Statistical Analysis Plan

Sponsor:	Bristol-Myers Squibb Research and Development
Protocol No:	IM024 005
Protocol Title:	A Double-Blind Randomized Placebo-Controlled Single and Multiple Ascending Doses Study of the Safety and Tolerability, pharmacokinetics (Including Bioavailability Comparison and Food Effect) and Pharmacodynamics of Oral BMS-986251 Administration in Healthy Subjects, with Efficacy Assessment of Multiple Doses in Patients with Moderate-to-Severe Psoriasis
PRA Project ID:	BMS616EC-176161
Version Date:	23-Aug-2018

2.0 Table of Contents

3.0 Introduction

This Statistical Analysis Plan (SAP) describes the statistical methods that will be used during the analysis and reporting of data collected under Bristol-Myers Squibb Research and Development (BMS) Protocol IM024 005.

This SAP should be read in conjunction with the study protocol and electronic case report form (eCRF). This version of the plan has been developed using the final protocol version 1.0 dated 21-Sep-2017 (including all amendments up to this protocol date) and the final eCRF(s) dated 12-Feb-2018 (single ascending dose [SAD]) and 01-Jun-2018 (multiple ascending dose [MAD]).

An approved and signed SAP is a requirement for database lock. An approved SAP is also required for unblinding of the study treatments.

This SAP only covers the results that will be processed by the PRA Early Development Services (EDS) Biostatistics Department.

PRA EDS will perform the pharmacokinetic (PK), pharmacodynamic (PD), and safety and tolerability evaluation.

This SAP was written after the clinical study was terminated due to non-clinical findings. The study was stopped after completion of Part A, Cohorts A1 – A4 and during dosing of the cohort A5 and the first cohort of Part B, B1. Cohort A6 and bioavailability (BA) / food effect (FE) cohort in Part A, cohorts B2-B4 in Part B and Part C were not conducted. In this SAP, only analyses applicable for the data collected are included.

This SAP supersedes the statistical considerations identified in the protocol; where considerations are substantially different, they will be so identified. Any post-hoc or unplanned analyses, or significant changes from the planned analysis in this SAP, will be clearly identified in Section 9.8.2 of the clinical study report (CSR). Changes to planned analyses do not require an updated SAP but will be included in the CSR if significant.

4.0 Changes from Previous Version of Approved SAP

This is the first version of the SAP.

5.0 Study Objectives

5.1 Primary

To evaluate the safety, tolerability and PK of escalating single and multiple ascending doses of BMS-986251 in healthy subjects, and of multiple doses of BMS-986251 in patients with moderate-to-seve re psoriasis.

5.1.1 Primary Endpoint

Safety and tolerability

- Number and percent of subjects that experience the following: SAE, death or an AE leading to study discontinuation, during the study participation or up to 1 month post discontinuation of dosing or last participation in the study for SAE.
- Number and percent of subjects with potentially clinically significant changes in ECG parameters, vital signs, or clinical laboratory parameters from Day 1 through the final follow visit.

  Other safety measures collected during the study are not considered among the primary endpoint and will be summarized as safety endpoints.

Pharmacokinetics

- Plasma concentrations of BMS-986251 and derived PK parameters as applicable

5.2 Secondary

- To evaluate the PD of escalating single and multiple ascending doses of BMS-986251 in healthy subjects, and of multiple doses of BMS-986251 in patients with moderate-to-severe psoriasis.
- To evaluate the oral bioavailability (BA) of an oral suspension of BMS-986251 relative to a liquid dosage form at a single dose level in healthy subjects.
- To evaluate the effect of a high-fat meal on the PK of an oral suspension of BMS-986251 at a single dose level in healthy subjects.
- To explore clinical effects of multiple doses of BMS-986251 in patients with moderate-to-severe psoriasis.

5.2.1 Secondary Endpoint

- The percentage ex-vivo inhibition (I) of interleukin (IL)-17 secretion in whole blood and derived PD parameters
- Plasma concentrations of BMS-986251 following oral suspension and derived PK parameters as applicable
- Plasma concentrations of BMS-986251 following high-fat meal and derived PK parameters as applicable

[redacted]

6.0 Planned Study Design

This is a double-blind, placebo-controlled, randomized SAD and MAD study in 3 parts in a planned number of approximately 103 participants: 88 healthy subjects and 15 patients with psoriasis. The present study is designed to evaluate the safety and tolerability, PK, PD and efficacy of BMS-986251. Part A and B are planned to enroll healthy subjects and is conducted at a single site. Part C was planned to enroll patients with psoriasis and to be conducted as a multi-center study in multiple countries. Part C was not executed due to study termination.

