Title Page

Title	**R**eal-World **O**ut**c**ome of Rheumatoid Arthritis Patients in **K**orea on **A**dalimumab (ROCKA Study)
Protocol Version Identifier	Amendment 01, 26 Dec 2017
Date of Last Version of Protocol	26 Dec 2017
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Procedure Number	Not applicable (Non-PASS PMOS)
Marketing Authorization Holder(s)	AbbVie Limited [redacted]
Joint PASS	Not applicable (Non-PASS PMOS)
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 Korea.
Country(ies) of Study	Korea
Author	[redacted]

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 Ltd [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**
AESI	**Adverse Event of Special Interest**
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]	
Statistics Manager/ CRO(S):		
Principal Investigator:	Investigator information is on file at AbbVie	
Sponsor:	[redacted]	
Clinical Project Manager:		
Emergency Contacts Safety Review Team		

PROTOCOL SIGNATURES

Investigator Signature:

I have read and agree to the Protocol Number 11006, "**R**eal-World **O**utcome of Rheumatoid Arthritis Patients in **K**orea on **A**dalimumab (ROCKA Study)". 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: **R**eal-World **O**ut**c**ome of Rheumatoid Arthritis Patients in **K**orea on **a**dalimumab (ROCKA Study).

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 in Korea.

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 Korea.

Results from study on the effect 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 Korea.

Research Question and Objectives: The objective of this non-interventional, observational study is to assess the effect of adalimumab on health-related QoL and work productivity in patients with Rheumatoid Arthritis (RA) in Korea. 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 Korea.

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 89 patients diagnosed with RA that meet the inclusion and exclusion criteria will be enrolled at approximately 9 sites in Korea.

To assess health and disability outcomes, the Health Assessment Questionnaire Disability Index (HAQ DI) will be assessed at baseline, Week 12 and Week 24 after treatment initiation with adalimumab. In addition, other PROs of work activity and well-being, including the WPAI, EuroQol 5 dimension (EQ-5D), and Short Form 36-Item Health Survey (SF-36), will also be assessed.

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 participating country.

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 89 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 subject ≥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 weeks 12 and weeks 24 weeks from the 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 • 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 **Additional Secondary Variable** • Change in HAQ DI score from baseline to 24 weeks • Changes in the disease severity and PROs from baseline to 24 weeks **Exploratory Variable** • Change in patient satisfaction questions from baseline to weeks 12 and 24
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 89 patients diagnosed with RA that meet the inclusion and exclusion criteria will be enrolled at approximately 9 sites in Korea. The sample size was calculated by assuming an alpha of 0.05 and a power of 0.80 in a one-sided test,

resulting in 36 subjects required to recognize a statistically significant improvement in HAQ DI (-0.21). Then, given the importance of other secondary endpoints, an improvement of 9.9±25 hours of work time lost requires 40 subjects. However, since it is expected that approximately half the study population may no longer be working due to their age, we assume a 50% employment rate in the study population and a drop-out rate of 10%, eventually approximately 89 patients will be required to achieve the required number of respondents.

Data Analysis:

Primary Endpoint Analysis

Change in HAQ DI score at 24 weeks after the initiation of adalimumab (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 other PROs (SF-36 domain scales, EQ-5D Index, WPAI total lost productivity) at weeks 12 and 24 after the initiation of adalimumab (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 (observed population).

Additional Secondary Endpoint Analysis

- Change in HAQ DI score at 24 weeks after the initiation of adalimumab (observed population), compared with those patients not continuing on adalimumab (non-observeds). The mean changes in these two groups will be compared using an independent t-test.
- HCRU 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)
- Associations between disease severity and PROs
- Associations between change in disease severity and change in PROs

Exploratory endpoint

- Change in patient satisfaction questions at weeks 12 and 24 after the initiation of adalimumab (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.
Milestones: Start of Data Collection : 19 Oct, 2015 End of Data Collection : 28 Feb, 2018 Study Progress Report : Not applicable Interim Report : Not applicable Registration in the EU PASS Register : Not Applicable Final Report of Study Results : 31 Aug, 2018

