions

Study Size: Approximately 100 patients diagnosed with RA will be recruited. The planned sample size provides at least 95% power for detecting a statistically significant improvement in HAQ-DI (ΔHAQ-DI < 0) assuming a mean ΔHAQ-DI of -0.21 and a standard deviation of 0.5 (reference 11), at two-sided significance level of 0.05 and accounting for a 10% dropout rate. The sample size also provides at least 95% power for detecting a statistically significant clinically meaningful improvement in HAQ-DI (ΔHAQ-DI < -0.22) assuming a mean ΔHAQ-DI of -0.5 and a standard deviation of 0.7, at two-sided significance level of 0.05 and accounting for a 10% dropout rate. For the secondary endpoint WPAI, the sample size provides 63% power for detecting a statistically significant improvement in "hours of work lost" at two-sided significance level of 0.05 and accounting

for a 10% dropout rate, assuming a mean change in "hours of work lost" of 10 and standard deviation of 30 and assuming a 55% employment rate in the study population.

Data Analysis:

Primary Endpoint Analysis

Change in HAQ DI score at 24 weeks after the initiation of adalimumab, in those patients continuing on adalimumab (as observed population). This change will be summarized as the mean and 95% confidence interval and will be tested with a paired t-test.

Secondary Endpoint Analysis

- Change in HAQ DI score at 12 weeks after the initiation of adalimumab, in those patients continuing on adalimumab (as observed population). This change will be summarized as the mean and 95% confidence interval and will be tested with a paired t-test.
- Change in other patient reported outcomes (SF-36 domain scales, EQ-5D Index, WPAI total lost productivity) at weeks 12 and 24 after the initiation of adalimumab, in those patients continuing on adalimumab (as observed population). These changes will be summarized as the means and 95% confidence intervals and will be tested with paired t-tests.
- Number and percent of patients achieving a clinically meaningful improvement on the HAQ DI, as defined by a -0.22 point improvement or greater, at weeks 12 and 24 after the initiation of adalimumab, in those patients continuing on adalimumab (as observed population).

Exploratory Endpoint Analysis

- Change in HAQ DI score at 24 weeks after the initiation of adalimumab, in those patients continuing on adalimumab (as observed population), compared with those patients not continuing on adalimumab (withdrawal population). The mean changes in these two groups will be compared using an independent t-test.
- Healthcare resource utilization will be described using number and percentage within each category (number of consultations, number of procedures received, number of surgeries, number of hospitalizations and length of stay, number of concomitant medications)
- Change in patient satisfaction questions at weeks 12 and 24 after the initiation of adalimumab, in those patients continuing on adalimumab (as observed population). These changes will be summarized as number and percentage of each response and compared with Kruskal–Wallis test. Satisfaction will also be dichotomized and analyzed over time with Cochrane-Armitage test for trends.
- Patient's impression of change at weeks 12 and 24 after the initiation of adalimumab, in those patients continuing on adalimumab (as observed population). These changes will be summarized as number and percentage of each response and compared with Kruskal–Wallis test.
- Associations between disease severity and PROs
- Associations between change in disease severity and change in PROs

Milestones:

Start of Data Collection (FPFV):	10 October 2015
End of Data Collection:	31 January 2017
Database Lock:	28 February 2017
Interim Database Lock:	nil
Interim Report:	nil
Final Report of Study Results:	30 June 2017

5.0 Amendments and Updates

Number	Date	Section of Study Protocol	Amendment or Update	Reason
11011	16/09/2015	n/a	Initial Protocol	n/a
11011	25/09/2015	Management and Reporting of Adverse Events/Adverse Reactions	Delete Pediatric, Malignancy, and Product Complaints	As per the comments of GMA-RC
11011	01/10/2015	Study size	Sample size calculation	As per the comments of GMA-RC
11011	28/10/2015	Management and Reporting of Adverse Events/Adverse Reactions	Amend the AE collection period, AE reporting and Pregnancy as the protocol standards	As per the comments of GMA safety management Subjects will be contacted approximately 70 days following the intake of the last dose of physician-prescribed treatment for an assessment of any new or ongoing AEs.

6.0 Milestones

Major study milestones and their planned dates are as follows:

Start of Data Collection (FPFV):	10 October 2015
End of Data Collection:	31 January 2017
Database Lock:	28 February 2017
Interim Database Lock:	Nil
Interim Report:	Nil
Final Report of Study Results:	30 June 2017

7.0 Rationale and Background

Disability has been defined as impairments, activity limitations and participation restrictions due to personal and environmental factors (1). The concept of disability is one where a physical health condition or disease is evaluated in terms of its impact, difficulties, or limitations on a range of tasks, activities, or roles that are considered typical of everyday life. Examples of affected activities include basic aspects of daily living such as eating, bathing, dressing, household chores and meal preparation, or participation in society, or participation in work.

For public health purposes disability is becoming increasingly important as an outcome measure. Despite this, there has been no data available, within our knowledge, on the effectiveness of adalimumab on health-related QoL and work productivity in patients with Rheumatoid Arthritis (RA) in Taiwan so far. Results from study of effect of adalimumab on Work Productivity and Activity Impairment (WPAI) scores and other Patient-Reported Outcomes (PROs) of work activity and well-being will be of interest to a variety of stakeholders in the healthcare system including patients, healthcare practitioners and payers in Taiwan.

Reimbursement in Taiwan is strongly influenced by local “real -world” evidence of the intervention’s impact on patient outcomes and economic endpoints. The Bureau of National Health Insurance (BNHI) in Taiwan endorsed Dose Tapering and Withdraw (DT&W) guideline that was effective in Jan 2013. Under the DT&W policy, it indicated that when a patient with RA who received 2 years biologics treatment with one of the following criteria: 1) disease activity score (DAS) 28 $\leqq$ 3.2 or 2) erythrocyte sedimentation rate (ESR) $\leqq$ 25mm/h and C-reactive protein (CRP) $\leqq$ 1mg/dL, the biological dose will be tapered to 50% less dosage and then be discontinued after one year of dose spacing. Full-dose biologicals can be re-applied only if a RA patient meets all of the following criteria after one year of dose spacing: (1) DAS28 raise > 1.2; (2) ESR > 25mm/h and (3) ESR raise > 25%.

The government aims to implement DT&W policy to reduce the total health care spending on the biologics. Although the policy was implemented since 2013, physicians as well as patients are generally reluctant to dose tapering. In this regard, it is acknowledged by both physician association and patients associations that there is an intense need to collect RWE to demonstrate the value of continued use of biologics as well as early biological treatment of RA patients to payers.

Abbvie collaborated with Taiwanese rheumatologists to implement the TAPER Study to assess the impact of DT&W policy on biological efficacy and social-economic endpoints by real-world chart review. The preliminary data was presented at the Asian Pacific League of Associations for Rheumatology (APLAR) 2015 Meeting. In addition, these data will be presented at the annual meeting of Taiwan Rheumatology Association

(TRA) in November 2015. We also plan to share the preliminary results of TAPER Study with the review committee of the BNHI to strengthen the importance of continuing biological therapy in RA patients and aim to loosen the DT&W guideline in Taiwan. This is a good example of local public health policy probably being influenced by the RWE.

Considering the particular reimbursement policy in Taiwan, having the more "real world evidence" (RWE) of local economic and health outcomes for the use of adalimumab in moderate to severe RA patients will be more valuable to support the reimbursement / pricing maintenance in Taiwan.

The objective of this non-interventional, observational study is to assess the effect of adalimumab on health-related QoL, work productivity, and healthcare resource utilization (HCRU) in patients with RA in Taiwan.

8.0 Research Question and Objectives

The objective of this study is to assess the effect of adalimumab on health and disability outcomes in patients with the immune-mediated inflammatory diseases of rheumatoid arthritis using the real world data as observed. The effect of adalimumab on health and disability outcomes in these patients will be assessed by the primary outcome measure which is the change in Health Assessment Questionnaire Disability Index (HAQ DI) score at 24 weeks after the initiation of adalimumab. The HAQ DI is selected as the primary point as it is commonly used to assess improvements in physical function in RA clinical trials and recommended by the US Food and Drug Administration (FDA) guidance on RA treatment development (3, 4). In addition, the HAQ-DI has been utilized as a predictor variable in investigations of productivity (5). The HAQ-DI has been demonstrated to be significantly correlated with work-related measures such as work capacity, household work performance, work task performance, and work disability (6-9). In addition, the effect of adalimumab will also be assessed by the secondary outcome measures which are changes to the WPAI, EuroQol 5 dimension (EQ-5D) score, and Short Form 36-Item Health Survey (SF-36) domain scores at 12 and 24 weeks after the initiation of adalimumab in RA.

8.1 Safety Information

Adalimumab therapy has a well-established and well described safety profile based on extensive postmarketing experience and continued clinical trial patient exposure since the first approved indication in 2002 for rheumatoid arthritis. AbbVie is committed to continue to collect safety information including those events that may occur in this trial 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 subjects/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 11.1.5 under Adverse Event Reporting.

9.0 Research Methods

9.1 Study Design

This study is designed as a prospective, observational study to assess the effect of adalimumab on health-related QoL and work productivity in patients with RA in Taiwan in clinical practice.
Note: This study is non-interventional and the subjects/investigators will follow the current clinical practice in each site and also the routine clinical follow up as determine by the treating physician.

This study is non-interventional. Patient therapy is not decided by the study protocol but falls within current medical practice, and the prescription of adalimumab is clearly separated from the decision to include the patient in this study. The subjects/investigator will follow the current clinical practice in each site and also the routine clinical follow up as determine by the treating physician.

RA patients will be recruited from within the clinical settings of each rheumatologist participating in the study. Approximately 100 patients diagnosed with RA that meet the inclusion and exclusion criteria will be enrolled at approximately 7 sites in Taiwan.

To assess health and disability outcomes, the HAQ DI at baseline, Week 12 and Week 24 after treatment initiation with adalimumab will be collected. In addition, other PROs of work activity and well-being, including the WPAI, EQ-5D, and SF-36, will also be collected. All above instruments have been validated for the Chinese version.

The HCRU will also be collected. This includes surgical procedures, hospitalizations, bed days in hospital, physician consultations etc. Costs will be assigned based on the HCRU using standardized costs for each participating centers.

The patients identified by the recruiting investigators based on the study selection criteria will be collected data as observed on QoL, functioning, work productivity,

treatment satisfaction, impression of change and HCRU. Data will be captured at baseline (D0), Week 12 and Week 24.

Subjects may discontinue adalimumab treatment at any time during study participation. Subjects that end study participation early will have a Termination Visit, which may be a routine follow-up visit at investigator's clinic. All subjects will have a data recorded approximately 70 days after the Week 24 dosing or after the last administration of adalimumab to obtain information on any new or ongoing AEs.

Primary Endpoint Analysis
Change in HAQ DI score at 24 weeks after the initiation of adalimumab, in those patients continuing on adalimumab (as observed population). This change will be summarized as the mean and 95% confidence interval and will be tested with a paired t-test.

Secondary Endpoint Analysis
- Change in HAQ DI score at 12 weeks after the initiation of adalimumab, in those patients continuing on adalimumab (as observed population). This change will be summarized as the mean and 95% confidence interval and will be tested with a paired t-test.
- Change in other patient reported outcomes (SF-36 domain scales, EQ-5D Index, WPAI total lost productivity) at weeks 12 and 24 after the initiation of adalimumab, in those patients continuing on adalimumab (as observed population). These changes will be summarized as the means and 95% confidence intervals and will be tested with paired t-tests.
- Number and percent of patients achieving a clinically meaningful improvement on the HAQ DI, as defined by a -0.22 point improvement or greater, at weeks 12 and 24 after the initiation of adalimumab, in those patients continuing on adalimumab (as observed population).

Exploratory Endpoint Analysis
- Change in HAQ DI score at 24 weeks after the initiation of adalimumab, in those patients continuing on adalimumab (as observed population), compared with those patients not continuing on adalimumab (withdrawal population). The mean changes in these two groups will be compared using an independent t-test.
- Healthcare resource utilization will be described using number and percentage within each category (number of consultations, number of procedures received, number of surgeries, number of hospitalizations and length of stay, number of concomitant medications)
- Change in patient satisfaction questions at weeks 12 and 24 after the initiation of adalimumab, in those patients continuing on adalimumab (as observed population). These changes will be summarized as number and percentage of

each response and compared with Kruskal–Wallis test. Satisfaction will also be dichotomized and analyzed over time with Cochrane-Armitage test for trends.

- Patient's impression of change at weeks 12 and 24 after the initiation of adalimumab, in those patients continuing on adalimumab (as observed population). These changes will be summarized as number and percentage of each response and compared with Kruskal–Wallis test.
- Associations between disease severity and PROs
- Associations between change in disease severity and change in PROs

Observation period

- Observation of safety till 70 days after the Week 24 dosing or after the last dose of adalimumab
- Observation of pregnancy till 150 days after the Week 24 dosing or after the last dose of adalimumab

9.1.1 Schedule of Events

Table 1 Data Collection/Observation

	Data Collection/Observation	Baseline[a]	Week 12 (V2) ± 7 days	Week 24 (V3) ± 7 days	Early Termination / Drop out	70 days after the Week 24 or the last dose	150 days after the Week 24 or the last dose
Clinician Packet	Inclusion/exclusion form	X					
	Clinical history/patient demographics	X					
	Comorbidities	X					
	DAS28 (ESR) or DAS28 (CRP)	X	X	X	X		
Patient Packet	EuroQoL 5-Dimension (EQ-5D)	X	X	X	X		
	Short Form 36-Item Health Survey (SF-36)	X	X	X	X		
	Health Assessment Questionnaire (HAQ)	X	X	X	X		
	Work Productivity and Activity Impairment Questionnaire (WPAI)	X	X	X	X		
	Healthcare Resource Utilization (HCRU)	X	X	X	X		
	Patient Global Impression of Change (PGIC)		X	X	X		
	Patient Treatment Satisfaction Questions	X	X	X	X		
Clinician	Adverse events	←				→	
	Pregnancy	←					→

a. The Baseline will serve as the reference date for all subsequent time-points. A ± 7 day window is permitted around scheduled data collection time-points.

9.2 Setting

The study will take place in single country (Taiwan) with multiple centers. The study sites will be identified and selected by AbbVie. The study population shall comprise of male and/or female patients who are attending a routine clinical visit and meet all of the inclusion criteria and none of the exclusion criteria. Overall, approximately 100 subjects with clinically diagnosed RA are planned to be enrolled in the study at up to 7 sites.