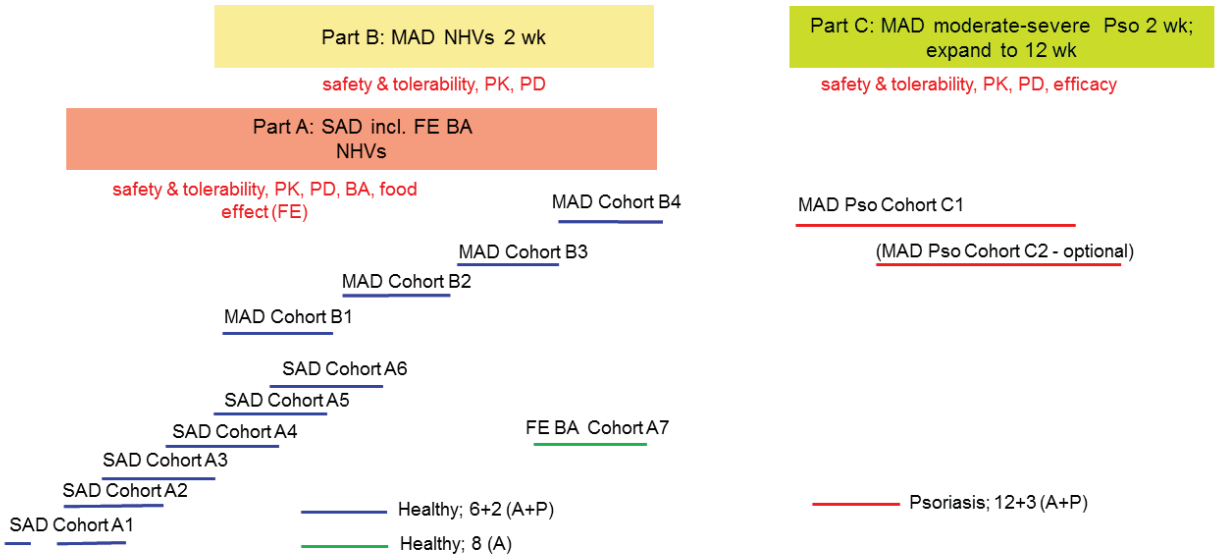
Part A is a SAD study in a planned number of 6 sequential cohorts of 8 healthy subjects (6 active + 2 placebo) each, receiving single escalating oral doses of BMS-986251. In the 1st cohort, sentinel dosing will be employed (1 active + 1 placebo, followed after 72 hours by the remaining subjects of the 1st cohort [5 active + 1 placebo]). In addition to the 6 ascending dose cohorts, a cohort of 8 healthy subjects (8 active) will be included to assess the relative BA of an oral suspension (under development; representative for the solid dosage form to be used in Part C) compared to the solution formulation, and to evaluate the effect of food on the BA of the oral suspension in a 3-period sequential design (BA/food effect [FE] cohort).

Part B is a MAD study in a planned number of 4 sequential cohorts of 8 healthy subjects (6 active + 2 placebo) each, receiving daily oral doses of escalating BMS-986251 for 2 weeks.

Part C is a multiple dose part in one cohort of 15 patients with moderate-to-severe psoriasis (12 active + 3 placebo), treated for 2 weeks, with a potential extension to 12 weeks by protocol amendment. Per protocol amendment, this study part may be extended with further cohorts, receiving lower repeated BMS-986251 doses than Cohort C1. A decision to extend the study with (a) lower-dosed cohort(s) will be based on the efficacy/safety balance of the 1st patient cohort. A high therapeutic response or, alternatively, poor safety or tolerability observed in the 1st patient cohort may be the basis to amend the study protocol for extension to a lower dosed cohort.

An overview of the study is provided in Figure 1, Table 1, Table 2 and Table 3.

Figure 1 Study Design Schematic



A = active; BA = bioavailability; FE = food effect; MAD = multiple ascending dose; NHV = healthy volunteers; P = placebo; PD = pharmacodynamics; PK = pharmacokinetics; Pso = psoriasis; SAD = single ascending dose; wk = week

Note: SAD Cohort A1 will have a sentinel dosing design with 2 subjects (1 active and 1 placebo) dosed 72 hours prior to the remaining subjects in the cohort.