5.0 Amendments and Updates

Number	Date	Section of Study Protocol	Amendment or Update	Reason
1	26 Dec 2017	- Sample size - Milestones	Amendment	Change of sample size and milestones (See Appendix L for details)

6.0 Milestones

Major study milestones and their planned dates are as follows:

Start of Data Collection (FPFV):	19 October 2015
End of Data Collection:	28 February 2018
Study Progress Report:	Not Applicable
Interim Report:	Not Applicable
Registration in the EU PAS register:	Not Applicable
Final Report of Study Results:	31 August 2018

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, no data, within our knowledge, on the effectiveness of adalimumab on health-related QoL and work productivity in patients with Rheumatoid Arthritis (RA) in Korea.

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 Korea.

Reimbursement in Korea is strongly influenced by local "real -world" evidence of the intervention's effects on outcomes and economic endpoints. Therefore, having the economic and health outcomes "real world evidence" (RWE) for the use of Humira in moderate RA patients from Korea will be valuable to support the reimbursement / pricing maintenance and expansion in Korea.

In Korea, Humira is reimbursed for both moderate and severe RA patients. However, the recent policy change in Korea indicated that the paradigm of using the ICER as the only value metric has been recently shifting toward considering other criteria such as patient reported outcomes, equity, innovation, and affordability. For example, the Korean government is in discussion with industry and academics to incorporate multi-criteria decision analysis (MCDA) such as including patient reported outcome into HTA for new medical technologies and post launch product price management. In this regard, generating the RWE is critical for the price re-negotiation and protection with the national payer, under current reimbursement and pricing policies in South Korea.

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 Korea.
The Humira's efficacy and patient's outcomes data from this study could be used to mitigate the tapering issues of biologics. The patients' work-productivity data aligned with global comparison could be used to keep the current co-payment ratio, 10% of patients. And aligned with T2T and fit for work data, we can pursue to expand the importance of early treatment of RA.

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. 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.

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 Korea 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.

RA patients will be recruited from within the clinical settings of each rheumatologist participating in the study. Approximately 89 patients diagnosed with RA that meet the inclusion and exclusion criteria will be enrolled at approximately 9 sites in Korea.

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

The patients identified by the recruiting investigators (specialty dependent on country/region; e.g. rheumatologist, internists, general practitioners, etc.) based on the study selection criteria will complete a set of patient questionnaires on QoL, functioning, work productivity, treatment satisfaction, impression of change and HCRU. Data will be captured at baseline (D0), Week 12 and Week 24.

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 countries.

Subjects may discontinue adalimumab treatment at any time during study participation. Subjects that end study participation early will have a Termination Visit. All subjects will have a follow-up phone call approximately 70 days after the last administration of adalimumab to obtain information on any new or ongoing AEs.
This protocol requires all SAEs and AESIs as outlined in protocol section 11.0 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.

As this is a postmarketing observational study, Abbvie is NOT involved in the product supply since the drug is being used according to the approved market label and is to be prescribed by the physician under usual and customary practice of physician prescription. This study is non-interventional and the subjects/investigator will follow the current clinical practice in each site. Not additional task will be required other than current practice to keep the data as “real world data collect.

Primary Endpoint
Change in HAQ DI score at 24 weeks after the initiation of adalimumab(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
- 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 (observed population).

Additional Secondary Endpoint Analysis
- Change in HAQ DI score at 24 weeks after the initiation of adalimumab (observed population), compared with those patients not continuing on adalimumab (non-observeds). 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)
- Associations between disease severity and PROs
- Associations between change in disease severity and change in PROs

- 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 (observed population). These changes will be summarized as the means and 95% confidence intervals and will be tested with paired t-tests.
- Change in patient satisfaction questions at weeks 12 and 24 after the initiation of adalimumab (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 analysed over time with Cochrane-Armitage test for trends.

All instruments used in the study are translationally validated for the country language.

9.1.1 Schedule of Events

Table 1 Study Activities (Day 1/Baseline Through 6 months)

	Study Activity	Baseline[a]	Week 12 (V2) ± 7 days	Week 24 (V3) ± 7 days	Early Termination / Drop out
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
Adverse events (including malignancy)		X	X	X	X

a. The Baseline visit date will serve as the reference for all subsequent visits. A ± 7 day window is permitted around scheduled study visits.