The recruiting investigators will select potentially eligible patients from consecutive visits within their clinic based on the inclusion and exclusion criteria (Section 9.2.1 and Section 9.2.2). It is the responsibility of each physician to ask every consecutive patient who meets the inclusion criteria of the study to participate to avoid selection bias, and if investigators hold different types of clinics (e.g. routine visit clinics versus emergency clinics), only patients visiting their routine clinics will be used for patient selection.

Site personnel should thoroughly assess the eligibility criteria and evidence of this should be stored with the source documentation at site. Where there is any deviation from the inclusion/exclusion criteria, the patient should be excluded from the study.

Subjects that initially screen fail for the study may be permitted to re-screen following re-consent. All screening procedures with the possible exceptions noted below will be repeated. The subject must meet all inclusion and none of the exclusion criteria at the time of re-screening in order to qualify for the study. There is no minimum period of time a subject must wait to re-screen for the study. If the subject had a complete record of eligible criteria including a PPD test (or equivalent), or Interferon-Gamma Release Assay (IGRA; QuantiFERON-TB Gold In-Tube test or T-SPOT TB test), Chest x-ray (if applicable) and ECG no more than 3 months (90 days) have passed, these data will not be required to be repeatedly collected for re-screening. As appropriate, sites are encouraged to contact the AbbVie Medical Monitor to confirm if subjects should or should not be re-screened.

9.2.1 Inclusion Criteria:

Patients meeting all of the following inclusion criteria at baseline will be included:

1. Subject has a diagnosis of RA as defined by the 1987 revised ACR classification criteria and/or the ACR/ the European League against Rheumatism (EULAR) 2010 classification criteria (any duration since diagnosis)
2. Male or female subjects ≥18 years of age (local definition according to adalimumab label) who is in compliance with eligibility for adalimumab based on the local label
3. Patients with moderate to severe RA defined as DAS28 (ESR) or DAS28 (CRP) > 3.2

4. Biologically treatment naïve and initiated adalimumab at baseline visit
5. Availability of clinical data of the previous 12 weeks prior to baseline
6. Ability to self-complete patient questionnaires
7. Subject must be able and willing to provide written informed consent and comply with the requirements of this study protocol

Additional Inclusion Criteria

8. Female subjects who are either not of childbearing potential, defined as postmenopausal for at least 1 year or surgically sterile (bilateral tubal ligation, bilateral oophorectomy and/or hysterectomy) or are of childbearing potential and are practicing an approved method of birth control throughout the study and for 150 days after the Week 24 dosing or the last dose of adalimumab.
9. Subjects judged to be in good health as determined by the Principal Investigator based upon the results of medical history, laboratory profile, physical examination, chest x-ray (CXR), and a 12-lead electrocardiogram (ECG) performed no more than 3 months (90 days) have passed.
10. Subjects have negative TB Screening records. If a subject has evidence of a latent TB infection, the subject must initiate and complete a minimum of 1 month (per Taiwan guideline) of an ongoing TB prophylaxis or have documented completion of a full course of TB prophylaxis, prior to Baseline

9.2.2 Exclusion Criteria:

Patients meeting any of the following exclusion criteria at baseline will be excluded:

1. Patients who are pregnant or breast feeding at enrolment or wish to become pregnant in the next 24 weeks
2. Participation in any RA-related clinical trial at the time of enrolment, at baseline or at any point during the past 24 weeks prior to baseline
3. Patients, who in the clinician's view, may not be able to accurately report their QoL or prior resource utilization
4. Patients, who in the clinician's view, may not be able to adhere to adalimumab therapy over 24 weeks

Additional Exclusion Criteria

5. Subject has been treated with any investigational drug of chemical or biologic nature within a minimum of 30 days or five half-lives (whichever is longer) of the drug prior to the Baseline Visit
6. Infection(s) requiring treatment with intravenous (IV) anti-infectives within 30 days prior to the Baseline Visit or oral anti-infectives within 14 days prior to the Baseline Visit
7. Prior exposure to biologics that have a potential or known association with PML (i.e., natalizumab (Tysabri®) or rituximab (Rituxan®)
8. Known hypersensitivity to adalimumab or its excipients

9. History of demyelinating disease (including myelitis) or neurologic symptoms suggestive of demyelinating disease
10. History of invasive infection (e.g. listeriosis and histoplasmosis), human immunodeficiency virus (HIV)
11. Subjects with any active viral infection that based on the investigator's clinical assessment makes the subject an unsuitable candidate for the study
12. Hepatitis B: HBs Ag positive (+) or detected sensitivity on the HBV-DNA PCR qualitative test for HBc Ab/HBs Ab positive subjects
13. Chronic recurring infections or active TB
14. History of moderate to severe congestive heart failure (NYHA class III or IV), recent cerebrovascular accident and any other condition which would put the subject at risk by participation in the study
15. Evidence of dysplasia or history of malignancy (including lymphoma and leukemia) other than a successfully treated non-metastatic cutaneous squamous cell or basal cell carcinoma or localized carcinoma in situ of the cervix
16. Positive pregnancy test at Screening or Baseline
17. History of clinically significant drug or alcohol abuse in the last 12 months
18. Clinically significant abnormal screening laboratory results as evaluated by the Investigator

9.2.3 Investigator Selection Criteria

Selection of investigators will be made based on qualification by training and experience. AbbVie will provide IMS with a list of clinicians that would be able to able to assist in recruiting in a timely manner. IMS will contact each clinician to obtain their participation in the study and provide an expected number of patients to be enrolled from that clinic. The ethical review boards recognized by the respective participating sites are required to review and approve the study and patient informed consent.

9.2.4 Study Procedures

The study procedures outlined in Table 1 will be discussed in detail in this section with the exception of adverse events procedures (discussed in Section 11.0).

9.2.4.1 Informed Consent

Following the current local regulations in Taiwan, informed consent forms (ICF; Appendix A) in local language will be given to every patient participating in the study before data collection commences. The recruiting clinicians or their representative(s) will provide each patient with the ICF to sign which includes consent to use the data for publication and information including their right to withdraw from the study without penalty or change in medical care the patient is otherwise entitled to.

Potential drug to drug interactions with oral contraceptives and need for alternative methods of birth control will be informed.

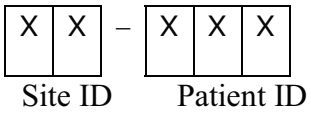
"If you are already using a method of birth control, you should check with the study doctor to make sure it is considered acceptable for this study. Certain drugs may interact with contraceptive agents and reduce their effectiveness, therefore you should inform the study doctor of all medications (prescription and over-the-counter) that you are currently taking or begin taking during the study."

9.2.4.2 Patient Assignment

Once the recruiting clinician has obtained the subject's authorization to release medical information and written consent to participate in the study, the clinician will be asked to complete an inclusion and exclusion form (

Appendix B) for patients, thus confirming the patient's eligibility to participate in this study.
Each participating patient will be assigned a 3-digit patient identification number. The numbers should be assigned in sequential, ascending order per site as shown below:

- Site ID; and
- Patient ID: First eligible patient number will be 001, and then the second patient number would be 002



9.2.4.3 Investigator Recruitment

AbbVie will provide IMS (CRO Division in IMS) with a list of clinicians that would be able to assist in recruiting in a timely manner. IMS will contact each clinician to obtain their participation in the study and provide an expected number of patients to be enrolled from that clinic. The ethical review boards recognized by the respective participating sites are required to review and approve the study and patient informed consent.

9.2.4.4 Study site monitoring

As the study entails patients completing PRO questionnaires and clinicians completing case report forms (CRFs), there is not a need for on-site monitoring visits. IMS will closely track enrolment progress for bi-monthly reporting. IMS will work closely with the study coordinator at each site to ensure they check the forms when returned from the patients and physicians (e.g., all questions were answered). IMS will also be available to answer questions and follow up with the sites if the recruitment process is slow or if there are any errors on the forms. Periodic phone follow-up will be conducted to ensure data collection completeness and quality.

9.2.4.5 Patient Selection

The recruiting investigators will select potentially eligible patients from consecutive visits within their clinic based on the inclusion and exclusion criteria (Section 9.2.1 and Section 9.2.2). It is the responsibility of each physician to ask every consecutive patient who meets the inclusion criteria of the study to participate to avoid selection bias, and if investigators hold different types of clinics (e.g. routine visit clinics versus emergency clinics), only patients visiting their routine clinics will be used for patient selection. The intent is to enroll patients who have been prescribed adalimumab upon the physicians' own discretion.

Medical and Surgical History
A detailed medical history with respect to TB exposure needs to be documented. This information needs to include BCG vaccination, cohabitation with individuals who have had TB, and/or who reside or work in TB endemic locations.

Physical Examination
Physical exam records at routine clinic visits will be collected at scheduled timepoints. Physical examination findings that are related or part of each subject's medical history should be captured on the appropriate eCRF page.

12-Lead Electrocardiogram (ECG)

Resting 12-lead ECG records will be collected at Baseline. A qualified physician will interpret the clinical significance of any abnormal finding, sign, and date each ECG. Any clinically significant findings will be documented in the source documents and later transcribed on to the appropriate eCRF.

For subjects with a normal ECG taken within 90 days prior to Baseline, a repeated ECG record before enrollment will not be required, provided all protocol required documentation is available. If there is any finding clinically significant, the Principal Investigator must contact the Medical Monitor before enrolling the subject.

Subjects can have a repeat ECG at any time during the study as warranted based on the opinion of the Investigator.

Chest X-ray (CXR)

A standard CXR (posterior-anterior [PA] and lateral views) report within 90 days prior to Baseline to rule out the presence of TB or other clinically relevant findings will be collected, provided all protocol required documentation is available at the site (as outlined below).

Subjects can have a repeated CXR at any time during the study as warranted based on the judgment of the Investigator. The Principal Investigator will indicate the clinical significance of any finding, including the presence or absence of (1) calcified granulomas, (2) pleural scarring/thickening, and (3) signs of active TB, and will sign and date the report.

Pregnancy Tests

At the Baseline Visit, subjects of childbearing potential should be confirmed as non-pregnant. A lactating or pregnant female will not be eligible for participation or continuation in this study.

9.2.4.6 Data Collection

IMS will coordinate data collection with each site. At study initiation (Baseline, D0), patients will be asked to provide their written informed consent. After signing consent, the patients' questionnaires as recorded will be collected. At Week 12 and 24 time-

points, the patients' questionnaires will be collected before them visiting their physicians. There will be a study coordinator or study nurse at each site to monitor the process. The study coordinator/nurse will collect the record of questionnaires directly. Physicians will not see the contents patients entered. The study coordinator/nurse will check to ensure all the forms are filled-in correctly.

In addition, physicians will also be asked to complete a clinical CRF in paper form based on the patient's medical records at baseline, 12 weeks, and 24 weeks. The CRF completed by physicians will be returned to the study coordinator/nurse at each site as well.

All data will be collected by the study coordinator/nurse at each site and returned directly to IMS. The data collection time is expected to be 10-13 months.

All patient and clinician data will be handled preserving confidentiality.

9.2.4.7 Study Documents

Clinical case report form (CRF)

The clinical CRF will document the patient's current status (moderate, severe RA), Disease Activity Score in 28 joints (DAS28), prior and current treatments and other relevant clinical and demographic data to be used in segmenting the population during analysis.

To calculate the DAS28 the physician or specialist nurse will:

1. Count the number of swollen joints (out of the 28)
2. Count the number of tender joints (out of the 28)
3. Record the blood test data of erythrocyte sedimentation rate (ESR) or C reactive protein (CRP) using the latest measurement in the medical records
4. Record the 'global assessment of health' of patients, which will be indicated by marking a 10 cm line between very good and very bad

The physician or specialist nurse will then mark each component score on the CRF and the DAS28 score if calculated (an online scoring calculator for the DAS28 can be found at [redacted]

The DAS28 will be scored using the following formula:

DAS28 ESR = *0.56 * sqrt(tender28) + 0.28 * sqrt(swollen28) + 0.70 * ln(ESR) + 0.014 * (Global assessment of Health in cm)*

DAS28 CRP = *0.56 * sqrt(tender28) + 0.28 * sqrt(swollen28) + 0.36 * ln(CRP) + 0.014 * (Global assessment of Health in cm)+0.96*

DAS28 scores will be interpreted using the following categorization:

- Remission: DAS28 ≤ 2.6
- Low Disease activity: 2.6 < DAS28 ≤ 3.2
- Moderate Disease Activity: 3.2 < DAS28 ≤ 5.1
- High Disease Activity: DAS28 >5.1

The full CRF is presented in Appendix C.

PRO questionnaires

The following PRO questionnaires will be included in the patient questionnaire packet.

Health Assessment Questionnaire Disability Index (HAQ DI)

The HAQ DI is a patient-reported questionnaire to assess functioning impacted by RA. It includes the categories of dressing and grooming, arising, eating, walking, hygiene, reach, grip and common daily activities. It asks patients about the amount of difficulty they experience in these activities as well as the use of aids and/or devices. The HAQ also has a numeric rating scale (NRS) (13) to assess pain on a scale from 0 to 10. Self-administered by the patient, the completion time is approximately 3-4 minutes. The full version of HAQ DI is presented in Appendix D.

Short Form (36) Health Survey (SF-36)

The SF-36 is a patient-reported questionnaire of patient health-related QoL. It measures generic health concepts relevant across age, disease, and treatment groups. There are 36 items in total and the recall period is the last 4 weeks. The SF-36 consists of eight scaled scores, which are the weighted sums of the questions in their section. Each scale is directly transformed into a 0-100 scale. Completion time for the SF-36 is approximately 10 minutes. The full version of SF-36 is presented in Appendix E.

EuroQol 5 dimension, 3 level quality of life questionnaire (EQ-5D-3L)

The EQ-5D-3L measures the patient's overall health state in a descriptive system of health-related QoL states consisting of five dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) each of which can take one of three responses. The responses record three levels of severity ('no problems', 'some problems', and 'extreme problems) within a particular EQ-5D-3L dimension (14, 15). In addition, a VAS rates current health state between 0-100. The EQ-5D-3L results can be converted to health utility scores. Completion time for the EQ-5D-3L is approximately 2-3 minutes. The full version of EQ-5D-3L is presented in Appendix F.

Work Productivity and Activity Impairment (WPAI)

The WPAI is a patient-reported questionnaire to measure work and activity impairment during the past seven days. It determines employment status, hours missed from work due to the disease (i.e. RA), hours missed from work for other reasons, hours actually worked, the degree to which the disease affected work productivity while at work and the degree to which the disease affected activities outside of work. Additional questions around employment status will be incorporated into the survey. The completion time for the WPAI is approximately 2-5 minutes. The full version of WPAI is presented in Appendix G.

