

STATISTICAL ANALYSIS PLAN

NCT Number: NCT04873700

Study Title: Real-world Data of Moderate to Severe Inflammatory Bowel Disease (UC and CD) in Mexico: a Multicenter, Non-interventional Study to Evaluate Disease Control, Treatment Patterns, Burden of Disease and Patient Reported Outcomes

Study Number: IBD-5010

SAP Version and Date:

Version 2.0: 08-June-2022

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Takeda Mexico S.A. de C.V.

Protocol #: IBD-5010

**Real World data of Moderate to Severe Inflammatory Bowel Disease (UC and CD)
in Mexico: a multicenter, non-interventional study to evaluate disease control,
treatment patterns, burden of disease and patient reported outcomes (RISE-MX)**

Statistical Analysis Plan (SAP)

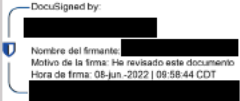

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03-Jun-2022

Corresponding to:

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Database lock	17-Jun-2022



1.0 Approvals

Sponsor	
Sponsor Name:	Takeda Mexico S.A de C.V.
Representative/ Title:	[REDACTED] / Clinical Operations [REDACTED]
Signature /Date:	<div>  <p>DocuSigned by: [REDACTED] Nombre del firmante: [REDACTED] Motivo de la firma: He revisado este documento. Hora de firma: 08-Jun-2022 08:58:44 CDT</p> </div>
ICON plc	
Biostatistician / Title:	[REDACTED], M.S. / [REDACTED]
Signature /Date:	<div>  <p>Signed by: [REDACTED] Reason: I am approving this document. Date & Time: 08 Jun 2022 10:23 AM -04:00</p> </div>

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3.0 Change History

Version / Date	Change Log
0.1 / 05-Nov-2021	First draft to Sponsor.
0.2 / 21-Dec-2021	Second draft to Sponsor (addresses comments received on first draft)
1.0 / 28-Jan-2022	Stable draft to Sponsor (addresses comments received on SAP V0.2)
1.1 / 29-Apr-2022	<p>Section 11.2: Years smoked as recorded on CRF (not derived).</p> <p>Section 12.1: Clarified definition of duration of disease.</p> <p>Section 12.3: Updated to report EIM for both CD and UC patients (not just UC).</p> <p>Section 12.4: Updated list of predictors for logistic regression based on comments received for dry-run TFLs.</p> <p>Section 13.2: Updated to include summaries on treatment combinations.</p> <p>Section 15.0: Corrected SF-36 questionnaire to V2 (not V1). To enable computation of IBDQ domains, clarified that qualitative responses will be converted to numeric as per choices printed on questionnaire</p> <p>Appendix 1: Deleted, as SF-36 V2 scoring is performed in Optum® software.</p> <p>Appendix 2: Appropriate parentheses added in algorithms for absenteeism, and absenteeism + presenteeism.</p>
2.0 / 03-Jun-2022	<p>Section 12.4: Included "Unknown" response values in the education level category of "Secondary school or less".</p> <p>Section 17.0: Included information about direct and indirect cost analysis.</p>

4.0 List of Abbreviations

Abbreviation	Definition
AE	Adverse event
BMI	Body Mass Index
CD	Crohn's Disease
CDAI	Crohn's Disease Activity Index
CI	Confidence Interval
CRF	Case Report Form
EIM	Extraintestinal Manifestation
HBI	Harvey-Bradshaw Index
IBD	Inflammatory Bowel Disease
IBDQ	Inflammatory Bowel Disease Questionnaire
ME	Margin of Error
MedDRA	Medical dictionary for regulatory affairs
PRO	Patient Reported Outcome
PT	Preferred term
QoL	Quality of Life
SAP	Statistical Analysis Plan
SF-36	36-item Short Form Health Survey
SOC	System organ class
TFLs	Tables, Figures, and Listings
UC	Ulcerative Colitis
WPAI	Work Productivity and Activity Impairment questionnaire

5.0 Introduction

This Statistical Analysis Plan (SAP) presents details of the statistical methods used for analyses and reporting of data collected under Takeda Mexico S.A de C.V. study Protocol number [IBD-5010](#). It should be read in conjunction with the study Protocol and Case Report Forms (CRFs), as any changes to these may necessitate updates to the SAP.