9.2 Setting

The study will take place in single country (Korea) 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 89 subjects with clinically diagnosed RA are planned to be enrolled in the study at up to 9 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.

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 $\geq$ 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

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

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 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 Section11.0).

9.2.4.1 Informed Consent

In local languages 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.

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

X	X	–	X	X	X
Site ID			Patient ID		

9.2.4.3 Investigator Recruitment

AbbVie will provide 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. This study is non-interventional and the subjects/investigator will follow the current clinical practice in each site. Not additional task will be required other than current practice to keep the data as "real world data collect.

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. The patient then will complete the study questionnaires in paper form. At all follow up visits (week 12 and 24), the patient will complete the study questionnaires while waiting for their appointment at their clinic, approximately 30 minutes before they visit their physicians. It is important that they complete the questionnaires prior to speaking with their clinician during the visit, as the clinician feedback might impact patient perceptions measured by the PRO instruments.

Patients must complete the survey by themselves without help from anyone. However, for patients who physically have difficulty filling out the questionnaires, help is allowed as long as there are no suggestions or discussion from the helpers
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 filled in by the patient and physician will be collected 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. Take blood to measure the erythrocyte sedimentation rate (ESR) or C reactive protein (CRP); the latest measurement in the medical records may also be used if a blood draw is not standard for that visit
4. Ask the patient to make a 'global assessment of health' 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 http://www.das-score.nl/das28/DAScalculators/dasculators.html).

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.

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.

All of the questionnaires will use the validated Korean version.

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.

9.3 Variables

Variables:
Primary Variable

- Change in HAQ DI score at weeks 12 and weeks 24 weeks from the 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 patient satisfaction questions from baseline to weeks 12 and 24

- 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

Additional Secondary Variable

- Change in HAQ DI score from baseline to 24 weeks
- Changes in the disease severity and PROs from baseline to 24 weeks

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 89 patients diagnosed with RA will be recruited. The sample size was calculated by assuming an alpha of 0.05 and a power of 0.80 in a one-sided test, Z (1-alpha) = 1.645 and Z (1-β) = 0.842. As to the primary variable, assuming a mean ΔHAQ-DI of -0.21 and a standard deviation (SD) of 0.5, according to the formula, 36 subjects are required. Then, given the importance of the secondary endpoint (WPAI), an improvement of 9.9±25 hours of work time lost (mean=9.9, SD=25) requires 40 subjects. However, we assume a 50% employment rate in the study population and a drop-out rate of 10%, eventually approximately 89 patients will be required (40/0.5/(1-0.1) = 89).

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 principle investigator or his/her designees 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 shared 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. The main analysis will be conducted on the pooled population, where appropriate, with each individual country analyzed separately as supportive data.

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 (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.

The primary 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 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 analysis 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 (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 (observed population).

9.7.6 Additional Secondary Endpoint Analysis

Additional efficacy analysis includes:

- Change in HAQ DI score at 24 weeks after the initiation of adalimumab, in those patients continuing on adalimumab, compared with those patients not continuing on adalimumab. 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)
- Associations between disease severity and PROs
- Associations between change in disease severity and change in PROs

Exploratory endpoint
Change in patient satisfaction questions at weeks 12 and 24 after the initiation of adalimumab (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.

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.

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 (LSLV).

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/device after it is released for distribution.

The investigational product in this trial contains both:

- Biologic compound(s) and
- Device component(s) (pre-filled syringe, pen).

Complaints associated with any component of this investigational product must be reported to the Sponsor (Section 11.2.2). For adverse events, please refer to Sections 11.1.1 through11.1.6. For product complaints, please refer to Section 11.2

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.

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 Serious Adverse Event Collection Period

Serious 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 30 days or 5 half-lives following the intake of the last dose of physician-prescribed treatment.

11.1.5 Serious Adverse Event Reporting

In the event of a serious adverse event, the physician will:

- For events from patients using and AbbVie product - notify the AbbVie contact person identified below within 24 hours of the physician becoming aware of the event.