All of the above questionnaires will use the validated Chinese version.

Patient Global Impression of Change (PGIC)

The PGIC measures the patient's perceptions of changes in their disease. It consists of one question asking about the change in their condition; for this study, the base will be "since you initiated your adalimumab treatment". The completion time for the PGIC is less than 1 minute. The full version of PGIC is presented in Appendix H.

Patient Treatment Satisfaction Questions

The patient treatment satisfaction questions were developed de novo for this study and are not considered "validated" questions. Self-administered by the patient, the completion time for the patient treatment satisfaction questions is approximately 1-2 minutes. The full version of patient treatment satisfaction questions are presented in Appendix I.

Healthcare Resource Utilization (HCRU) Questionnaire

The HCRU questionnaire will collect data on the healthcare resources consumed in the prior 3 months, as recall beyond 3 months may be problematic in an older population (16). HCRU collection will include data such as the number of physician visits and to which physician (GP, specialist), Emergency Department visits, hospitalizations, and other drugs as well as devices and aids purchased to assist in their mobility due to RA. The HCRU questionnaire will be part of the patient questionnaire and will be distributed to patients together with the PRO questionnaires (Appendix D to Appendix I). The full HCRU questionnaire is presented in Appendix J.

9.2.5 Adverse Events

Adverse events, whether in response to a query, observed by site personnel, or reported spontaneously by the subject will be recorded. Adverse events definition and serious adverse event categories are described in detail in Section 11.0.

9.2.6 Removal of Subjects from Therapy or Assessment

1. Discontinuation of Individual Subjects

A subject may withdraw from the study at any time. The Investigator may discontinue any subject's participation for any reason, including an adverse event, safety concerns or failure to comply with the protocol.

Subjects will be withdrawn from the study immediately if any one of the following occurs:

- Clinically significant abnormal laboratory result(s) or adverse event(s), as determined by the Investigator in consultation with the AbbVie Medical Monitor.
- The Investigator believes it is in the best interest of the subject.
- The subject requests withdrawal from the study.
- Inclusion and exclusion criteria violation was noted after the subject started study drug, when continuation of the study drug would place the subject at risk as determined by the AbbVie Medical Monitor (see *Section 5.2 and Section 7.0*).
- Introduction of prohibited medications or dosages when continuation of adalimumab would place the subject at risk as determined by the AbbVie Medical Monitor.
- Subject is non-compliant with TB prophylaxis.
- The subject becomes pregnant during the study period.
- Subject has dysplasia of the gastrointestinal tract or a malignancy, except for localized non-melanoma skin cancer. Discontinuation for carcinoma in-situ of the cervix is at the discretion of the Investigator.
- Subject is diagnosed with lupus-like syndrome, multiple sclerosis or demyelinating disease.
- Subject is significantly non-compliant with clinical follow-up which would put the subject at risk for continued participation in the trial, as determined by the Investigator, in consultation with the AbbVie Medical Monitor.

The subject will be treated in accordance with the Investigator's best clinical judgment. If the subject prematurely dropped out from the study, the pre-defined Terminal Visit data should be collected within 2 weeks of the last dose of adalimumab, and preferably prior to the initiation of another therapy. However, these data collection should not interfere with the initiation of any new treatments or therapeutic modalities that the Investigator feels are necessary to treat the subject's condition. A final data of a subject will be recorded

approximately 70 days after the Week 24 dosing or the last dose of adalimumab to determine the status of any ongoing AEs/SAEs or the occurrence of any new AEs/SAEs. The information will be recorded on the appropriate in eCRF page.

For subjects that are considered lost to follow-up, reasonable attempts must be made to obtain information on the final status of the subject. At a minimum, two phone calls must be made and one certified letter must be sent.

9.3 Variables

Variables (as observed)**:**
Primary Variable

- Change in HAQ DI score at week 24 from baseline

Secondary Variable

- Change in other PROs (SF-36 domain scales, EQ-5D Index, Work Productivity and Activity Impairment Questionnaire [WPAI]) from baseline to weeks 12 and 24
- Change in HAQ DI score at week 12 from baseline
- Number and percent of patients achieving a clinically meaningful improvement on the HAQ DI, from baseline to weeks 12 and 24
- Healthcare Resource Utilization (HCRU) at baseline, 12 and 24 weeks

Exploratory Variable

- Difference of the change in HAQ DI score from baseline to 24 weeks between as observed population and withdrawal population
- Change in patient satisfaction questions from baseline to weeks 12 and 24
- Patient's impression of change at weeks 12 and 24 from baseline
- Association between disease severity and PROs
- Association between change in disease severity and change in PROs

9.4 Data Sources

Case Report Forms (CRFs) and patient questionnaires.

Collection of data includes but not limited to subject demographics, clinical history, comorbidities, spontaneous adverse events, and concomitant medications. The following questionnaires will be utilized to collect data directly from participating subjects:

- EQ-5D
- SF-36
- HAQ DI
- WPAI

- HCRU
- Patient Global Impression of Change (PGIC)
- Patient Treatment Satisfaction Questions

9.5 Study Size

Approximately 100 patients diagnosed with RA will be recruited. The planned sample size provides at least 95% power for detecting a statistically significant improvement in HAQ-DI (ΔHAQ-DI < 0) assuming a mean ΔHAQ-DI of -0.21 and a standard deviation of 0.5 (reference 11), at two-sided significance level of 0.05 and accounting for a 10% dropout rate. The sample size also provides at least 95% power for detecting a statistically significant clinically meaningful improvement in HAQ-DI (ΔHAQ-DI < -0.22) assuming a mean ΔHAQ-DI of -0.5 and a standard deviation of 0.7, at two-sided significance level of 0.05 and accounting for a 10% dropout rate. For the secondary endpoint WPAI, the sample size provides 63% power for detecting a statistically significant improvement in "hours of work lost" at two-sided significance level of 0.05 and accounting for a 10% dropout rate, assuming a mean change in "hours of work lost" of 10 and standard deviation of 30 and assuming a 55% employment rate in the study population.

9.6 Data Management and Storage Process

9.6.1 Data Management

Data management and data quality check will be performed to remove errors and inconsistencies in order to assure the appropriateness of the study data set to assess the study objectives. Data entry screens will be developed and tested prior to initiating data collection to reduce data entry errors. If required, IMS will provide AbbVie with data for analysis.

Each site coordinator will be instructed to answer patients' queries which may arise in relation to the questionnaires and check the patients' input to make sure all questions are answered.

9.6.2 Storage Process

Following data quality checks, each dataset will be converted to SAS and merged for analysis. All information included in the CRF and the patients' questionnaires will be checked in order to detect possible queries to solve and will be extracted to a specifically designed database, where it will be validated by IMS personnel to ensure its quality. Finally, data analysis will be conducted and final results reported.

The databases will be stored in IMS data servers. Data servers are submitted to daily backups in order to increase the security on all data managed in the collection process.

All paper based questionnaires will be stored in a secured, locked area for a period of seven (7) years, after which all data will be shred using an agency specialized in disposal of confidential documents.

9.7 Data Analysis

9.7.1 Statistical and Analytic plans

A statistical analysis plan (SAP) will be developed describing the specific analysis that will be performed including, and in addition to, the analysis described here. All analysis will be performed in accordance with the approved analysis plan. The following provides an overview of some of the analysis.

The scoring of the PRO questionnaires will be done in accordance to the developers' recommendations.

A separate statistical analysis plan will be developed describing the specific analysis that will be performed including and in addition to the analysis described here.

9.7.2 Analyzable population

All subjects who received at least one dose of adalimumab during the study will be included.

9.7.3 Planned Methods of Statistical Analysis

All statistical tests will be two-tailed with a significance level of 0.05. Descriptive statistics will be provided. Descriptive analysis will be conducted on all key parameters and presented as mean, standard deviation, minimum, maximum, and median when continuous and as "n" and percent when categorical. Change from adalimumab initiation to 24 weeks will be calculated and evaluated for significant improvements using paired t-tests / ANOVA for parametric and Wilcoxon signed-rank for non-parametric data. Analysis will be also be conducted by severity level (moderate vs severe), disease duration quartile (to compare to prior work) and up to two (2) other subgroups. Cochran-Armitage test of trends or other similar methods may be used to compare categories of subjects.

9.7.4 Primary Endpoint Analysis

The primary endpoint variable will be the change in HAQ DI score at 24 weeks after the initiation of adalimumab, in those patients continuing on adalimumab (as observed population).

The objective of the primary endpoint analysis will be to demonstrate that treatment with adalimumab improves functioning as measured by the HAQ DI in subjects with RA following treatment initiation. This change will be summarized as the mean and 95% confidence interval and will be tested with a paired t-test without adjusting for baseline disease severity. For sensitivity analysis, the mean change in HAQ DI at Week 24 will be analyzed using ANOVA adjusting for baseline disease severity.

9.7.5 Secondary Endpoint Analysis

The main secondary endpoint variable will be the change in HAQ DI at 12 weeks after the initiation of adalimumab.

The objective of endpoint analysis will be to demonstrate that treatment with adalimumab improves functioning as measured by HAQ DI in subjects with RA compared to baseline.

The main secondary analysis will be summarized as the mean and 95% confidence interval and will be tested with a paired t-test without adjusting for baseline disease severity. For sensitivity analysis, the mean change in HAQ DI at Week 12 will be analyzed using ANOVA adjusting for baseline disease severity.

Other secondary analyses include:

- Change in other patient reported outcomes (SF-36 domain scales, EQ-5D Index, WPAI total lost productivity) at weeks 12 and 24 after the initiation of adalimumab, in those patients continuing on adalimumab (as observed population). These changes will be summarized as the means and 95% confidence intervals and will be tested with paired t-tests.
- Number and percent of patients achieving a clinically meaningful improvement on the HAQ DI, as defined by a -0.22 point improvement or greater, at weeks 12 and 24 after the initiation of adalimumab, in those patients continuing on adalimumab (as observed population).

9.7.6 Exploratory Endpoint Analysis

Additional analyses include:

- Change in HAQ DI score at 24 weeks after the initiation of adalimumab, in those patients continuing on adalimumab (as observed population), compared with those patients not continuing on adalimumab (withdrawal population). The mean changes in these two groups will be compared using an independent t-test.
- Healthcare resource utilization will be described using number and percentage within each category (number of consultations, number of procedures received, number of surgeries, number of hospitalizations and length of stay, number of concomitant medications)
- Change in patient satisfaction questions at weeks 12 and 24 after the initiation of adalimumab, in those patients continuing on adalimumab (as observed population). These changes will be summarized as number and percentage of each response and compared with Kruskal–Wallis test. Satisfaction will also be dichotomized and analyzed over time with Cochrane-Armitage test for trends.
- Patient's impression of change at weeks 12 and 24 after the initiation of adalimumab, in those patients continuing on adalimumab (as observed population). These changes will be summarized as number and percentage of each response and compared with Kruskal–Wallis test.
- Associations between disease severity and PROs
- Associations between change in disease severity and change in PROs

9.7.7 Safety Analysis

Adverse events occurring while participants are on adalimumab will be coded using Common Terminology Criteria for Adverse Events (CTCAE) classification individually listed by indication groups. The incidences and percentages of individuals experiencing AEs and SAEs within each indication will be summarized by System Organ Class (SOC) with further summaries by severity and relatedness (causality) categories. Adverse events leading to discontinuation and concomitant medications will also be listed and summarized.

9.7.8 Additional Analysis

Additional analysis will explore the potential modifying effects of baseline measures on the changes in primary and secondary efficacy outcomes. These measures will include age, gender, baseline severity, and other diagnoses/co-morbidities. The analysis will specifically test for differential changes across the subgroups defined by the potential modifiers using general linear models.

9.7.9 Missing Data

Efficacy measures are not assessed after a participant discontinues adalimumab. The exception to this will be the analysis of proportion of patients at 24 weeks who remain on adalimumab. Item level data on the PROs will be imputed according to the developers' recommendations. There will be no other imputation for missing data.

9.7.10 Interim Analysis

There is no interim analysis planned for this study.

9.8 Quality Control

9.8.1 Ethics and Quality

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

9.8.2 Quality Assurance

Prior to the initiation of the study, physician and site personnel will be trained on the study. Training will include a detailed discussion of the protocol, performance of study procedures, and completion of the CRFs and paper questionnaires.

All sites will be monitored during the course of study participation. One hundred percent (100%) source document review for safety will be performed.

All clinical data will be documented via the CRF. Study coordinators at each site will check the paper CRFs completed by the physicians and questionnaires completed by patients (e.g., all questions were answered). Data entry will be conducted by IMS. After entry of the data, computer logic checks will be run to check for inconsistent data. Any necessary corrections will be made to the database and documented via addenda, queries, and source data clarification forms.

Steps to be taken to ensure the accuracy and reliability of data include the selection of qualified investigators and appropriate study centers, review of protocol procedures with the investigator and associated personnel before the study and periodic monitoring visits by the sponsor. Written instructions will be provided for administration and collection of study questionnaires.

Guidelines for CRF completion will be provided and reviewed with study personnel before the start of the study. The sponsor will review CRFs and patient questionnaires for accuracy and completeness after transmission to the sponsor; any discrepancies will be resolved with the investigator or designee, as appropriate. After upload of the data into the clinical study database they will be verified for accuracy and consistency with the data sources.

Protocol Deviation

For the purposes of this protocol, reportable deviations are defined as:

- Subject entered into the study even though she/he did not satisfy entry criteria
- Subject who developed withdrawal criteria during the study and was not withdrawn
- Subject who received excluded or prohibited concomitant treatment

9.9 Limitations of the Research Methods

The study is to be performed as a non-interventional study. Unlike clinical studies, obtainable data are limited and there is a possibility of missing data.

9.10 Other Aspects

9.10.1 Note To File

The Principal Investigator or designee will be responsible for documenting study relevant information and occurrences that affects the course of the study. The information and occurrences are not protocol deviations but will be documented in a note to file and will be communicated to the sponsor.

9.10.2 Training Log

All designated study personnel must be trained on the study protocol and procedures. Training and retraining are documented on the Training Log.

9.10.3 Visitor Log

All Sponsor or other related individuals who visit the study site must sign the Visitor Log.

9.10.4 Responsibilities of the Principal Investigator

The Principal Investigator is responsible for oversight of enrolment, the patient consent process, study related procedures, compliance with the protocol, all institutional, state and local guidelines.