Protocol [IBD-5010](#) is a non-interventional study with a purpose to assess disease characteristics of patients in Mexico diagnosed with moderate to severe inflammatory bowel disease (IBD) as presented in form of Crohn's disease (CD) or Ulcerative Colitis (UC). Additionally, it aims to understand how patients are managed, treatment patterns employed (particularly with respect to available biologic therapies) and obtain patients' perspective on how the disease impacts their quality of life (QoL) and work productivity.

This SAP has been developed and approved prior to database lock and data analysis. All analyses will be conducted after clinical data are entered in the database, discrepancies resolved, and the database is locked to further changes.

Production and quality control of statistical analyses and accompanying Tables, Figures, and Listings (TFLs) for this study will be the responsibility of ICON plc, located in Blue Bell, Pennsylvania, United States.

6.0 Protocol Objectives and Estimands

The Protocol lists the following primary and secondary objectives of the study. Details on the attributes of estimands can be found in relevant sections to follow in this Plan.

Objective	Estimand
Primary:	
• To evaluate disease activity at Day 1 among UC and CD patients diagnosed with moderate to severe disease.	<ul style="list-style-type: none"> - Proportion of UC patients with active disease (defined as 9-point partial Mayo score ≥ 5) at Day 1. - Proportion of CD patients with active disease (defined as Harvey Bradshaw Index (HBI) score ≥ 8 or Crohn's Disease Activity Index (CDAI) ≥ 220) at Day 1.
Secondary:	
1. To characterize socio-demographic and clinical features of UC and CD patients, overall and by disease activity at Day 1.	<ul style="list-style-type: none"> - Distribution of socio-demographic and clinical characteristics in UC patients with moderate/severe versus mild/no disease activity at Day 1 - Distribution of socio-demographic and clinical characteristics in CD patients with moderate/severe versus mild/no disease activity at Day 1.
2. For UC and CD, to compare patients with moderate to severe disease activity with no or mild activity, regarding socio-demographic and clinical variables and treatment patterns at Day 1.	<ul style="list-style-type: none"> - Distribution of clinical features and treatment patterns at Day 1 in UC patients with moderate/severe versus mild/no disease activity . - Distribution of clinical features and treatment patterns at Day 1 in CD patients with moderate/severe versus mild/no disease activity.
3. To characterize treatment patterns for UC and CD in the 3 year prior to Day 1, including use of biologic and conventional therapies and failure to these therapies (if any), overall and by disease activity at Day 1.	<ul style="list-style-type: none"> - By disease activity at Day 1 (moderate/severe or mild/none), distribution of treatments utilized in past 3 years by UC patients. - By disease activity at Day 1 (moderate/severe or mild/none), distribution of treatments employed in past 3 years by CD patients.
4. To evaluate QoL in UC and CD patients, overall and by disease activity at Day 1.	<ul style="list-style-type: none"> - Mean scores of all measured dimensions of 36-item Short Form Survey (SF-36) overall and by disease activity at Day 1 for UC and CD patients.

	- Mean total and individual domain scores as assessed by Inflammatory Bowel Disease Questionnaire (IBDQ) in UC and CD patients by disease activity at Day 1.
5. To evaluate work productivity and activity impairment experienced by UC and CD patients, overall and by disease activity at Day 1.	<ul style="list-style-type: none"> - Mean total percentage of work productivity and activity impairment (WPAI), in hours, for patients with moderate to severe activity compared with patients with no or mild activity. - Mean work time missed (WPAI), in hours, for patients with moderate to severe activity compared with patients with no or mild activity. - Mean productivity impairment while working (WPAI), in hours, for patients with moderate to severe activity compared with patients with no or mild activity. - Mean total activity impairment (WPAI). - Proportion of patients who quit their job due to IBD (UC or CD) and have not been able to return to work.
6. To describe burden of disease in terms of healthcare resources utilization and costs (direct and indirect) related to management of UC and CD in 3 years prior to Day 1.	- Distribution of surgeries, hospitalizations, medical appointments, imaging and laboratory testing in the 3 years prior to Day 1.

7.0 Study Design

This is a multicenter, non-interventional, cross-sectional study aiming primarily to descriptively evaluate CD and UC activity in IBD patients in Mexico.

Over a period of six months, approximately 10 - 12 sites across the country that follow CD and UC patients in ambulatory care will identify patients consecutively as they attend routine clinical appointments with their physician.