[redacted]

11.1.6 Pregnancy Reporting

In the event of a pregnancy occurrence in the patient, the physician will notify AbbVie contact person identified in Section 11.1.5 within 24 hours of the physician becoming aware of the pregnancy.

11.1.7 Malignancy Reporting

In the event of any non-serious event of malignancy in subjects 30 years of age and younger, whether related to adalimumab or not, the investigator will notify AbbVie Emergency contact person identified at the beginning of the protocol within 24 hours of the site being made aware of the event.
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. A detailed discussion of the pre-clinical toxicology, metabolism, pharmacology and safety experience with adalimumab can be found in the current Investigator's Brochure. 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 11.7 under Malignancy Reporting.

11.2 Product Complaint

11.2.1 Definition

A Product Complaint is any Complaint (see Section 11.0 for the definition) related to the biologic or drug component of the product or to the medical device component(s).

For a product this may include, but is not limited to, damaged/broken product or packaging, product appearance whose color/markings do not match the labeling, labeling discrepancies/inadequacies in the labeling/instructions (example: printing illegible), missing components/product, device not working properly, or packaging issues.

For medical devices, a product complaint also includes all deaths of a patient using the device, any illness, injury, or adverse event in the proximity of the device, an adverse event that could be a result of using the device, any event needing medical or surgical intervention including hospitalization while using the device and use errors.

Any information available to help in the determination of causality by the device to the events outlined directly above should be captured.

11.2.2 Reporting

Product Complaints concerning the investigational product and/or device must be reported to the Sponsor within 24 hours of the study site's knowledge of the event via local Product Complaint reporting practices. Product Complaints occurring during the study will be followed-up to a satisfactory conclusion. All follow-up information is to be reported to the Sponsor (or an authorized representative) and documented in source as required by the

Sponsor. Product Complaints associated with adverse events will be reported in the study summary. All other complaints will be monitored on an ongoing basis.

Product complaints involving a non-Sponsor investigational product and/or device should be reported to the identified contact or manufacturer, as necessary per local regulations.

Product Complaints may require return of the product with the alleged complaint condition (syringe, pen, etc.). In instances where a return is requested, every effort should be made by the investigator to return the product within 30 days. If returns cannot be accommodated within 30 days, the site will need to provide justification and an estimated date of return.

The description of the complaint is important for AbbVie in order to enable AbbVie to investigate and determine if any corrective actions are required.

12.0 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 Korea. 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 Specialist 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 each country.

13.0 Confidentiality

13.1 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.

13.2 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.

14.0 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.

15.0 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.

16.0 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.

17.0 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 as follows :

- SAE : reported to Abbvie within 24 hours of physician awareness

- Non-serious AE : reported to Abbvie within 24 hours of PMOS physician awareness.

18.0 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.

19.0 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.

20.0 References

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21.0 Appedndices

Appendix A. Patient Informed Consent Form (ICF)

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: IMS Japan K.K. **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：**

1023259 Informed Consent Form (EN) v3_0 1

1023259 Real-World Impact of RA

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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.

1023259 Real-World Impact of RA

		-			
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.

1023259 Real-World Impact of RA

		-			
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

imshealth
INTELLIGENCE APPLIED

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:

1023259 Real-World Impact of RA

Site number | Participant ID

imshealth INTELLIGENCE APPLIED.

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

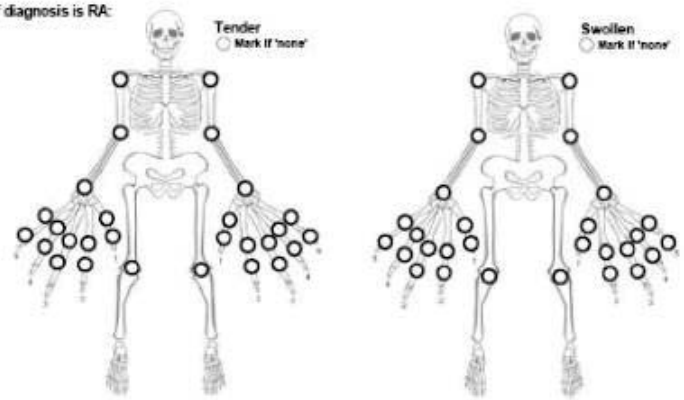
Please provide the information below.	
1. When was the patient diagnosed with Rheumatoid Arthritis?	Year
2. What is the patient's current disease status?	▫ Moderate ▫ Severe

1023259 Clinician Case Report Form (Baseline) v9_0 1

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

imshealth
INTELLIGENCE APPLIED.