It is the responsibility of the Principal Investigator to select, supervise, and delegate responsibility for study conduct to staff members. The Principal Investigator is responsible for determining the appropriate staff qualifications required for specific study-related tasks to be delegated. Study-related tasks delegated to staff members will be documented on the Site Signature and Delegation Log.

9.10.5 End of Trial

End of Trial is defined as last subject's last visit (LPLV).

10.0 Protection of Human Subjects

This study must be conducted in compliance with the recommendations of the Declaration of Helsinki, 2008 (World Medical Association). In addition, this study will adhere to all general and local legal and regulatory requirements applicable to non-interventional studies.

Informed consent will be obtained from each subject before the subject can participate in the study. The contents and process of obtaining informed consent will be in accordance with all applicable regulatory requirements.

As required by applicable local regulations, the sponsor's Regulatory Affairs group will ensure all legal regulatory aspects are covered, and obtain approval of the appropriate regulatory bodies, prior to study initiation in regions where an approval is required.

This study is non-interventional and falls outside the scope of the EU Directive 2001/20/EC, the EU Directive 2005/28/EC and International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines.

This study complies with the EU Directive 95/46/EC of the European Parliament and of the Council of 24 October 1995 on the protection of individuals with regard to the processing of personal data and on the free movement of such data.

11.0 Management and Reporting of Complaints

A Complaint is any written, electronic, or oral communication that alleges deficiencies related to the physical characteristics, identity, quality, purity, potency, durability, reliability, safety, effectiveness, or performance of a product after it is released for distribution.

11.1 Medical Complaints

11.1.1. Adverse Event Definition and Serious Adverse Event Categories

An adverse event (AE) is defined as any untoward medical occurrence in a patient, which does not necessarily have a causal relationship with their treatment. An adverse event 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 adverse event.

This protocol requires all SAEs as outlined in this section to be actively solicited. The safety profile of adalimumab which has over 3.5 million patient years of post-marketing exposure is stable and well established; non-serious events will not be actively solicited as these events are not likely to contribute to the further understanding of the safety profile of the product. Any non-serious AEs will be collected as spontaneous reports if AbbVie is notified.

If an adverse event meets any of the following criteria, it is considered a serious adverse event (SAE):

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 study 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 study 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). Additionally, any elective or spontaneous abortion or stillbirth is considered an important medical event. 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.

11.1.2 Severity

The following definitions will be used to rate the severity for any adverse event being collected as an endpoint/data point in the study and for all serious adverse events.

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.

11.1.3 Relationship to Pharmaceutical Product

The following definitions will be used to assess the relationship of the adverse event to the use of product:

Reasonable Possibility An adverse event where there is evidence to suggest a causal relationship between the product and the adverse event.

No Reasonable Possibility An adverse event where there is no evidence to suggest a causal relationship between the product and the adverse event.

If no reasonable possibility of being related to product is given, an alternate etiology must be provided for the adverse event.

11.1.4 Adverse Event Collection Period

Adverse events will be reported to AbbVie from the time the physician obtains the patient's authorization to use and disclose information (or the patient's informed consent) until 70 days following the intake of the last dose of physician-prescribed treatment will be collected, whether solicited or spontaneously reported by the subject. In addition, serious adverse events will be collected from the time the subject signed the study-specific informed consent. Adverse event information will be collected and recorded on the appropriate eCRFs.

Subjects will be contacted approximately 70 days following the intake of the last dose of physician-prescribed treatment for an assessment of any new or ongoing AEs.

All SAEs, as defined by AbbVie, reported during the 70-day follow-up phone call must be captured in the clinical database.

11.1.5 Adverse Event Reporting

In the event of a serious adverse event, and additionally, any non-serious event of malignancy in subjects/patients 30 years of age and younger, whether related to AbbVie product or not, the Investigator will notify the AbbVie Emergency contact person

(Taiwan ASR) identified at the beginning of the protocol within 24 hours of the physician becoming aware of the event.

11.1.6 Pregnancy Reporting

Pregnancy in a study subject must be reported to AbbVie within 1 working day of the site becoming aware of the pregnancy. Subjects who become pregnant during the study must be discontinued (Section 9.2.6). Pregnancies will be collected from the date of the first dose through 150 days following the last dose of adalimumab.

Information regarding a pregnancy occurrence in a study subject and the outcome of the pregnancy will be collected.

Pregnancy in a study subject 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 to AbbVie within 24 hours of the site becoming aware of the event.

12.0 Plans for Disseminating and Communicating Study Results

At the end of this observational study, a report will be written by AbbVie or a CRO working on behalf of AbbVie. The required standard study report template will be followed. This report will contain a description of the objectives of the study, the methodology and its results and conclusions. The completed eCRFs, [patient questionnaires, interim assessments], the final study output and study report are 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 study results will be submitted to local authorities per local laws and regulations.

The results of this PMOS may be published by AbbVie or by any one of the participating investigators after agreement with AbbVie.

12.1 Ethical and Legal Consideration

All participant data will be handled in a manner compliant with all local regulatory and privacy laws. All parties will ensure protection of subject personal data and will not include subject names on any sponsor forms, reports, publications, or in any other disclosures, except where required by law. Appropriate role-based access to minimum necessary information will be maintained so that only authorized individuals have access to protected health information (PHI).

AbbVie shall comply with all applicable laws regarding the reporting of spontaneous adverse events (AEs) to the relevant local authorities in Taiwan. AbbVie will follow the

International Conference on Harmonization of Good Clinical Practice (ICH-GCP) guidelines for AE reporting and report all spontaneously reported AEs within the required timeframe (usually within 24 hours of discovery).

All IMS staff working directly with patient data and/or having direct contact with healthcare practitioners will have received formal training to ensure they have a clear understanding of how to recognize an AE and inform Affiliate Safety Representative so that they are in full compliance with local laws regarding AE reporting.

The study will be reviewed and approved by the appropriate Ethics Committee(s) at each site prior to the start of patient recruitment, according to the specific legal requirements in Taiwan.

12.2 Confidentiality

12.2.1 Patient confidentiality

Information on patients' identity shall be considered as confidential for all effects and purposes. Each site and patient will have a code in the study. Sites will be automatically coded by IMS. Patients will be assigned a sequential number by the site coordinator upon meeting all inclusion and no exclusion criteria.

The patients' identity should not be revealed nor published under any circumstances. Patient data recorded in the CRF will be documented anonymously, coded with a patient number in such a way that only the investigator and site staff may associate particular data with an identified or identifiable individual or his/her medical record. All other parties involved in data management, analysis and storage will receive, and subsequently analyze, non-identifiable patient data.

12.2.2 Data confidentiality

By signing the investigator's confidentiality agreement, the investigator affirms to AbbVie/IMS that information furnished by AbbVie/IMS to the investigator will be kept in confidence and such information will be divulged to any expert committee, affiliated institution, and employees only under an appropriate understanding of confidentiality with such committee, affiliated institution and employees.

12.3 Study administration

The entire study will be managed by an international project coordinator at IMS Japan K.K. who will coordinate the project and maintain fluid communication with the study sponsor, the study team and the director at IMS Japan K.K.

As part of the monitoring plan, regular phone calls (at least every two weeks) will be made between IMS and local site coordinator in order to check inclusion status, resolve any issues, check data plausibility, etc.

12.4 Investigators compliance

By signing the investigator's agreement, the investigator agrees to conduct the study in an efficient and diligent manner and in conformance with this protocol, generally accepted standards of good clinical practice and all applicable laws, rules and regulations relating to the conduct of the study.

The investigator shall prepare and maintain complete and accurate study documentation in compliance with applicable national and local laws, rules and regulations and, for each patient participating in the study, promptly record all data in the CRF as required by this protocol.

12.5 Risks

This is a non-interventional observational study. It does not involve any direct patient intervention with respect to laboratory tests, examinations or drug treatment. Patients will be asked to complete questionnaires related to their RA, QoL, functioning, work productivity, treatment satisfaction, and healthcare resource utilization at their clinic during their visit three times over the course of 6 months, requiring approximately 30 minutes of their time each time.

12.6 Discontinuation or Drop-out

Patients' participation in the study is completely voluntary, and they are allowed to withdraw or discontinue from the study. The following three situations will be counted as study drop-out:

1) Patient is switched off Adalimumab
2) Patient is not willing to continue participation in the study
3) Patient disappears and cannot be contacted anymore

For the first two situations, the Early Termination Form (Appendix K) will be provided for the patients and their physicians to fill in.

Patients not completing questionnaires will not be classified as drop-out. For example, if a patient missed Week 12 questionnaires for some reason, he/she can still fill in Week 24 questionnaires.

Once a subject is dropped out from the study, no further information for that subject will be collected. However, the reason for drop-out will be collected and, if the reason for treatment discontinuation is due to as adverse event, the event will be reported to Abbvie within 24 hours of physician awareness.

12.7 Quality control and audit

Steps to be taken to ensure the accuracy and reliability of data include the selection of qualified investigators and appropriate study centers, review of protocol procedures with the investigator and associated personnel before the study and periodic monitoring visits by the sponsor. Written instructions will be provided for administration and collection of study questionnaires.

Guidelines for CRF completion will be provided and reviewed with study personnel before the start of the study. The sponsor will review CRFs and patient questionnaires for accuracy and completeness during on-site monitoring visits and after transmission to the sponsor; any discrepancies will be resolved with the investigator or designee, as appropriate. After upload of the data into the clinical study database they will be verified for accuracy and consistency with the data sources.

The study will be performed following the IMS and AbbVie Standard Operating Procedures (SOPs) for Observational Studies.

12.8 Communication of findings

AbbVie / IMS shall retain ownership of all screeners, case report forms, data analysis, and reports which result from this study.

All information obtained as a result of the study will be regarded as confidential, until appropriate analysis and review by AbbVie and the investigator(s) are completed. The results of the study may be published or presented by the investigator(s) after the review by, and in consultation and agreement with AbbVie, such that confidential or proprietary information is not disclosed.

Prior to publication or presentation, a copy of the final text should be forwarded by the investigator(s) to AbbVie for comment. Such comments shall aim to ensure the scientific content of the proposed publications and/or presentations and ensure that the data and material receive fair, accurate, and reasonable presentation.

13.0 References

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16 Evans C, Crawford B. Patient self-reports in pharmacoeconomic studies. Their use and impact on study validity. PharmacoEconomics. 1999 Mar;**15**(3):241-56.

Annexure 1. Following the current local regulations in Taiwan, informed consent forms (ICF; 錯誤! 書籤的自我參照不正確。

Appendix A. Patient Informed Consent Form (ICF)

- (If you are already using a method of birth control, you should check with the study doctor to make sure it is considered acceptable for this study. Certain drugs may interact with contraceptive agents and reduce their effectiveness, therefore you should inform the study doctor of all medications (prescription and over-the-counter) that you are currently taking or begin taking during the study.

NOTE: This Informed Consent Form will be adapted to meet the ethics requirements at participating sites in each country, and the local version in local language will be submitted to ethics committees. This is the English version developed based on general templates provided by IMS China, IMS Korea, and IMS Taiwan.

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

INFORMED CONSENT FORM

We are inviting you to participate in this research study, titled "REAL-WORLD IMPACT OF HUMIRA ON RHEUMATOID ARTHRITIS PATIENTS IN CHINA, SOUTH KOREA, AND TAIWAN". It has been approved by the ethics committee. This Informed Consent form (ICF) contains important information of the research study. The study staff will explain it to you and answer any questions you have. Please review the information carefully before you sign the ICF. You can only participate in this study unless the ICF is signed.

STUDY TITLE: REAL-WORLD IMPACT OF HUMIRA ON RHEUMATOID ARTHRITIS PATIENTS IN CHINA, SOUTH KOREA, AND TAIWAN
Study organization: [redacted] **Sponsor:** AbbVie Pte. Ltd. **Investigator:** [To insert study investigator name and contact information] **Site(s):** [To insert study site] ***24 hour emergency contact:** [To insert emergency phone number]
Participant name： **Gender：** **Date of birth:** **Medical record number：** **Address：** **Phone：**

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		-			
Site number			Participant ID		

I. Study Purpose This is a longitudinal, observational, non-interventional, multinational, multi-centre study. The purpose of the study is to investigate the benefits associated with Humira use in patients with Rheumatoid Arthritis (RA) in China, South Korea, and Taiwan.
II. Participant Selection All participants for this study are selected by the investigator based on the inclusion and exclusion criteria defined in the study protocol. The selection criteria include a diagnosis of RA, RA treatment experience, and other requirements based on the investigator's assessment.
III. Study methodology The entire study period is approximately 24 weeks. Approximately 100 patients diagnosed with RA will be recruited per country. We will invite you to fill in the study questionnaires in paper forms today, at week 12 and week 24 before you see your doctor. It will take approximately 30 minutes to complete the questionnaires. The study questionnaires are on your quality of life, functioning, work productivity, treatment satisfaction, impression of changes and healthcare resource utilization. Please follow the instruction of study staff to complete the questionnaires. Please also relax and do not have any pressure. Your response to the questionnaires will not impact on your rights.
IV. Data management and storage process All study data will be stored in IMS data servers. Data servers are submitted to daily backups in order to increase the security on all data managed in the collection process. All paper based questionnaires will be stored in a secured, locked area for a period of seven (7) years, after which all data will be shred using an agency specialized in disposal of confidential documents.

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Site number Participant ID

V. Risks

This is a non-interventional observational study. It does not involve any direct patient intervention with respect to laboratory tests, examinations or drug treatment. If you feel uncomfortable because of the length of the questionnaires, please feel free to ask the study staff for help. You can also withdraw from the study at any time. We fully respect your decision.

VI. Expected Benefits

Humira may be beneficial in treating RA and improve the quality of life of RA patients, but this cannot be guaranteed. While you may not personally benefit from being in this study, the information learned from this study may help researchers to find out if Humira will help other people with RA.

VII. Confidentiality

Information on your identity will be considered as confidential for all effects and purposes. Your identity will not be revealed nor published under any circumstances. Your data will be documented anonymously and coded with a patient number. All other parties involved in data management, analysis and storage will only receive, and subsequently analyze non-identifiable data. However, research records and medical records identifying you may be inspected by the study investigator or the ethics committee for the purpose of monitoring the research to ensure it follows related laws and legal requirements. However, no records identifying you will be allowed to be revealed or published by these parties.

VIII. Compensation

1. As this study only requires you to fill out the questionnaires, there is no risk of injury resulting from this study.
2. There is no compensation for you to fill out the questionnaires.
3. You will not lose any of your legal rights by signing this ICF.