On the day of the appointment (Day 1), written informed consent will be obtained from patients who meet all eligibility criteria and data collection will include cross-sectional evaluation as well as a retrospective chart review.

[Figure 1](#) illustrates the study design scheme.

Cross-sectional data regarding demographics, disease activity, and treatment started will be collected from medical records and patients will be asked to complete the QoL instruments (SF-36 and IBDQ), and work productivity questionnaire (WPAI).

Additional retrospective data will be harvested from 3 years prior referring to previous IBD (CD and UC) treatments (drug, dose, treatment duration, and drug changes), medical history and comorbidities, and healthcare resources utilization (surgeries, hospitalizations, medical appointments, laboratory and imaging tests).

Due to the observational nature of the study, no impact is expected on the subjects except for collection of informed consent and patient-reported outcome (PRO) tools, and use of historical data. The usual care provided to the subjects should remain unchanged.

Start of the study will be marked by the date of last Protocol signature, followed by a recruitment period of at least 6 months, and the end defined as the date of collection of the last data point for the last patient enrolled.

This study design with no control group is deemed suitable and feasible to address the descriptive objectives of the study.

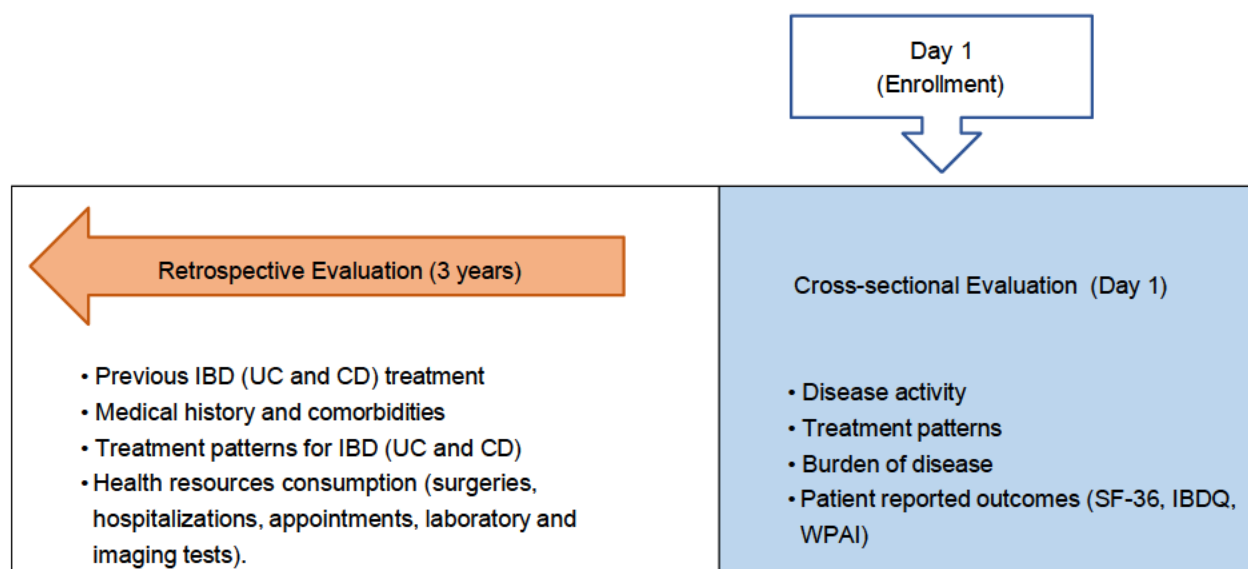


Figure 1: Study Design Scheme

7.1 Study Population

A total of approximately 335 patients who meet all inclusion criteria will be enrolled at participating sites in Mexico. Patients will be male or female, at least 18 years of age, and been diagnosed with moderate to severe CD or UC at least six months prior to Day 1 appointment.

7.2 Sample Size Considerations

Approximately 335 patients regardless of IBD type (CD or CD) will be enrolled from 10 – 12 public/private reference hospitals from regions of Mexico.

Since there is no information available regarding the rate of CD and UC control in the country, this sample size makes a reasonable assumption of uncontrolled disease rate (p) of 50% in the population and a margin of error (ME) of less than 5.5%.