Table 1 Part A Dose Cohorts

Cohort	Number of Subjects (Active / Placebo)	Period	Dose of BMS-986251	Fasted / Fed	Formulation
A1	1 / 1 (sentinel group)	1	2 mg	Fasted	Oral solution
	5 / 1	1	2 mg	Fasted	Oral solution
A2	6 / 2	1	6 mg	Fasted	Oral solution
A3	6 / 2	1	15 mg	Fasted	Oral solution
A4	6 / 2	1	30 mg	Fasted	Oral solution
A5	6 / 2	1	60 mg	Fasted	Oral solution
A6	6 / 2	1	120 mg	Fasted	Oral solution
A7 (BA/FE)	8	1	tbd	Fasted	Oral solution
		2	tbd	Fasted	Oral suspension (under development)
		3	tbd	Fed	Oral suspension (under development)

BA = bioavailability; FE = food effect; tbd = to be determined

Doses maybe adjusted based on data obtained in previous cohorts.

Table 2 Part B Dose Cohorts

Cohort	Subjects (Active / Placebo)	Dose of BMS-986251	Duration	Fasted/Fed	Formulation
B1	6 / 2	6 mg QD	14 days	Fasted	Oral solution
B2	6 / 2	tbd QD	14 days	Fasted	Oral solution
B3	6 / 2	tbd QD	14 days	Fasted	Oral solution
B4	6 / 2	60 mg QD	14 days	Fasted	Oral solution

QD = once daily; tbd = to be determined upon reviewed data
Doses maybe adjusted based on data obtained in previous cohorts.

Table 3 Part C Dose Cohort

Cohort	Subjects (Active / Placebo)	Dose of BMS-986251	Duration	Fasted/Fed	Formulation
C1	12 / 3	60 mg QD	14 days	tbd	Oral tablet

QD = once daily; tbd = to be determined upon reviewed data
Dose may be adjusted based on data obtained in previous study parts.

6.1 Sample Size Considerations

Part A and B – SAD and MAD cohorts

The current design of 8 subjects per cohort with 6 subjects assigned to active treatment is a commonly used design for SAD and MAD studies and is considered sufficient to achieve the study objectives. Although this number of is not based on statistical power considerations, administration of BMS-986251 to 6 subjects in each dose cohort provides approximately 80% probability of observing at least one occurrence of any AE which would occur with approximately 24% incidence in the population from which the sample is drawn.

Part A – BA/FE cohort

The planned number of 8 subjects on active treatment to be enrolled in the BA/FE cohort (in which BA and FE of an oral suspension will be evaluated in a 3-period sequential design), has not been based on formal statistical sample size calculations. This number of subjects is a commonly accepted number of subjects for this type of exploratory study and is considered sufficient to achieve the study objectives.

Part C – Psoriasis patients

Like Parts A and B, Part C is also an exploratory study. Therefore, no formal statistical sample size calculation has been performed and the sample size is not based on a power calculation. The planned number of 15 subjects with 12 subjects on active treatment is a commonly accepted number of subjects for this type of exploratory study. Formal statistical hypotheses were not set up. Any statistical test performed will be exploratory.

6.2 Randomization

Within each cohort (excluding the BA/FE cohort of Part A), subjects will be randomized to receive either BMS-986251 or placebo. All subjects who sign informed consent and are enrolled (including those not subsequently randomized or treated) will be assigned sequential subject numbers. Eligible subjects will be randomized according to a computer-generated randomization scheme. Subjects in Cohort A7 in Part A will be assigned sequential subject numbers in the order of enrollment. Eligible subjects will be treated in accordance with the study design.

Part A, SAD in Healthy Volunteers:

Approximately 48 subjects (8 in each cohort) enrolling in Cohorts A1 to A6 will be randomized to BMS-986251 or matching placebo in a 3:1 randomization ratio. All subjects in BA/FE Cohort A7 will receive BMS-986251.

Part B, MAD in Healthy Volunteers:

Approximately 32 subjects will be enrolled in 4 dose cohorts during the MAD study. Each dose cohort will randomize 8 subjects in a 3:1 ratio to receive BMS-986251 or matching placebo.

Part C, Multiple Dosing in Psoriasis Patients:

Approximately 15 subjects in one planned dose cohort will be randomized in a randomization ratio of 4:1 to receive BMS-986251 or matching placebo.

7.0 Overview of Planned Analysis

7.1 Changes from Protocol

This study was terminated on June 25, 2018 prior to completion of dosing in all planned cohorts and subjects within cohort. Following cohorts have been dosed before the termination:

Part A

Cohort A1 (2mg): n=8

Cohort A2 (6 mg): n=8

Cohort A3 (15 mg): n=8

Cohort A4 (30 mg): n=8

Cohort A5 (60 mg): n=4

Part B

Cohort B1 (3 mg QD): n=2 (dosing till Day 10)

Summary tables of disposition, demographics and adverse events will be provide for Part B, but data from Part B subjects will be presented in all listings with data for Part B.