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		-			

Site number Participant ID

IX. Participant Rights

1. In the study process, any important findings related to your health or condition that would impact your continuous participation in the study will be provided to you immediately.
2. This study has been approved by the ethics committee, who reviews the benefits, risks, confidentiality and other related aspects of the study. If you have doubts regarding the study purpose, your own rights as a study participant or any damage caused by the participation, you may consult the ethics committee for help. The contact is: [Phone number of ethics committee].
3. If you have any questions or concerns about the study now, please feel free to ask the study staff now or call [to insert phone number] (24 hour emergency contact).
4. There are two (2) copies of this ICF. The study investigator has given you the copy and clearly explained the study information to you. The study investigator has also answered your questions related to the study.
5. Data obtained from you in this research study will be anonymized and may be used for commercial purposes. It is the policy of IMS and Abbvie not to provide financial compensation to you should this occur.

X. Withdrawal or Discontinuation

Your participation in this research is entirely voluntary. You may withdraw your consent or quit from this study at any time. If you decide to enter the study and to withdraw at any time in the future, there will be no penalty or loss of benefits to which you are otherwise entitled, and your future medical care will not be affected. The study investigator may decide to discontinue the study at any time, or withdraw you from the study at any time, if they feel that it is necessary or in your best interests. If you enter the study and then decide to withdraw at a later time, all data collected about you during your enrolment in the study will still be retained for analysis.

1023259 Real-World Impact of RA

		-			

Site number Participant ID

XI. Signature

1. The study investigator has explained the study purpose, methodology, benefits and risks clearly.

   Study investigator name:
   Study investigator signature:
   Date:

2. I have fully understood the study methodology and the possible benefits and risks related to it. All my questions related to the study have been answered by the study investigator. I voluntarily consent to participate in this research study.

   Participant name:
   Participant signature:
   Date:

Appendix B. Inclusion/Exclusion Form

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

[redacted]

Patient Inclusion/Exclusion Form

Today's date: ☐☐ / ☐☐ / ☐☐☐☐ (Month / Day / Year)

Please check if the patient meets all of the following inclusion criteria.

• Subject has a diagnosis of RA as defined by the 1987 revised ACR classification criteria and/or the ACR/EULAR 2010 classification criteria (any duration since diagnosis)	☐1 Yes ☐0 No
• Male or female subject ≥18 years of age (local definition according to adalimumab label) who is in compliance with eligibility for adalimumab based on the local label	☐1 Yes ☐0 No
• With moderate to severe RA defined as DAS28 (ESR) or DAS28 (CRP)>3.2	☐1 Yes ☐0 No
• Biologically treatment naïve and initiated adalimumab at baseline visit	☐1 Yes ☐0 No
• Availability of clinical data of the previous 12 weeks prior to baseline	☐1 Yes ☐0 No
• Ability to self-complete patient questionnaires	☐1 Yes ☐0 No
• Subject must be able and willing to provide written informed consent and comply with the requirements of the study protocol	☐1 Yes ☐0 No

The patient can only be enrolled with 'Yes' checked for all inclusion criteria above.

Please check if the patient meets any of the following exclusion criteria.

• The patient is pregnant or breast feeding at enrolment or wishes to become pregnant in the next 24 weeks	☐1 Yes ☐0 No
• Participation in any RA-related clinical trial at the time of enrolment, at baseline or at any point during the past 24 weeks prior to baseline	☐1 Yes ☐0 No
• The patient, who in your view, may not be able to accurately report their quality of life or prior resource utilization	☐1 Yes ☐0 No
• The patient, who in your view, may not be able to adhere to adalimumab therapy over 24 weeks	☐1 Yes ☐0 No

The patient can only be enrolled with 'No' checked for all exclusion criteria above.

Patient Inclusion Exclusion Form v2.0

Appendix C. Clinical Case Report Form (CRF)

Baseline:

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		-			
Site number			Participant ID		

[redacted]

Clinician Case Report Form
(Baseline)

All of the following information must be completed by the clinician or his/her representative.

Clinician name: _____

Clinician signature: _____

Patient ID	Site # - Participant #
Today's date	Day / Month / Year

Please provide the information below.	
1. When was the patient diagnosed with Rheumatoid Arthritis?	Year
2. What is the patient's current disease status?	▫ Moderate ▫ Severe

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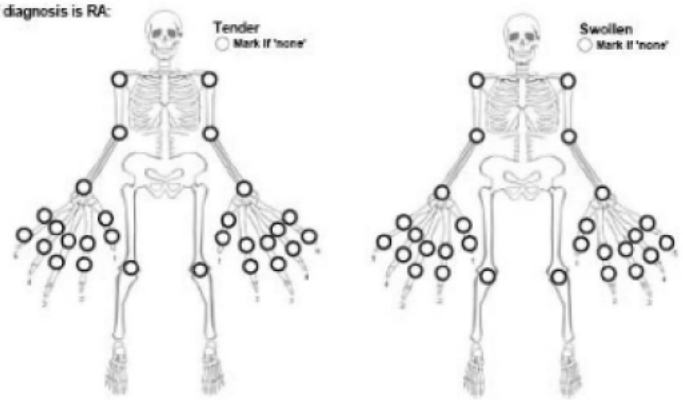
		-			
Site number			Participant ID		

[redacted]

Please provide the information below.	
3. Please perform a swollen and tender joint examination on your patient using the figure below and record the total number of tender/swollen joints in the appropriate boxes on the right.	Tender Joint Count ☐☐ Swollen Joint Count ☐☐
If diagnosis is RA: 	
4. Please record the most recent Erythrocyte Sedimentation Rate (ESR) (in mm/hour) or C-reactive protein (CRP) (in mg/L) of this patient.	☐☐ ESR (mm/hour) Test Date (DD/MM/YYYY): ___/___/_____ ☐☐ CRP (mg/L) Test Date (DD/MM/YYYY): ___/___/_____
5. Please record the latest DAS28 score*, if calculated	☐

* For calculation instruction, please refer to study protocol, page 21, clinical case report form (CRF).

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

[redacted]

6. Please check all the comorbidities this patient has currently.
☐0 No comorbidity
☐1 Myocardial infarction
☐2 Congestive heart failure
☐3 Peripheral vascular disease
☐4 Cerebrovascular disease
☐5 Dementia
☐6 Chronic pulmonary disease
☐7 Connective tissue disease
☐8 Ulcer disease
☐9 Mild liver disease
☐10 Diabetes
☐11 Hemiplegia
☐12 Moderate or severe renal disease
☐13 Diabetes with end-organ damage
☐14 Any tumor
☐15 Leukemia
☐16 Lymphoma
☐17 Moderate or severe liver disease
☐18 Metastatic solid tumor
☐19 AIDS

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		-			

Site number Participant ID

[redacted]

7. Please check all the prior medications this patient has received for her/his Rheumatoid Arthritis in the last 6 months.
(No response option for biologics is given as the current study recruits only patients with no history of any biologics prior to the study).

Drug Name	Average number of pills per day	Dose strength	Times per month
Disease Modifying Antirheumatic Drug (DMARD)			
☐1 Auranofin (Ridaura, Myochrysine)	_____	_____mg	_____
☐2 Azathioprine (Imuran)	_____	_____mg	_____
☐3 Cyclosporine (Sandimmune and Neoral)	_____	_____mg	_____
☐4 Hydroxychloroquine (Plaquenil)	_____	_____mg	_____
☐5 Leflunomide (Arava)	_____	_____mg	_____
☐6 Methotrexate (Rheumatrex, Folex)	_____	_____mg	_____
☐7 Minocycline (Minocin, Dynacin and Vectrin)	_____	_____mg	_____
☐8 Sulfasalazine (Azulfidine)	_____	_____mg	_____
☐9 Others	_____	_____mg	_____
Anti-inflammatory Drug (NSAID)			
☐10 Ibuprofen (Advil, Motrin, Nuprin)	_____	_____mg	_____
☐11 Naproxen (Naprosyn, Anaprox, Aleve)	_____	_____mg	_____
☐12 Celecoxib (Celebrex)	_____	_____mg	_____
☐13 Aspirin (ASA)	_____	_____mg	_____
☐14 Diclofenac (Voltaren)	_____	_____mg	_____
☐15 Indomethacin (Indocid)	_____	_____mg	_____
☐16 Others	_____	_____mg	_____
Others			
☐17 Steroids	_____	_____mg	_____
☐18 Stomach or gastric medications	_____	_____mg	_____

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

[redacted]

8. Please check all the prior surgeries this patient has received for her/his Rheumatoid Arthritis in the last 6 months.			
☐0 No surgery performed			
☐1 Yes →	**Type of Surgery** (Please input the number of the list below)	**Length of Stay***	**Date of Surgery (DD/MM/YYYY)**
	☐1 _____	_____days	____/____/_____
	☐2 _____	_____days	____/____/_____
	☐3 _____	_____days	____/____/_____
	☐4 _____	_____days	____/____/_____
	☐5 _____	_____days	____/____/_____

List of common surgeries for rheumatoid arthritis:

1. Arthroscopy
2. Carpal tunnel release
3. Cervical spinal fusion
4. Total knee replacement
5. Total hip replacement
6. Knee arthrodesis (fusion)
7. Hip arthrodesis (fusion)
8. Synovectomy
9. Other:_____

* For day surgeries, please input 0 days.

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

[redacted]

9. Please check any Hylan G-F 20 (Synvisc) injection this patient has received for her/his Rheumatoid Arthritis in the last 6 months.			
☐0 No injection performed			
☐1 Yes →	**Injection Place**	**Dosage**	**Number of Shots**
	☐1 Hip	_____ml	_____
	☐2 Knee	_____ml	_____

10. Please provide the dosing information for the first injection of Adalimumab (Humira) this patient has received for her/his Rheumatoid Arthritis.	
First time administration (DD/MM/YYYY):	**Dosage**
___/___/_____	_____mg

1023259 Real-World Impact of RA

		-			

Site number Participant ID

[redacted]

11. Please record the current medications this patient has received for her/his Rheumatoid Arthritis.			
Drug Name	**Average number of pills per day**	**Dose strength**	**Times per month**
Disease Modifying Antirheumatic Drug (DMARD)			
☐1 Auranofin (Ridaura, Myochrysine)	_____	_____mg	_____
☐2 Azathioprine (Imuran)	_____	_____mg	_____
☐3 Cyclosporine (Sandimmune and Neoral)	_____	_____mg	_____
☐4 Hydroxychloroquine (Plaquenil)	_____	_____mg	_____
☐5 Leflunomide (Arava)	_____	_____mg	_____
☐6 Methotrexate (Rheumatrex, Folex)	_____	_____mg	_____
☐7 Minocycline (Minocin, Dynacin and Vectrin)	_____	_____mg	_____
☐8 Sulfasalazine (Azulfidine)	_____	_____mg	_____
☐9 Others	_____	_____mg	_____
Anti-inflammatory Drug (NSAID)			
☐10 Ibuprofen (Advil, Motrin, Nuprin)	_____	_____mg	_____
☐11 Naproxen (Naprosyn, Anaprox, Aleve)	_____	_____mg	_____
☐12 Celecoxib (Celebrex)	_____	_____mg	_____
☐13 Aspirin (ASA)	_____	_____mg	_____
☐14 Diclofenac (Voltaren)	_____	_____mg	_____
☐15 Indomethacin (Indocid)	_____	_____mg	_____
☐16 Others	_____	_____mg	_____
Others			
☐17 Steroids	_____	_____mg	_____
☐18 Stomach or gastric medications	_____	_____mg	_____

Thank you for completing the Clinician Case Report Form.
Please return this form to the IMS representative.

1023259 Clinician Case Report Form (Baseline) v9_0 7

Follow-up:

1023259 Real-World Impact of RA

		-			

Site number Participant ID

[redacted]

Clinician Case Report Form
(Follow-up)

All of the following information must be completed by the clinician or his/her representative.

Clinician name: _____

Clinician signature: _____

Site & participant ID | | | - | | | | Site # / Participant #

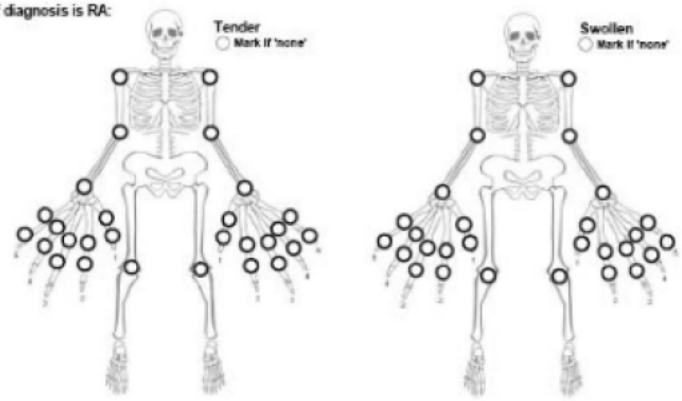
Today's date: | | / | | | / | | | | Day / Month / Year

Please provide the information below.	
1. What is the patient's current disease status?	☐ Moderate ☐ Severe

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

[redacted]

Please provide the information below.	
2. Please perform a swollen and tender joint examination on your patient using the figure below and record the total number of tender/swollen joints in the appropriate boxes on the right.	Tender Joint Count: ☐☐ Swollen Joint Count: ☐☐
If diagnosis is RA: 	
3. Please record the most recent Erythrocyte Sedimentation Rate (ESR) (in mm/hour) or C-reactive protein (CRP) (in mg/L) of this patient.	☐☐ ESR (mm/hour) Test Date (DD/MM/YYYY): ___/___/_____ ☐☐ CRP (mg/L) Test Date (DD/MM/YYYY): ___/___/_____
4. Please record the latest DAS28 score*, if calculated	☐

* For calculation instruction, please refer to study protocol, page 21, clinical case report form (CRF).

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

[redacted]

5. Please check all the surgeries this patient has received for her/his Rheumatoid Arthritis since the last completed survey.			
☐0 No surgery performed			
☐1 Yes →	**Type of Surgery** (Please input the number of the list below)	**Length of Stay***	**Date of surgery (DD/MM/YYYY)**
	☐1 _____	_____days	____/____/_____
	☐2 _____	_____days	____/____/_____
	☐3 _____	_____days	____/____/_____
	☐4 _____	_____days	____/____/_____
	☐5 _____	_____days	____/____/_____

List of common surgeries for rheumatoid arthritis:

1. Arthroscopy
2. Carpal tunnel release
3. Cervical spinal fusion
4. Total knee replacement
5. Total hip replacement
6. Knee arthrodesis (fusion)
7. Hip arthrodesis (fusion)
8. Synovectomy
9. Other:_____

* For day surgeries, please input 0 days.