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 Clinician Case Report Form (Baseline) v9_0 2

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

imshealth™ INTELLIGENCE APPLIED.

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

1023259 Real-World Impact of RA

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Site number			Participant ID		

imshealth
INTELLIGENCE APPLIED.

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		

imshealth™ INTELLIGENCE APPLIED.

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		

imshealth™ INTELLIGENCE APPLIED.

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		

imshealth
INTELLIGENCE APPLIED.

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.

Follow-up:

1023259 Real-World Impact of RA

Site number | Participant ID

imshealth INTELLIGENCE APPLIED.

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 #)

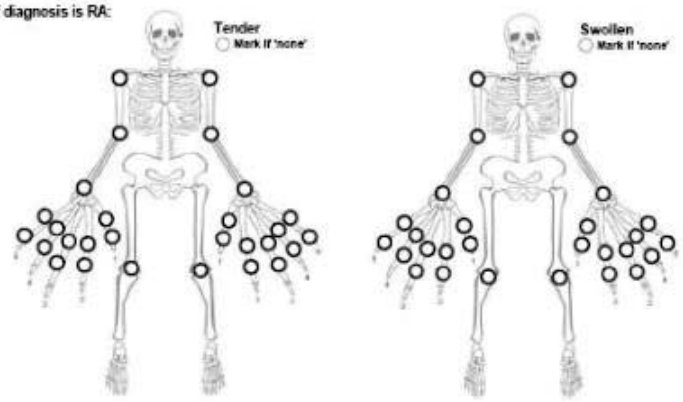
Today's date: ☐☐ / ☐☐ / ☐☐☐☐ (Day / Month / Year)

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		

imshealth
INTELLIGENCE APPLIED.

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		

imshealth™ INTELLIGENCE APPLIED.

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		

imshealth™ INTELLIGENCE APPLIED.

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)	

1023259 Real-World Impact of RA

		-			

Site number Participant ID

imshealth™ INTELLIGENCE APPLIED.

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.

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

SAMPLE

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

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(SF-36v2 Standard, US Version 2.0)

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

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(SF-36v2 Standard, US Version 2.0)

SAMPLE

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

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SAMPLE

6. **During the <u>past 4 weeks</u>, 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 <u>bodily</u> pain have you had during the <u>past 4 weeks</u>?**

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

8. **During the <u>past 4 weeks</u>, how much did <u>pain</u> 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

SAMPLE

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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

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SAMPLE

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!

SAMPLE

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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

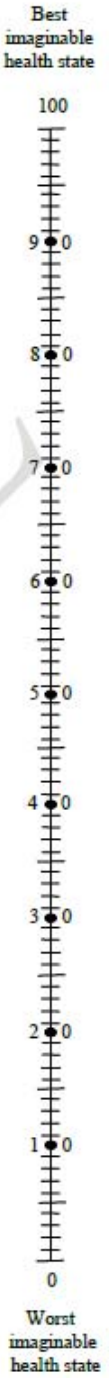
- I am not anxious or depressed ❑
- I am moderately anxious or depressed ❑
- I am extremely anxious or depressed ❑

SAMPLE

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



SAMPLE

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

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

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

imshealth™ INTELLIGENCE APPLIED.

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 IMS representative.

Appendix J. Healthcare resource utilization (HCRU) questionnaire

Baseline:

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

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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.**

1023259 HCRU Questionnaire (Baseline) v6_0 1

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

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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

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

imshealth™ INTELLIGENCE APPLIED.

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

1023259 HCRU Questionnaire (Baseline) v6_0 3

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

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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.