The following formula was used:

$$1.96^2 \times p \times (1 - p) / ME^2$$

$$1.96^2 \times 0.5 \times (1 - 0.5) / 0.055^2$$

$$= 317.35$$

An additional 17 patients would be required to account for a non-evaluable rate of 5%, increasing the total sample size to 335.

7.3 Population Sets

All patients who provide written informed consent and fulfill the study eligibility criteria will comprise the Enrolled Population Set and their data used for purposes of all analyses.

Patients for whom written consent is not available will not be included or deleted from the database. If erroneously, a patient is included in the study more than once, only the data relating to the first inclusion will be retained and available for analysis.

8.0 General Analytical Considerations

8.1 Study Visits

Study Day 1 will be the date of patient's routine clinical appointment with their physician.

8.2 Missing Data

Although retrospective data collection is susceptible to the quality of medical records, it is expected that treatment patterns and hospitalization will be recorded without significant missingness. Unless stated otherwise in sections below, missing data will not be replaced with imputed values.

8.3 Data Display Characteristics

Data displays produced for this study will include presentations in the form of summary tables, figures (as needed), and listings.

Unless stated otherwise, by-patient data listings will be produced for all recorded data. Data listings will simply list the data recorded on the CRF or derived for each patient. They will be ordered by IBD type (CD or UC) and date and time of assessment, where applicable. When expedient, additional levels of hierarchy may reflect subsets of assessments within subject.

Summary tables will be based on the Enrolled Population Set and presented either by IBD type (CD or UC) and overall, or stratified by disease activity at Day 1 for CD and UC (i.e., moderate/severe or mild/no activity). Statistics displayed will be a function of the type of data associated with the summarized assessment. That is, continuous measures will be summarized with the number of non-missing values, mean, standard deviation, median, first and third quartiles, minimum and maximum values. Categorical data will be summarized with frequencies and corresponding percentages.

Where applicable, P-values from standard statistical tests for two-group comparisons (t-test or its non-parametric analog, Mann-Whitney if a continuous variable is not normally distributed; chi-square or Fisher's exact test if expected cell counts are less than 5 for categorical variables) with two-sided significance and a Type 1 error rate of 0.05 will be reported in summary tables.

All programming code and analysis outputs will be generated using SAS/STAT and SAS/GRAPH software, version 9.4 or higher of the SAS system for Windows. Copyright © [2013] SAS Institute Inc. SAS and all other SAS Institute Inc. product or service names are registered trademarks or trademarks of SAS Institute Inc., Cary, NC, USA.

9.0 Interim Analysis

No interim analysis is planned for this study.

10.0 Patient Disposition

A listing will be provided for all patients who provide informed consent for the study. Protocol version under which consent was obtained, whether all admission criteria were met, and date of study Day 1 will be included.

10.1 Protocol Deviations

A listing will be provided for all protocol deviations.

11.0 Patient Characteristics

The study population will be described by disease activity at Day 1 for CD and UC patients using the following socio-demographic (**Secondary Objective 1**), anthropometric, and medical history characteristics.

11.1 Socio-demographic and Anthropometrics

- Age: calculated as number of years elapsed between birth date and date of Day 1 visit.
- Sex
- Professional status
- Number of patients who quit their job due to IBD and have not been able to return to work.
- Education level
- Patient income
- Height (cm)
- Weight (kg)
- BMI (kg/m²)

11.2 Medical History

- Smoking Habits: Patient use of tobacco (never, current, former), start date, type of substance (cigarettes, cigars, smokeless tobacco, pipes), years smoked, amount and frequency use will be listed. A summary table will present these characteristics by disease activity at Day 1 for CD and UC patients.
- Family History of IBD: Whether a relevant family history of IBD (CD or UC) exists in parents, siblings or children, and relationship to patient, will be noted in a listing. By disease activity at Day 1, this information will also be summarized for CD and UC patients.
- Medical History/Comorbidities: A listing will display all entries for relevant patient medical history (other than IBD), comorbidities or extraintestinal manifestations (EIM), with specific condition(s), start/end dates, whether ongoing, treated, and treatment name. CD and UC patients reporting at least one relevant medical history event will be summarized by disease activity at Day 1, including total number of conditions per patient.