6. Please check any Hylan G-F 20 (Synvisc) injections this patient has received for her/his Rheumatoid Arthritis since the last completed survey.			
☐0 No injection performed			
☐1 Yes →	**Injection Place**	**Dosage**	**Number of shots**
	☐1 Hip	_____ml	_____
	☐2 Knee	_____ml	_____

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

[redacted]

7. Please check any adalimumab (Humira) injection this patient has received for her/his Rheumatoid Arthritis since the last completed survey.		
☐0 No, no injection performed		
☐1 Yes →	**Dosage**	**Number of Times**
	_____mg	_____
Administration stop date (if stopped)	___/___/_____ (DD/MM/YYYY)	

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Site number Participant ID

[redacted]

8. Please record all of the medications this patient has received for her/his Rheumatoid Arthritis since the last completed survey			
Drug Name	**Average number of pills per day**	**Dose strength**	**Times per month**
Disease Modifying Antirheumatic Drug (DMARD)			
☐1 Auranofin (Ridaura, Myochrysine)	_____	_____mg	_____
☐2 Azathioprine (Imuran)	_____	_____mg	_____
☐3 Cyclosporine (Sandimmune and Neoral)	_____	_____mg	_____
☐4 Hydroxychloroquine (Plaquenil)	_____	_____mg	_____
☐5 Leflunomide (Arava)	_____	_____mg	_____
☐6 Methotrexate (Rheumatrex, Folex)	_____	_____mg	_____
☐7 Minocycline (Minocin, Dynacin and Vectrin)	_____	_____mg	_____
☐8 Sulfasalazine (Azulfidine)	_____	_____mg	_____
☐9 Others	_____	_____mg	_____
Anti-inflammatory Drug (NSAID)			
☐10 Ibuprofen (Advil, Motrin, Nuprin)	_____	_____mg	_____
☐11 Naproxen (Naprosyn, Anaprox, Aleve)	_____	_____mg	_____
☐12 Celecoxib (Celebrex)	_____	_____mg	_____
☐13 Aspirin (ASA)	_____	_____mg	_____
☐14 Diclofenac (Voltaren)	_____	_____mg	_____
☐15 Indomethacin (Indocid)			
☐16 Others	_____	_____mg	_____
Others			
☐17 Steroids	_____	_____mg	_____
☐18 Stomach or gastric medications	_____	_____mg	_____

Thank you for completing the Clinician Case Report Form.
Please return this form to the IMS representative.

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Appendix D. Health Assessment Questionnaire Disability Index (HAQ DI)

HEALTH ASSESSMENT QUESTIONNAIRE (HAQ-DI)©

Name: _____ Date: _____

Please place an "x" in the box which best describes your abilities OVER THE PAST WEEK:

	WITHOUT ANY DIFFICULTY	WITH SOME DIFFICULTY	WITH MUCH DIFFICULTY	UNABLE TO DO
DRESSING & GROOMING				
Are you able to:				
Dress yourself, including shoelaces and buttons?	☐	☐	☐	☐
Shampoo your hair?	☐	☐	☐	☐
ARISING				
Are you able to:				
Stand up from a straight chair?	☐	☐	☐	☐
Get in and out of bed?	☐	☐	☐	☐
EATING				
Are you able to:				
Cut your own meat?	☐	☐	☐	☐
Lift a full cup or glass to your mouth?	☐	☐	☐	☐
Open a new milk carton?	☐	☐	☐	☐
WALKING				
Are you able to:				
Walk outdoors on flat ground?	☐	☐	☐	☐
Climb up five steps?	☐	☐	☐	☐

Please check any AIDS OR DEVICES that you usually use for any of the above activities:

☐ Devices used for Dressing (button hook, zipper pull, etc.)
☐ Built up or special utensils
☐ Crutches
☐ Cane
☐ Wheelchair
☐ Special or built up chair
☐ Walker

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

☐ Dressing and grooming ☐ Arising ☐ Eating ☐ Walking

Please place an "x" in the box which best describes your abilities OVER THE PAST WEEK:

	WITHOUT ANY DIFFICULTY	WITH SOME DIFFICULTY	WITH MUCH DIFFICULTY	UNABLE TO DO
HYGIENE				
Are you able to:				
Wash and dry your body?	☐	☐	☐	☐
Take a tub bath?	☐	☐	☐	☐
Get on and off the toilet?	☐	☐	☐	☐
REACH				
Are you able to:				
Reach and get down a 5 pound object (such as a bag of sugar) from above your head?	☐	☐	☐	☐
Bend down to pick up clothing from the floor?	☐	☐	☐	☐
GRIP				
Are you able to:				
Open car doors?	☐	☐	☐	☐
Open previously opened jars?	☐	☐	☐	☐
Turn faucets on and off?	☐	☐	☐	☐
ACTIVITIES				
Are you able to:				
Run errands and shop?	☐	☐	☐	☐
Get in and out of a car?	☐	☐	☐	☐
Do chores such as vacuuming or yard work?	☐	☐	☐	☐

Please check any AIDS OR DEVICES that you usually use for any of the above activities:

☐ Raised toilet seat ☐ Bathtub bar ☐ Long-handled appliances for reach

☐ Bathtub seat ☐ Long-handled appliances in bathroom ☐ Jar opener (for jars previously opened)

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

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

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

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

Your PAIN: How much pain have you had IN THE PAST WEEK?

On a scale of 0 to 10 (where zero represents "no pain" and 10 represents "worst pain imaginable"), please mark the number below.

0	1	2	3	4	5	6	7	8	9	10

Appendix E. Short Form (36) Health Survey (SF-36)

Your Health and Well-Being

This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. ***Thank you for completing this survey!***

For each of the following questions, please mark an ☒ in the one box that best describes your answer.

1. In general, would you say your health is:

Excellent	Very good	Good	Fair	Poor
☐1	☐2	☐3	☐4	☐5

2. <u>Compared to one year ago</u>, how would you rate your health in general <u>now</u>?

Much better now than one year ago	Somewhat better now than one year ago	About the same as one year ago	Somewhat worse now than one year ago	Much worse now than one year ago
☐1	☐2	☐3	☐4	☐5

3. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

	Yes, limited a lot	Yes, limited a little	No, not limited at all
a. Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports	☐ 1	☐ 2	☐ 3
b. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐ 1	☐ 2	☐ 3
c. Lifting or carrying groceries	☐ 1	☐ 2	☐ 3
d. Climbing several flights of stairs	☐ 1	☐ 2	☐ 3
e. Climbing one flight of stairs	☐ 1	☐ 2	☐ 3
f. Bending, kneeling, or stooping	☐ 1	☐ 2	☐ 3
g. Walking more than a mile	☐ 1	☐ 2	☐ 3
h. Walking several hundred yards	☐ 1	☐ 2	☐ 3
i. Walking one hundred yards	☐ 1	☐ 2	☐ 3
j. Bathing or dressing yourself	☐ 1	☐ 2	☐ 3

4. **During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?**

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Cut down on the amount of time you spent on work or other activities	☐1	☐2	☐3	☐4	☐5
b. Accomplished less than you would like	☐1	☐2	☐3	☐4	☐5
c. Were limited in the kind of work or other activities	☐1	☐2	☐3	☐4	☐5
d. Had difficulty performing the work or other activities (for example, it took extra effort)	☐1	☐2	☐3	☐4	☐5

5. **During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?**

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Cut down on the amount of time you spent on work or other activities	☐1	☐2	☐3	☐4	☐5
b. Accomplished less than you would like	☐1	☐2	☐3	☐4	☐5
c. Did work or other activities less carefully than usual	☐1	☐2	☐3	☐4	☐5

6. **During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors, or groups?**

Not at all	Slightly	Moderately	Quite a bit	Extremely
☐1	☐2	☐3	☐4	☐5

7. **How much bodily pain have you had during the past 4 weeks?**

None	Very mild	Mild	Moderate	Severe	Very Severe
☐1	☐2	☐3	☐4	☐5	☐6

8. **During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?**

Not at all	A little bit	Moderately	Quite a bit	Extremely
☐1	☐2	☐3	☐4	☐5

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks...

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a. Did you feel full of life?	☐1	☐2	☐3	☐4	☐5
b. Have you been very nervous?	☐1	☐2	☐3	☐4	☐5
c. Have you felt so down in the dumps that nothing could cheer you up?	☐1	☐2	☐3	☐4	☐5
d. Have you felt calm and peaceful?	☐1	☐2	☐3	☐4	☐5
e. Did you have a lot of energy?	☐1	☐2	☐3	☐4	☐5
f. Have you felt downhearted and depressed?	☐1	☐2	☐3	☐4	☐5
g. Did you feel worn out?	☐1	☐2	☐3	☐4	☐5
h. Have you been happy?	☐1	☐2	☐3	☐4	☐5
i. Did you feel tired?	☐1	☐2	☐3	☐4	☐5

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

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐1	☐2	☐3	☐4	☐5

11. How TRUE or FALSE is <u>each</u> of the following statements for you?

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
a. I seem to get sick a little easier than other people	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b. I am as healthy as anybody I know	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c. I expect my health to get worse	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d. My health is excellent	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

THANK YOU FOR COMPLETING THESE QUESTIONS!

Appendix F. EuroQol 5 dimension, 3 level quality of life questionnaire (EQ-5D-3L)

By placing a tick in one box in each group below, please indicate which statements best describe your own health state today.

Mobility

I have no problems in walking about ❑
I have some problems in walking about ❑
I am confined to bed ❑

Self-Care

I have no problems with self-care ❑
I have some problems washing or dressing myself ❑
I am unable to wash or dress myself ❑

Usual Activities (*e.g. work, study, housework, family or leisure activities)*

I have no problems with performing my usual activities ❑
I have some problems with performing my usual activities ❑
I am unable to perform my usual activities ❑

Pain/Discomfort

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

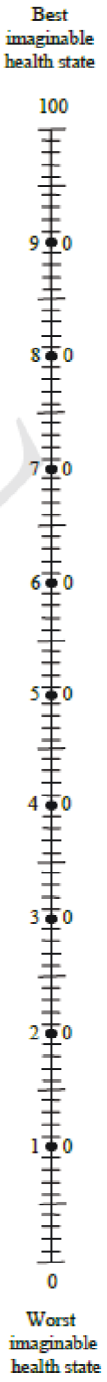
Anxiety/Depression

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

To help people say how good or bad a health state is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale how good or bad your own health is today, in your opinion. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your health state is today.

Your own health state today



Appendix G. Work Productivity and Activity Impairment (WPAI)

Work Productivity and Activity Impairment Questionnaire: Rheumatoid arthritis V2.0 (WPAI:RA)

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

1. Please check your current employment status.

☐1	Full time (working for pay)
☐2	Part time (working for pay)
☐3	Volunteering
☐4	Stopped working because of my RA
☐5	Stopped working for other reasons
☐6	Retired

If your response is 1 or 2, continue the survey.
If your response is 3-6, skip to question 6.

The next questions refer to 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 rheumatoid arthritis? *Include hours you missed on sick days, times you went in late, left early, etc., because of your rheumatoid arthritis. 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 annual leave, holidays, time off to participate in this study?

_____ HOURS

1

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 rheumatoid arthritis 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 rheumatoid arthritis affected your work only a little, choose a low number. Choose a high number if rheumatoid arthritis affected your work a great deal.

Consider only how much rheumatoid arthritis affected productivity while you were working.

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

CIRCLE A NUMBER

2

6. During the past seven days, how much did your rheumatoid arthritis problems affect your ability to perform your normal daily activities, other than work at a job?

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

Consider only how much rheumatoid arthritis affected your ability to perform your normal daily activities, other than work at a job.

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

CIRCLE A NUMBER

3

Appendix H. Patient Global Impression of Change (PGIC)

Patients' Global Impression of Change (PGIC) Scale

Since you initiated your Humira treatment, how would you describe the change in your rheumatoid arthritis? (Tick one box)

☐1	☐2	☐3	☐4	☐5	☐6	☐7
Very much better	Much better	A little better	No change	A little worse	Much worse	Very much worse

Appendix I. Patient Treatment Satisfaction Questions

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		-			

Site number Participant ID

[redacted]

Patient Treatment Satisfaction Questions

Today's date: ☐☐ / ☐☐ / ☐☐☐☐

Day Month Year

Please answer the questions below.	Very satisfied	Somewhat satisfied	Neither satisfied nor dissatisfied	Somewhat dissatisfied	Very dissatisfied
1. Over the last 4 weeks, how satisfied have you been with the way your rheumatoid arthritis treatment improves your morning stiffness in and around the joints?	☐	☐	☐	☐	☐
2. Over the last 4 weeks, how satisfied have you been with the way your rheumatoid arthritis treatment improves your mobility?	☐	☐	☐	☐	☐
3. Over the last 4 weeks, how satisfied have you been with the way your rheumatoid arthritis treatment improves your ability to perform daily living requiring fine motor skills (i.e. writing, using utensils, dressing)?	☐	☐	☐	☐	☐
4. Over the last 4 weeks, how satisfied have you been with your rheumatoid arthritis treatment overall?	☐	☐	☐	☐	☐

Thank you for completing the Patient Treatment Satisfaction Questions.
Please return this form to the [redacted]epresentative.