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

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INTELLIGENCE APPLIED.

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	_____

1023259 Real-World Impact of RA

		-			

Site number Participant ID

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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	_____

1023259 HCRU Questionnaire (Baseline) v8_0 6

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

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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	_____

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

imshealth INTELLIGENCE APPLIED

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

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

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INTELLIGENCE APPLIED.

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

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

imshealth™ INTELLIGENCE APPLIED.

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

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

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INTELLIGENCE APPLIED

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: _____

1023259 Real-World Impact of RA

		-			

Site number Participant ID

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INTELLIGENCE APPLIED

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: _____

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

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INTELLIGENCE APPLIED

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 HCRU Questionnaire (Baseline) v8_0 13

1023259 Real-World Impact of RA

		-			

Site number Participant ID

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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		

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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		

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INTELLIGENCE APPLIED

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

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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		

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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

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INTELLIGENCE APPLIED

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 HCRU Questionnaire (Follow-up) v8_0 5

1023259 Real-World Impact of RA

		-			

Site number Participant ID

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INTELLIGENCE APPLIED

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) v6_0 6

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

imshealth™
INTELLIGENCE APPLIED

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

imshealth™ INTELLIGENCE APPLIED.

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 IMS representative.

Appendix K. Early Termination Form

For Physician:

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

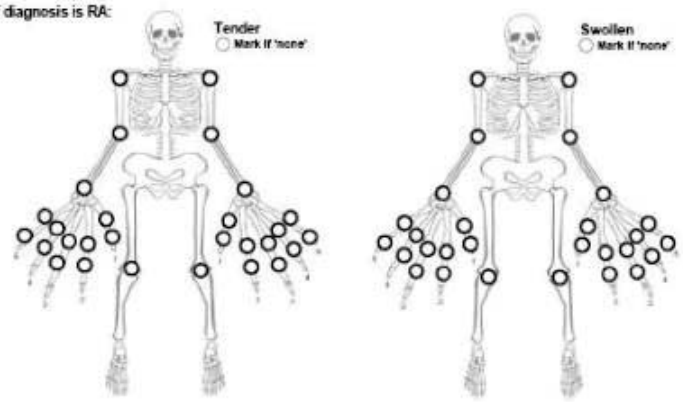
Please provide the information below.	
1. What is the patient's current disease status?	☐ Moderate ☐ Severe

1023259 Early Termination Form (Physician) v4_0 1

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

imshealth
INTELLIGENCE APPLIED.

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 Early Termination Form (Physician) v4_0 2

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

imshealth™ INTELLIGENCE APPLIED.

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		

imshealth
INTELLIGENCE APPLIED.

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** _____mg	**Number of Times** _____
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

imshealth INTELLIGENCE APPLIED.

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 IMS representative.

For Patient:

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

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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		

imshealth
INTELLIGENCE APPLIED.

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

imshealth INTELLIGENCE APPLIED.

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 Early Termination Form (Patient) v5_0 3

1023259 Real-World Impact of RA

		-			
Site number			Participant ID		

imshealth INTELLIGENCE APPLIED

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		

imshealth
INTELLIGENCE APPLIED.

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

imshealth INTELLIGENCE APPLIED.

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		

imshealth™ INTELLIGENCE APPLIED.

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		

imshealth INTELLIGENCE APPLIED

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 IMS representative.

Appendix L. Amendment 01 Changes

Summary of Amendment changes:

- Change of sample size
- Change of milestones

Section 4.0 Abstract

Previously read:

Study Design
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 9 sites in Korea.

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.

Study Size
Approximately 100 patients diagnosed with RA that meet the inclusion and exclusion criteria will be enrolled at approximately 9 sites in Korea. The sample size was calculated by assuming an alpha of 0.05 and a power of 0.80 in a two-sided test, resulting in 52 subjects required to recognize a statistically significant improvement in HAQ DI (-0.21). Given the importance of other secondary endpoints, an improvement of 9.9±25 hours of work time lost requires 58 subjects, assuming an alpha of 0.05 and a power of 0.80 in a two-sided test. However, since it is expected that approximately half the study population may no longer be working due to their age, approximately twice this number (100 patients) will be required to achieve the required number of respondents. We have also assumed a drop-out rate of 13% (assuming between 10%-15%).