12.0 Disease Status

Disease status of study patients will be assessed at Day 1 and results reported in data listings and summary tables as follows:

12.1 IBD Type

For each patient, IBD type (CD or UC), date of diagnosis, criteria for diagnosing moderate to severe CD or UC, age at diagnosis, and objective criteria considered for diagnosis will be listed. Information on steroid behavior at Day 1 (steroid-dependent, steroid refractory disease, unclassified use) will also be presented.

Separately for CD and UC, these characteristics will be summarized for patients with moderate/severe activity at Day 1 versus those with mild/no activity.

Duration of disease, in months, will be derived as the difference between date of diagnosis of CD or UC and Day 1 visit date / 30.5.

P-values for formal two-group comparisons will be reported.

12.2 Disease Activity at Day 1

Disease activity at Day 1 will be determined on the basis of HBI or CDAI scores for CD patients and partial Mayo score for UC patients. Patient responses to individual items as well as overall scores will be included in data listings.

A summary table will present the proportion of CD and UC patients by disease activity at Day 1 (**Primary Objective**), determined as follows:



IBD Type	Day 1 Disease Activity	
	Moderate/Severe	Mild/No
Crohn's disease	HBI \geq 8 or CDAI \geq 220	HBI $<$ 8 or CDAI $<$ 220
Ulcerative colitis	Partial Mayo \geq 5	Partial Mayo $<$ 5

The percentage of patients with active disease will be calculated as:

$$(\text{CD patients with HBI } \geq 8 \text{ or CDAI } \geq 220 / \text{Total CD patients}) * 100$$

$$(\text{UC patients with partial Mayo score } \geq 5 / \text{Total UC patients}) * 100$$

For both groups of patients, 95% confidence intervals for binomial proportions will be reported using the Wald method.

12.3 Clinical Characteristics of IBD

Location of disease, disease behavior, perianal or ileal disease, and EIM (for CD), and location of disease, disease behavior, and EIM (for UC) will be included in data listings. CD and UC patient subgroups of moderate/severe versus mild/no activity will be compared on these characteristics (**Secondary Objectives 2, 3**) in a summary table, with P-values reported for group differences.

12.4 Risk Factors Associated with IBD

Multivariate logistic regression models will be constructed to ascertain if moderate/severe disease activity in CD and UC is significantly associated with certain patient and clinical characteristics. The following risk factors for the binary outcome of moderate/severe versus mild/no disease will be included in separate models for CD and UC:

- Age at diagnosis of moderate/severe disease (in years, categorized as < 30 , $30 - 50$, > 50).
- Sex (Female versus Male).
- Ever used tobacco (current or former versus never).
- Any relevant medical history (other than IBD) comorbidity or extra intestinal manifestation (No, Yes).
- Use of immunosuppressors treatment during retrospective period (categorized 'Yes' if a previous regimen included azathioprine, mercaptopurine, methotrexate, cyclosporine, or tacrolimus; otherwise 'No').
- Steroid behavior at Day 1 (no previous use, steroid-dependent, steroid-refractory disease, unknown or unclassified use).
- Education level (Higher education not completed or higher (including CRF categories "Higher education", "Higher education not completed", and "Post-graduate/MBA") versus secondary education or less (including CRF categories "Unknown", "Not literate", "Primary school", "Primary school not completed", "Secondary school" and "Secondary school not completed").
- Subject income (< 3 SM ($< \$12,753.00$), $3 - 5$ SM ($\$12,753.00 - \$21,255.00$), > 5 SM ($> \$21,255.00$)).

- Retrospective biologic IBD treatment which is ongoing (categorized 'Yes' if treatment included infliximab, adalimumab, vedolizumab, certolizumab, golimumab, or ustekimumab; otherwise 'No').
- First treatment after diagnosis of moderate to severe disease (categorized as Biologic therapy/ aminosaliucilates (including infliximab, adalimumab, vedolizumab, certolizumab, golimumab, ustekimumab, sulphassalazine, mesalazine, olsalazine or mesalazine extended release) or Other (including hydrocortisone, prednisone, prednisolone, budesonide, or methylprednisolone, azathioprine, mercaptopurine, methotrexate, cyclosporine, tacrolimus, metronidazole, ciprofloxacin, enteral nutrition or parenteral nutrition, other).

Regression models will be run on complete cases, i.e., where data are not missing for any of the above listed predictors and results reported as odds ratios (OR) with 95% confidence intervals (CI), and P-values.