Appendix J. Healthcare resource utilization (HCRU) questionnaire

Baseline:

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Site number			Participant ID		

[redacted]

Healthcare Resource Utilization &
Demographic Questionnaire
(Baseline)

Patient ID	Site # - Participant #
Today's date	Day / Month / Year

<Request on entering>
1. Please use ballpoint pen.
2. On selecting the item, please check surely in ☐ or enter into ( ).
3. On correcting, please cross out with a double line (=) and **initial and date.**

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Site number Participant ID

[redacted]

1. When did you first start experiencing the symptoms of rheumatoid arthritis?
☐0 Do not remember
☐1 Year: _____

2. When did you first start visiting healthcare professionals for treatment of your rheumatoid arthritis ?
☐0 Do not remember
☐1 Year: _____

3. In the last 6 months, were there any consultations/visits to healthcare professionals for treatment of your rheumatoid arthritis? (Check all that apply)

☐0 No visit in the last 6 months

☐1 Yes →

☐1 General Practitioner (**Taiwan:** Family Medicine)	_____times
☐2 Rheumatologist	_____times
☐3 Gerontologist	_____times
☐4 Orthopedist	_____times
☐5 Internist	_____times
☐6 Emergency department	_____times
☐7 Traditional Medicine	_____times
☐8 Physical therapist (**Taiwan:** Rehabilitation Medicine)	_____times
☐9 Other: _____	_____times

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		-			
Site number			Participant ID		

[redacted]

4. In the last 6 months, when you visited the healthcare professional(s) for treatment of your rheumatoid arthritis, were there any procedures performed?		
☐0 No, consultation only		
☐1 Yes →	☐1 Chest X-Ray	_____times
	☐2 Spine X-Ray	_____times
	☐3 Neck X-Ray	_____times
	☐4 Shoulder X-Ray	_____times
	☐5 Hand X-Ray	_____times
	☐6 Knee X-Ray	_____times
	☐7 MRI	_____times
	☐8 CT scan	_____times
	☐9 Electrocardiogram	_____times
	☐10 Blood sample taken	_____times
	☐11 Urine test	_____times
	☐12 Endoscopy	_____times
	☐13 Bone scan	_____times
	☐14 Liver function test	_____times
	☐15 Tuberculin Skin Test	_____times
	☐16 Sputum tests	_____times
	☐17 Other:_____	_____times

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		-			
Site number			Participant ID		

[redacted]

5. In the last 6 months, when you visited the healthcare professional(s) for treatment of your rheumatoid arthritis, were there any surgeries performed?

☐0 No, consultation only

☐1 Yes →

	Type of surgery (Please input the number of the list below)	**Length of stay***	**Date of surgery (DD/MM/YYYY)**
☐1	_____	_____days	____/____/_____
☐2	_____	_____days	____/____/_____
☐3	_____	_____days	____/____/_____
☐4	_____	_____days	____/____/_____
☐5	_____	_____days	____/____/_____

List of common surgeries for rheumatoid arthritis:

1. Arthroscopy
2. Carpal tunnel release
3. Cervical spinal fusion
4. Total knee replacement
5. Total hip replacement
6. Knee arthrodesis (fusion)
7. Hip arthrodesis (fusion)
8. Synovectomy
9. Other:_____

* For day surgeries, please input 0 days.

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		-			
Site number			Participant ID		

[redacted]

6. In the last 6 months, when you visited the healthcare professional(s) for treatment of your rheumatoid arthritis, did you receive any Hylan G-F 20 (Synvisc) injection?		
☐0 No, consultation only		
☐1 Yes →	**Injection Place**	**Number of shots**
	☐1 Hip	_____
	☐2 Knee	_____

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		-			
Site number			Participant ID		

[redacted]

7. In the last 6 months, have you taken any medications for your rheumatoid arthritis?			
Drug name	**Average number of pills per day**	**Dose strength**	**Times per month**
Disease Modifying Antirheumatic Drug (DMARD)			
☐1 Auranofin (Ridaura, Myochrysine)	_____	_____mg	_____
☐2 Azathioprine (Imuran)	_____	_____mg	_____
☐3 Cyclosporine (Sandimmune and Neoral)	_____	_____mg	_____
☐4 Hydroxychloroquine (Plaquenil)	_____	_____mg	_____
☐5 Leflunomide (Arava)	_____	_____mg	_____
☐6 Methotrexate (Rheumatrex, Folex)	_____	_____mg	_____
☐7 Minocycline (Minocin, Dynacin and Vectrin)	_____	_____mg	_____
☐8 Sulfasalazine (Azulfidine)	_____	_____mg	_____
☐9 Others	_____	_____mg	_____
Anti-inflammatory Drug (NSAID)			
☐10 Ibuprofen (Advil, Motrin, Nuprin)	_____	_____mg	_____
☐11 Naproxen (Naprosyn, Anaprox, Aleve)	_____	_____mg	_____
☐12 Celecoxib (Celebrex)	_____	_____mg	_____
☐13 Aspirin (ASA)	_____	_____mg	_____
☐14 Diclofenac (Voltaren)	_____	_____mg	_____

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		-			

Site number Participant ID

[redacted]

7. In the last 6 months, have you taken any medications for your rheumatoid arthritis?			
Drug name	**Average number of pills per day**	**Dose strength**	**Times per month**
☐15 Indomethacin (Indocid)	_____	_____mg	_____
☐16 Others	_____	_____mg	_____
Others			
☐17 Steroids	_____	_____mg	_____
☐18 Stomach or gastric medications	_____	_____mg	_____

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		-			

Site number Participant ID

[redacted]

8. In the last 6 months, were you hospitalized in relation to your rheumatoid arthritis other than surgery? If yes, how many days did you stay at the hospital for your rheumatoid arthritis?		
☐$_0$ No hospitalization in the last 6 months		
Most recent hospitalization Admission date: ____/____/_____ (DD/MM/YYYY)	☐$_1$ Intensive care unit (ICU) ☐$_2$ General ward ☐$_3$ Both ☐$_4$ Other: _____	☐ Total days in hospital
Next hospitalization Admission date: ____/____/_____ (DD/MM/YYYY)	☐$_1$ Intensive care unit (ICU) ☐$_2$ General ward ☐$_3$ Both ☐$_4$ Other: _____	☐ Total days in hospital
Next hospitalization Admission date: ____/____/_____ (DD/MM/YYYY)	☐$_1$ Intensive care unit (ICU) ☐$_2$ General ward ☐$_3$ Both ☐$_4$ Other: _____	☐ Total days in hospital

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		-			
Site number			Participant ID		

[redacted]

9. Please check all the medical conditions you have been diagnosed with.
☐0 No comorbidity
☐1 Myocardial infarction
☐2 Congestive heart failure
☐3 Peripheral vascular disease
☐4 Cerebrovascular disease
☐5 Dementia
☐6 Chronic pulmonary disease
☐7 Connective tissue disease
☐8 Ulcer disease
☐9 Mild liver disease
☐10 Diabetes
☐11 Hemiplegia
☐12 Moderate or severe renal disease
☐13 Diabetes with end-organ damage
☐14 Any tumor
☐15 Leukemia
☐16 Lymphoma
☐17 Moderate or severe liver disease
☐18 Metastatic solid tumor
☐19 AIDS

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		-			

Site number Participant ID

[redacted]

10. Please answer the questions below.		
A) Do you need assistance with your daily tasks?	☐0 No	☐1 Yes
B) Do you have a caregiver or somebody to assist you day-to-day?	☐0 No	☐1 Yes
C) Have you made any modifications to your home due to your rheumatoid arthritis?	☐0 No	☐1 Yes

11. How old are you this year?
_____ years old

12. What is your gender?
☐1 Male
☐2 Female

13. What is your current marital status?
☐1 Unmarried
☐2 Married

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		-			
Site number			Participant ID		

[redacted]

14. What is the highest level of education you have attained?
Mainland China: ☐1 Junior high school and below ☐2 Senior high school/ Vocational training school ☐3 Associate degree ☐4 Bachelor degree ☐5 Graduate degree or above ☐6 Other: _____ **Taiwan:** ☐1 Elementary school ☐2 Junior high school ☐3 Senior high school ☐4 Community college/ business school ☐5 College/ University or above ☐6 Other: _____ **South Korea:** ☐1 Elementary School education ☐2 Middle School education ☐3 High School education ☐4 College(2-years course) degree ☐4 Bachelor degree ☐5 Master's degree ☐6 Doctoral degree ☐7 Other: _____

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		-			
Site number			Participant ID		

[redacted]

15. What type of medical insurance coverage do you have? (Check all that apply)
☐1 National/Public Insurance
☐2 Private Insurance
☐3 Employer benefits
☐4 Do not have insurance
☐5 Other: _____

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		-			
Site number			Participant ID		

[redacted]

16. Please check your household income
Mainland China:
☐1 Below RMB 8,000
☐2 RMB 8,000-11,999
☐3 RMB 12,000-14,999
☐4 RMB 15,000-19,999
☐5 RMB 20,000-29,999
☐6 RMB 30,000 and above
☐0 Prefer not to tell
Taiwan:
☐1 Less than NT$250,000
☐2 NT$250,000 – 649,999
☐3 NT$650,000 – NT$1199,999
☐4 NT$1,200,000 – NT$1,799,999
☐5 NT$1,800,000 – NT$2,499,999
☐6 More than NT$2,500,000
☐0 Prefer not to tell
Korea:
☐1 0 – 999,999 KRW
☐2 1,000,000 – 1,999,999 KRW
☐3 2,000,000 – 2,999,999 KRW
☐4 3,000,000 – 3,499,999 KRW
☐5 3,500,000 – 3,999,999 KRW
☐6 4,000,000 – 4,499,999 KRW
☐7 4,500,000 – 5,499,999 KRW
☐8 5,500,000 – 6,499,999 KRW
☐9 6,500,000 – 9,999,999 KRW
☐10 10,000,000 + KRW
☐0 Prefer not to tell

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

[redacted]

Thank you for completing the Healthcare Resource Utilization Questionnaire.
Please return this form to the IMS representative.

Follow-up:

1023259 Real-World Impact of RA

		-			

Site number Participant ID

[redacted]

Healthcare Resource Utilization & Demographic Questionnaire
(Follow-up)

Patient ID	☐☐ - ☐☐☐ Site # Participant #
Today's date	☐☐ / ☐☐ / ☐☐☐☐ Day Month Year

<Request on entering>
1. Please use ballpoint pen.
2. On selecting the item, please check surely in ☐ or enter into ( ).
3. On correcting, please cross out with a double line (=) and **initial and date.**

1023259 Real-World Impact of RA

		-			

Site number Participant ID

[redacted]

1. Since you last filled out this questionnaire, did you have any consultations/visits to healthcare professionals for treatment of your rheumatoid arthritis? (Check all that apply)		
☐0 No visit since you last filled out this questionnaire		
☐1 Yes →	☐1 General Practitioner (**Taiwan:** Family Medicine)	_____times
	☐2 Rheumatologist	_____times
	☐3 Gerontologist	_____times
	☐4 Orthopedist	_____times
	☐5 Internist	_____times
	☐6 Emergency department	_____times
	☐7 Traditional Medicine	_____times
	☐8 Physical therapist (**Taiwan:** Rehabilitation Medicine)	_____times
	☐9 Other: _____	_____times

1023259 Real-World Impact of RA

		-			

Site number Participant ID

[redacted]

2. Since you last filled out this questionnaire, when you visited the healthcare professional(s) for treatment of your rheumatoid arthritis, were there any procedures performed?		
☐0 No, consultation only		
☐1 Yes →	☐1 Chest X-Ray	_____times
	☐2 Spine X-Ray	_____times
	☐3 Neck X-Ray	_____times
	☐4 Shoulder X-Ray	_____times
	☐5 Hand X-Ray	_____times
	☐6 Knee X-Ray	_____times
	☐7 MRI	_____times
	☐8 CT scan	_____times
	☐9 Electrocardiogram	_____times
	☐10 Blood sample taken	_____times
	☐11 Urine test	_____times
	☐12 Endoscopy	_____times
	☐13 Bone scan	_____times
	☐14 Liver function test	_____times
	☐15 Tuberculin Skin Test	_____times
	☐16 Sputum tests	_____times
	☐17 Other:_____	_____times

1023259 HCRU Questionnaire (Follow-up) v8_0 3

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

[redacted]

3. Since you last filled out this questionnaire, when you visited the healthcare professional(s) for treatment of your rheumatoid arthritis, were there any surgeries performed?

☐0 No, consultation only

☐1 Yes →

	Type of Surgery (Please input the number of the list below)	**Length of stay***	**Date of surgery (DD/MM/YYYY)**
☐1	_____	_____days	____/____/_____
☐2	_____	_____days	____/____/_____
☐3	_____	_____days	____/____/_____
☐4	_____	_____days	____/____/_____
☐5	_____	_____days	____/____/_____

List of common surgeries for rheumatoid arthritis:

1. Arthroscopy
2. Carpal tunnel release
3. Cervical spinal fusion
4. Total knee replacement
5. Total hip replacement
6. Knee arthrodesis (fusion)
7. Hip arthrodesis (fusion)
8. Synovectomy
9. Other:_____

* For day surgeries, please input 0 days.

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

[redacted]

4. Since you last filled out this questionnaire, when you visited the healthcare professional(s) for treatment of your rheumatoid arthritis, did you receive any Hylan G-F 20 (Synvisc) injection?		
☐0 No, consultation only		
☐1 Yes →	**Injection Place**	**Number of shots**
	☐1 Hip	_____
	☐2 Knee	_____

5. Since you last filled out this questionnaire, when you visited the healthcare professional(s) for treatment of your rheumatoid arthritis, did you receive any adalimumab (Humira)?		
☐0 No injection performed		
☐1 Yes →	**Dosage**	**Times per month**
	_____mg	_____
If you have stopped using Adalimumab, when did you stop?	____/____/_____ (DD/MM/YYYY)	

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

[redacted]

6. Since you last filled out this questionnaire, have you taken any medications for your rheumatoid arthritis?			
Drug name	**Average number of pills per day**	**Dose strength**	**Times per month**
Disease Modifying Antirheumatic Drug (DMARD)			
☐1 Auranofin (Ridaura, Myochrysine)	_____	_____mg	_____
☐2 Azathioprine (Imuran)	_____	_____mg	_____
☐3 Cyclosporine (Sandimmune and Neoral)	_____	_____mg	_____
☐4 Hydroxychloroquine (Plaquenil)	_____	_____mg	_____
☐5 Leflunomide (Arava)	_____	_____mg	_____
☐6 Methotrexate (Rheumatrex, Folex)	_____	_____mg	_____
☐7 Minocycline (Minocin, Dynacin and Vectrin)	_____	_____mg	_____
☐8 Sulfasalazine (Azulfidine)	_____	_____mg	_____
☐9 Others	_____	_____mg	_____
Anti-inflammatory Drug (NSAID)			
☐10 Ibuprofen (Advil, Motrin, Nuprin)	_____	_____mg	_____
☐11 Naproxen (Naprosyn, Anaprox, Aleve)	_____	_____mg	_____
☐12 Celecoxib (Celebrex)	_____	_____mg	_____
☐13 Aspirin (ASA)	_____	_____mg	_____
☐14 Diclofenac (Voltaren)	_____	_____mg	_____

1023259 HCRU Questionnaire (Follow-up) v8_0 6

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

[redacted]

6. Since you last filled out this questionnaire, have you taken any medications for your rheumatoid arthritis?			
Drug name	**Average number of pills per day**	**Dose strength**	**Times per month**
☐15 Indomethacin (Indocid)	_____	_____mg	_____
☐16 Others	_____	_____mg	_____
Others			
☐17 Steroids	_____	_____mg	_____
☐18 Stomach or gastric medications	_____	_____mg	_____

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

[redacted]

7. Since you last filled out this questionnaire, when you were hospitalized in relation to your rheumatoid arthritis, how many days did you stay at the hospital for your rheumatoid arthritis		
☐0 No hospitalization since you last filled out this questionnaire		
Most recent hospitalization Admission date: ____/____/_____ (DD/MM/YYYY)	☐1 Intensive care unit (ICU) ☐2 General ward ☐3 Both ☐4 Other: _____	☐ Total days in hospital
Next hospitalization Admission date: ____/____/_____ (DD/MM/YYYY)	☐1 Intensive care unit (ICU) ☐2 General ward ☐3 Both ☐4 Other: _____	☐ Total days in hospital
Next hospitalization Admission date: ____/____/_____ (DD/MM/YYYY)	☐1 Intensive care unit (ICU) ☐2 General ward ☐3 Both ☐4 Other: _____	☐ Total days in hospital

8. Please answer the questions below.		
A) Do you need assistance with your daily tasks?	☐0 No	☐1 Yes
B) Do you have a caregiver or somebody to assist you day-to-day?	☐0 No	☐1 Yes
C) Have you made any modifications to your home due to your rheumatoid arthritis?	☐0 No	☐1 Yes

Thank you for completing the Healthcare Resource Utilization Questionnaire.
Please return this form to the [redacted]epresentative.