Milestones
Start of Data Collection: 19 Oct, 2015
End of Data Collection: 31 Jan, 2017
Study Progress Report: Not applicable
Interim Report: Not applicable

Registration in the EU PASS Register: Not Applicable
Final Report of Study Results: 31 Jul, 2017

Has been changed to read:

Study Design
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 89 patients diagnosed with RA that meet the inclusion and exclusion criteria will be enrolled at approximately 9 sites in Korea.

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 89 patients diagnosed with RA will be recruited.

Study Size
Approximately 89 patients diagnosed with RA that meet the inclusion and exclusion criteria will be enrolled at approximately 9 sites in Korea. The sample size was calculated by assuming an alpha of 0.05 and a power of 0.80 in a one-sided test, resulting in 36 subjects required to recognize a statistically significant improvement in HAQ DI (-0.21). Then, given the importance of other secondary endpoints, an improvement of 9.9±25 hours of work time lost requires 40 subjects. However, since it is expected that approximately half the study population may no longer be working due to their age, we assume a 50% employment rate in the study population and a drop-out rate of 10%, eventually approximately 89 patients will be required to achieve the required number of respondents.

Milestones
Start of Data Collection: 19 Oct, 2015
End of Data Collection: 28 Feb, 2018
Study Progress Report: Not applicable
Interim Report: Not applicable
Registration in the EU PASS Register: Not Applicable
Final Report of Study Results: 31 Aug, 2018

Section 6.0 Milestones

Previously read:
Major study milestones and their planned dates are as follows:
Start of Data Collection (FPFV): 19 October 2015
End of Data Collection: 31 January 2017
Study Progress Report: Not Applicable
Interim Report: Not Applicable
Registration in the EU PAS register: Not Applicable
Final Report of Study Results: 31 July 2017

Has been changed to read:
Major study milestones and their planned dates are as follows:
Start of Data Collection (FPFV): 19 October 2015
End of Data Collection: 28 February 2018
Study Progress Report: Not Applicable
Interim Report: Not Applicable
Registration in the EU PAS register: Not Applicable
Final Report of Study Results: 31 August 2018

Section 9.1 Study Design

Previously read:
Approximately 100 patients diagnosed with RA that meet the inclusion and exclusion criteria will be enrolled at approximately 9 sites in Korea.

Has been changed to read:
Approximately 89 patients diagnosed with RA that meet the inclusion and exclusion criteria will be enrolled at approximately 9 sites in Korea.

Section 9.2 Setting

Previously read:
Overall, approximately 100 subjects with clinically diagnosed RA are planned to be enrolled in the study at up to 9 sites.

Has been changed to read:
Overall, approximately 89 subjects with clinically diagnosed RA are planned to be enrolled in the study at up to 9 sites.

Section 9.5 Study Size

Previously read:
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.

Has been changed to read:
Approximately 89 patients diagnosed with RA will be recruited. The sample size was calculated by assuming an alpha of 0.05 and a power of 0.80 in a one-sided test, Z (1-alpha) = 1.645 and Z (1-β) = 0.842. As to the primary variable, assuming a mean ΔHAQ-DI of -0.21 and a standard deviation (SD) of 0.5, according to the formula, 36 subjects are required. Then, given the importance of the secondary endpoint (WPAI), an improvement of 9.9±25 hours of work time lost (mean=9.9, SD=25) requires 40 subjects. However, we assume a 50% employment rate in the study population and a drop-out rate of 10%, eventually approximately 89 patients will be required (40/0.5/(1-0.1) = 89).

AbbVie Inc. (AbbVie)

Post Marketing Observational Study

P15-777 Protocol

Real-World Outcome of Rheumatoid Arthritis Patients in Korea on Adalimumab
(ROCKA Study)

Amendment 01

Approved by:

[redacted]

05 Mar 2018
Date

5 Mar 2018
Date

3 Mar 2018
Date

Apr 12th, 2018
Date