13.0 Disease Treatment

Information on treatment patterns observed in the study population will be reported as described below:

13.1 First Treatment After Diagnosis

First treatment received after diagnosis of moderate/severe CD or UC, including treatment name, dose, route of administration, and frequency will be listed by IBD type (CD or UC) and overall.

13.2 Previous Treatments or Regimens

For CD and UC patients, all recorded information on IBD-related treatment regimens utilized in past three years, including, treatment name, start/end dates, whether ongoing, dose, frequency, and reason for discontinuation will be listed. For each IBD type (CD, UC), summary tables will be presented for patient subgroups of moderate/severe and mild/no activity at Day 1 (**Secondary Objective 3**). Individual treatment regimens checked on CRF will be summarized along with the number of patients who utilize the following combination therapies:

- Salicylic derivatives + immunosuppressants (sulphassalazine, mesalazine, olsalazine, mesalazine extended release, azathioprine, mercaptopurine, methotrexate, cyclosporine, or tacrolimus).
- Biologic therapy + immunosuppressants (infliximab, adalimumab, vedolizumab, certolizumab, golimumab, ustekimumab, azathioprine, mercaptopurine, methotrexate, cyclosporine, or tacrolimus)
- Salicylic derivatives + immunosuppressants + biologic therapy (any regimen noted in the above two categories).

13.3 Treatment Started at Day 1

A listing will be provided for patients who start treatment at Day 1 (Yes/No), name of treatment, date started, dose, route of administration, and frequency.

14.0 Safety Analysis

14.1 Adverse Events

Any AE that occurs on Day 1 visit for current or new treatments considered in medical strategy to treat the patient will be noted in CRF.



Verbatim terms used to document AEs will be coded using MedDRA version 21.1 (or the most current version available at time of last-patient-last-visit).

By IBD type, all AEs will be listed, including start and end date/time, whether ongoing, serious, severity, relationship to treatment, action taken, and if patient discontinued study due to the event. The listing will hierarchically display start date of the event, MedDRA system organ class (SOC) represented in the data, and within each SOC, each unique preferred term (PT).

AEs presented in listing will be tabulated by SOC and PT for CD and UC patients, as well as overall. At each level of summation (SOC, PT), patients reporting more than one AE will only be counted once.

14.2 Prior and Concomitant Medications

Any concomitant medications used by patients will be recorded on CRF. Indication for use, start and end date, ongoing, dose, frequency and route of administration will be noted.

Verbatim terms from CRF will be mapped to Anatomical/Therapeutic Chemical class and Generic drug names using the WHODRUG Global March 2021 B3 coding dictionary (or the most current version available at time of last-patient-last-visit). For each IBD type, a listing will display all entries for medications, ordered by start date, and present the anatomical main class (1st level) of each coded medication and within that the preferred term.

15.0 Health-Related Quality of Life and Work Productivity

Health-related quality of life and work productivity will be ascertained at Day 1 via three standard and validated instruments. Patients will complete the [SF-36](#), [IBDQ](#) and [WPAI:GH](#) during their routine medical appointment.

SF-36 Version 2: A general health QoL questionnaire, this survey evaluates 8 health dimensions:

- Physical functioning
- Bodily pain
- Role physical (limitations due to physical problems)
- Role emotional (limitations due to personal/emotional problems)
- Mental health
- Social functioning
- Vitality
- General health

Raw data noted on CRF will be processed using the Optum® PRO CoRE scoring software and aggregate scores computed for the above mentioned eight domains (see Section 6.3.3 of Data Management Plan). Domain scores may range from 0 to 100, with higher scores denoting a more favorable health state.

Patient scores for each scale will be listed by IBD type. By disease activity at Day 1, CD and UC patients will be compared on all dimensions of the survey (**Secondary Objective 4**) and P-values reported for statistical significance.

Inflammatory Bowel Disease Questionnaire: A disease-specific questionnaire, IBDQ measures four dimensions:

- Bowel function
- Emotional status
- Systemic symptoms
- Social function

Within each dimension, each question presents seven possible points. Qualitative responses will be converted to numeric as per choices printed on questionnaire and score for each dimension calculated from sum of points for specific questions ([Appendix 1](#)). Hence, total scores can range from 32 to 224, with higher scores representing better QoL.