Appendix K. Early Termination Form

For Physician:

1023259 Real-World Impact of RA

Site number - Participant ID

[redacted]

Early Termination Form
(Clinician)

All of the following information must be completed by the clinician or his/her representative.

Clinician name: _____

Clinician signature: _____

Site & participant ID ☐☐ - ☐☐☐ (Site # - Participant #)

Today's date: ☐☐ / ☐☐ / ☐☐☐☐ (Day / Month / Year)

Please provide the information below.	
1. What is the patient's current disease status?	☐ Moderate ☐ Severe

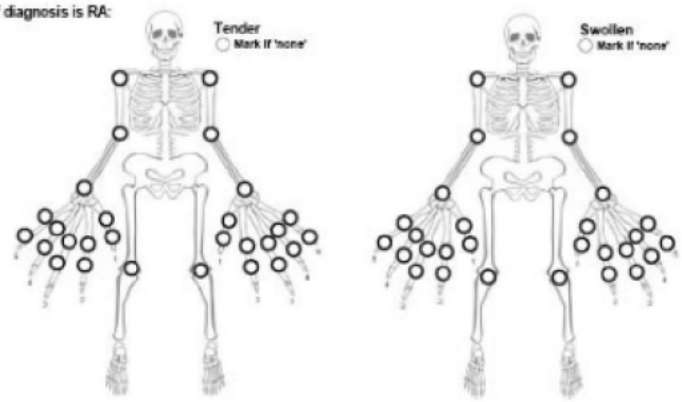
1023259 Early Termination Form (Physician) v4_0 1

1023259 Real-World Impact of RA

		-			

Site number Participant ID

[redacted]

Please provide the information below.	
2. Please perform a swollen and tender joint examination on your patient using the figure below and record the total number of tender/swollen joints in the appropriate boxes on the right.	Tender Joint Count: ☐☐ Swollen Joint Count: ☐☐
If diagnosis is RA: 	
3. Please record the most recent Erythrocyte Sedimentation Rate (ESR) (in mm/hour) or C-reactive protein (CRP) (in mg/L) of this patient.	☐☐ ESR (mm/hour) Test Date (DD/MM/YYYY): ___/___/_____
	☐☐ CRP (mg/L) Test Date (DD/MM/YYYY): ___/___/_____
4. Please record the latest DAS28 score*, if calculated	☐

* For calculation instruction, please refer to study protocol, page 21, clinical case report form (CRF).

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

[redacted]

5. Please check all the surgeries this patient has received for her/his Rheumatoid Arthritis since the last completed survey.

☐0 No surgery performed

☐1 Yes →

Type of Surgery (Please input the number of the list below)	Length of Stay*	Date of surgery (DD/MM/YYYY)
☐1 _____	_____days	____/____/_____
☐2 _____	_____days	____/____/_____
☐3 _____	_____days	____/____/_____
☐4 _____	_____days	____/____/_____
☐5 _____	_____days	____/____/_____

List of common surgeries for rheumatoid arthritis:

1. Arthroscopy
2. Carpal tunnel release
3. Cervical spinal fusion
4. Total knee replacement
5. Total hip replacement
6. Knee arthrodesis (fusion)
7. Hip arthrodesis (fusion)
8. Synovectomy
9. Other:_____

* For day surgeries, please input 0 days.

6. Please check any Hylan G-F 20 (Synvisc) injections this patient has received for her/his Rheumatoid Arthritis since the last completed survey.

☐0 No injection performed

☐1 Yes →

Injection Place	Dosage	Number of shots
☐1 Hip	_____ml	_____
☐2 Knee	_____ml	_____

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

[redacted]

7. Please check any adalimumab (Humira) injection this patient has received for her/his Rheumatoid Arthritis since the last completed survey.		
☐0 No, no injection performed		
☐1 Yes →	**Dosage**	**Number of Times**
	_____mg	_____
Administration stop date (if stopped)	___/___/_____ (DD/MM/YYYY)	
Reason why adalimumab (Humira) is stopped (if stopped): ☐1 Progression of disease ☐2 Adverse event (AE) ☐3 Patient withdrew		

1023259 Real-World Impact of RA

		-			

Site number Participant ID

[redacted]

8. Please record all of the medications this patient has received for her/his Rheumatoid Arthritis since the last completed survey			
Drug Name	**Average number of pills per day**	**Dose strength**	**Times per month**
Disease Modifying Antirheumatic Drug (DMARD)			
☐1 Auranofin (Ridaura, Myochrysine)	_____	_____mg	_____
☐2 Azathioprine (Imuran)	_____	_____mg	_____
☐3 Cyclosporine (Sandimmune and Neoral)	_____	_____mg	_____
☐4 Hydroxychloroquine (Plaquenil)	_____	_____mg	_____
☐5 Leflunomide (Arava)	_____	_____mg	_____
☐6 Methotrexate (Rheumatrex, Folex)	_____	_____mg	_____
☐7 Minocycline (Minocin, Dynacin and Vectrin)	_____	_____mg	_____
☐8 Sulfasalazine (Azulfidine)	_____	_____mg	_____
☐9 Others	_____	_____mg	_____
Anti-inflammatory Drug (NSAID)			
☐10 Ibuprofen (Advil, Motrin, Nuprin)	_____	_____mg	_____
☐11 Naproxen (Naprosyn, Anaprox, Aleve)	_____	_____mg	_____
☐12 Celecoxib (Celebrex)	_____	_____mg	_____
☐13 Aspirin (ASA)	_____	_____mg	_____
☐14 Diclofenac (Voltaren)	_____	_____mg	_____
☐15 Indomethacin (Indocid)			
☐16 Others	_____	_____mg	_____
Others			
☐17 Steroids	_____	_____mg	_____
☐18 Stomach or gastric medications	_____	_____mg	_____

Thank you for completing the Early Termination Form.
Please return this form to the [redacted] representative.

For Patient:

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

[redacted]

Early Termination Form

Patient ID	Site # - Participant #
Today's date	Day / Month / Year

<Request on entering>

1. Please use ballpoint pen.
2. On selecting the item, please check surely in ☐ or enter into ( ).
3. On correcting, please cross out with a double line (=) and **initial and date.**

1023259 Real-World Impact of RA

		-			

Site number Participant ID

[redacted]

1. Since you last filled out this questionnaire, did you have any consultations/visits to healthcare professionals for treatment of your rheumatoid arthritis? (Check all that apply)		
☐0 No visit since you last filled out this questionnaire		
☐1 Yes →	☐1 General Practitioner (**Taiwan:** Family Medicine)	_____times
	☐2 Rheumatologist	_____times
	☐3 Gerontologist	_____times
	☐4 Orthopedist	_____times
	☐5 Internist	_____times
	☐6 Emergency department	_____times
	☐7 Traditional Medicine	_____times
	☐8 Physical therapist (**Taiwan:** Rehabilitation Medicine)	_____times
	☐9 Other: _____	_____times

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

[redacted]

2. Since you last filled out this questionnaire, when you visited the healthcare professional(s) for treatment of your rheumatoid arthritis, were there any procedures performed?		
☐0 No, consultation only		
☐1 Yes →	☐1 Chest X-Ray	_____times
	☐2 Spine X-Ray	_____times
	☐3 Neck X-Ray	_____times
	☐4 Shoulder X-Ray	_____times
	☐5 Hand X-Ray	_____times
	☐6 Knee X-Ray	_____times
	☐7 MRI	_____times
	☐8 CT scan	_____times
	☐9 Electrocardiogram	_____times
	☐10 Blood sample taken	_____times
	☐11 Urine test	_____times
	☐12 Endoscopy	_____times
	☐13 Bone scan	_____times
	☐14 Liver function test	_____times
	☐15 Tuberculin Skin Test	_____times
	☐16 Sputum tests	_____times
	☐17 Other:_____	_____times

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

[redacted]

3. Since you last filled out this questionnaire, when you visited the healthcare professional(s) for treatment of your rheumatoid arthritis, were there any surgeries performed?			
☐0 No, consultation only			
☐1 Yes →	**Type of surgery** (Please input the number of the list below)	**Length of stay***	**Date of surgery (DD/MM/YYYY)**
	☐1 _____	_____days	____/____/_____
	☐2 _____	_____days	____/____/_____
	☐3 _____	_____days	____/____/_____
	☐4 _____	_____days	____/____/_____
	☐5 _____	_____days	____/____/_____

List of common surgeries for rheumatoid arthritis:

1. Arthroscopy
2. Carpal tunnel release
3. Cervical spinal fusion
4. Total knee replacement
5. Total hip replacement
6. Knee arthrodesis (fusion)
7. Hip arthrodesis (fusion)
8. Synovectomy
9. Other:_____

* For day surgeries, please input 0 days.

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

[redacted]

4. Since you last filled out this questionnaire, when you visited the healthcare professional(s) for treatment of your rheumatoid arthritis, did you receive any Hylan G-F 20 (Synvisc) injection?		
☐0 No, consultation only		
☐1 Yes →	**Injection place**	**Number of shots**
	☐1 Hip	_____
	☐2 Knee	_____

5. Since you last filled out this questionnaire, when you visited the healthcare professional(s) for treatment of your rheumatoid arthritis, did you receive any adalimumab (Humira)?		
☐0 No injection performed		
☐1 Yes →	**Dosage**	**Times per month**
	_____mg	_____
If you have stopped using Adalimumab, when did you stop?	____/____/_____ (DD/MM/YYYY)	

1023259 Real-World Impact of RA

		-			

Site number Participant ID

[redacted]

6. Since you last filled out this questionnaire, have you taken any medications for your rheumatoid arthritis?			
Drug name	**Average number of pills per day**	**Dose strength**	**Times per month**
Disease Modifying Antirheumatic Drug (DMARD)			
☐1 Auranofin (Ridaura, Myochrysine)	_____	_____mg	_____
☐2 Azathioprine (Imuran)	_____	_____mg	_____
☐3 Cyclosporine (Sandimmune and Neoral)	_____	_____mg	_____
☐4 Hydroxychloroquine (Plaquenil)	_____	_____mg	_____
☐5 Leflunomide (Arava)	_____	_____mg	_____
☐6 Methotrexate (Rheumatrex, Folex)	_____	_____mg	_____
☐7 Minocycline (Minocin, Dynacin and Vectrin)	_____	_____mg	_____
☐8 Sulfasalazine (Azulfidine)	_____	_____mg	_____
☐9 Others	_____	_____mg	_____
Anti-inflammatory Drug (NSAID)			
☐10 Ibuprofen (Advil, Motrin, Nuprin)	_____	_____mg	_____
☐11 Naproxen (Naprosyn, Anaprox, Aleve)	_____	_____mg	_____
☐12 Celecoxib (Celebrex)	_____	_____mg	_____
☐13 Aspirin (ASA)	_____	_____mg	_____
☐14 Diclofenac (Voltaren)	_____	_____mg	_____

1023259 Early Termination Form (Patient) v5_0 6

1023259 Real-World Impact of RA

		-			

Site number Participant ID

[redacted]

6. Since you last filled out this questionnaire, have you taken any medications for your rheumatoid arthritis?			
Drug name	**Average number of pills per day**	**Dose strength**	**Times per month**
☐15 Indomethacin (Indocid)	_____	_____mg	_____
☐16 Others	_____	_____mg	_____
Others			
☐17 Steroids	_____	_____mg	_____
☐18 Stomach or gastric medications	_____	_____mg	_____

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

[redacted]

7. Since you last filled out this questionnaire, when you were hospitalized in relation to your rheumatoid arthritis, how many days did you stay at the hospital for your rheumatoid arthritis		
☐0 No hospitalization since you last filled out this questionnaire		
Most recent hospitalization Admission date: ____/____/_____ (DD/MM/YYYY)	☐1 Intensive care unit (ICU) ☐2 General ward ☐3 Both ☐4 Other: _____	☐ Total days in hospital
Next hospitalization Admission date: ____/____/_____ (DD/MM/YYYY)	☐1 Intensive care unit (ICU) ☐2 General ward ☐3 Both ☐4 Other: _____	☐ Total days in hospital
Next hospitalization Admission date: ____/____/_____ (DD/MM/YYYY)	☐1 Intensive care unit (ICU) ☐2 General ward ☐3 Both ☐4 Other: _____	☐ Total days in hospital

8. Please answer the questions below.		
A) Do you need assistance with your daily tasks?	☐0 No	☐1 Yes
B) Do you have a caregiver or somebody to assist you day-to-day?	☐0 No	☐1 Yes
C) Have you made any modifications to your home due to your rheumatoid arthritis?	☐0 No	☐1 Yes

Thank you for completing the Healthcare Resource Utilization Questionnaire.
Please return this form to the [redacted] representative.

AbbVie Inc. (AbbVie)

Post Marketing Observational Study

P15-778 Protocol

Real-World Outcome of Adalimumab on Rheumatoid Arthritis Patients in Taiwan.

Approved by:

[redacted]

Date

Oct 22, 2015

Name [redacted]

Date

[redacted]

Date

Name [redacted]

Date

Oct 21, 2015