Patient responses to the four questionnaire dimensions and total score will be listed. Summary statistics will be provided for patient subgroups of moderate/severe versus mild/no disease activity for CD and UC (**Secondary Objective 4**) and P-values reported for group-comparisons.

Work Productivity and Activity Impairment Questionnaire (WPAI:GH) Version 3.0: Based on a recall period of past 7 days, the six items of this questionnaire will assess the impact of IBD on work productivity and daily activities. The following scores/components will be derived as per [\(Appendix 2\)](#).

- For currently employed patients:
 - ◊ Percentage of work time missed (absenteeism)
 - ◊ Percentage of impairment while working (presenteeism)
 - ◊ Total percentage of overall work impairment (absenteeism + presenteeism)
- For all patients:
 - ◊ Percentage of impairment in activities performed outside of work

Patient responses to the six items of the questionnaire will be listed by IBD type. Relevant item responses as well as the above derived components will be summarized by disease activity at Day 1 and P-values reported for comparison of moderate/severe versus mild/no activity patient subgroups.

16.0 Medical Resource Utilization

Healthcare resources utilized in past three years will be listed by IBD type and summarized by disease activity at Day 1 (**Secondary Objective 6**) for the following events:

- Previous surgeries for IBD (date and name of procedure).
- IBD-related hospitalizations (type of visit, admission/discharge dates, number and total duration of emergency room visits/hospital admissions).
- Previous medical appointments related to IBD (date and type of appointment, total number of appointments and treatment changes).
- Previous calprotectin levels and colonoscopy (if available).
- Previous imaging, laboratory including PCR, and histology testing (if available).

17.0 Changes from Protocol

Direct and indirect cost analysis utilizing data from Mexican administrative databases or other sources will be conducted separately by Takeda Mexico S.A. de CV.

18.0 Appendices

18.1 Appendix 1 Inflammatory Bowel Disease Questionnaire scoring scheme

Scale	Sum of Items
Bowel function	1 5 9 13 17 20 22 24 26 29
Emotional status	3 7 11 15 19 21 23 25 27 30 31 32
Systemic symptoms	2 6 10 14 18
Social function	4 8 12 16 28

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18.2 Appendix 2 Work Productivity and Activity Impairment Questionnaire scoring scheme

Component	Derivation
Percentage of work time missed (absenteeism)	$(Q2 / (Q2 + Q4)) * 100$
Percentage of impairment while working (presenteeism)	$(Q5 / 10) * 100$
Total percentage of overall work impairment (absenteeism + presenteeism)	$Q2 / (Q2 + Q4) + [(1 - (Q2 / (Q2 + Q4))) * Q5 / 10] * 100$
Percentage of impairment in activities performed outside of work	$(Q6 / 10) * 100$

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19.0 References

1. PRA-408128-DFinal+Clean+V2.0_+22Sep20+Rise-Mx+protocol.pdf
2. [Ware JE, Kosinski M. SF-36 Physical and Mental Health Summary Scales: A Manual for Users of Version 1. 2nd ed. Lincoln, Rh Quality Metric Incorporated; 2001.](#)
3. <http://www.flintbox.com/public/project/641>
4. http://www.reillyassociates.net/WPAI_General.html

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Document Type: Approval of Documents by 3rd parties

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Información sobre confidencialidad de registros y firmas electrónicos:

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Eventos de firmante en persona**Firma****Fecha y hora****Eventos de entrega al editor****Estado****Fecha y hora****Eventos de entrega al agente****Estado****Fecha y hora****Eventos de entrega al intermediario****Estado****Fecha y hora****Eventos de entrega certificada****Estado****Fecha y hora****Eventos de copia de carbón****Estado****Fecha y hora****Eventos del testigo****Firma****Fecha y hora****Eventos de notario****Firma****Fecha y hora****Eventos de resumen de sobre****Estado****Marcas de tiempo**

Sobre enviado

Con hash/cifrado

08/06/2022 9:56:51

Certificado entregado

Seguridad comprobada

08/06/2022 9:57:44

Eventos de resumen de sobre	Estado	Marcas de tiempo
Firma completada	Seguridad comprobada	08/06/2022 9:59:05
Completado	Seguridad comprobada	08/06/2022 9:59:05
Eventos del pago	Estado	Marcas de tiempo

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