Cohort A6 and BA/FE cohort in Part A, cohorts B2-B4 in Part B and Part C were not conducted.

7.2 Planned Analyses

7.2.1 Preliminary Analysis

Interim PK blinded results were provided after each cohort to the study team. A non-project team member PK Scientist will be the only team member to have access to the unblinded results.

7.2.2 Final Analysis

The full set of draft table, figures and listings (TFLs) will be provided after database lock. After comments have been incorporated on the draft TFLs, the TFLs will be finalized and incorporated in the CSR.

8.0 Definitions and General Analysis Methods

8.1 Analysis Data Presentation

8.1.1 Rounding

In listings, data will be presented with the same precision as the original data. Derived data will be rounded for presentation purposes.

For all summaries (with the exception of PK), the mean will be presented to 1 decimal greater than the original data, the standard deviation (SD) to 2 decimals greater than the original data, and the median, minimum (min) and maximum (max) values will be presented to the same number of decimal places as the original data.

For PK summaries, mean, SD, median, min, and max values ≥ 100 will be presented as integers and values < 100 ≥ 10 will be presented with 1 decimal, Values < 10 but ≥ 1 will be presented with 2 decimals, and Values < 1 will be presented with 3 decimals. Ratios will be presented with 2 decimals. Coefficient of variation (%CV) will be presented with 1 decimal.

For listing presentation purposes, PK parameters will be rounded in the same manner as noted above for summaries. The Tmax will be reported with 2 decimals.

P-values will be reported to 4 decimal places; p-values less than 0.0001 will be reported as p <0.0001.

Percentages will be rounded to 1 decimal, except 100% which will be displayed without any decimal places.

8.1.2 Imputation

Unless otherwise noted (section 15.2.1 and 17.1.1), data will not be imputed.

8.1.3 Descriptive Statistics

Unless otherwise indicated in specific data type sections, continuous variables will be summarized with the following descriptive statistics: n (number of observations), (arithmetic) mean, SD, median, min, and max.

Categorical data will be summarized with frequencies and percentages. Percentages by categories will be based on the number of subjects within a treatment group. Percentages will be rounded to 1 decimal, except 100% which will be displayed without any decimal places. Percentages will not be displayed for zero counts. Categories will be presented in the tables exactly as they appear in the eCRF / Database.

8.1.4 Pooling

Summary statistics will be calculated by study part, treatment (and time point, if applicable). Placebo data will be pooled across cohorts in Part A for descriptive statistics.

8.1.5 Unscheduled Measurements

Unscheduled measurements will be included in the listings. With the exception of unscheduled measurements used for baseline, unscheduled measurements will be excluded from the descriptive statistics and statistical analysis.

8.2 Analysis Data Definitions

8.2.1 Baseline Definition

Unless otherwise stated, baseline for post-dose evaluations within each period is defined as the last observation recorded before the first study drug administration in each period. The last observation can be an unscheduled / repeated measurement.

8.2.2 Treatment/Subject Grouping

Label	Grouping
Study Drug	BMS-986251, Placebo
Treatment	Part A SAD cohorts: oral BMS-986251 Part B MAD cohorts: oral BMS-986251
Dose Level	Part A SAD cohorts: 2 mg, 6 mg, 15 mg, 30 mg, 60 mg Part B MAD cohorts: 3 mg QD

8.2.3 Common Variable Derivations

Variable	Dataset	Definition/Calculation
Change from Baseline	All	Post-dose Observation minus Baseline Observation
Percent Change from Baseline	All	Post-dose Observation minus Baseline Observation then divided by Baseline Observation
Analysis Period	All	Interval of time during which treatment is constant.
Duration	AE	Stop date/time minus start date/time plus 1, presented in dd:hh:mm.

8.2.4 QC

The analysis datasets and the TFLs will be quality control (QC)'d according to the PRA EDS QC plan that is developed according to the EDSREP 009 SOP.

8.2.4.1 Critical Data

The QC plan requires datasets be classified as critical or non-critical. As key objectives of this study are to characterize the pharmacokinetics and assess safety and tolerability, the datasets considered critical are subject level, pharmacokinetic, and adverse events (ADSL, ADPC, ADPP, and ADAE). As these are related to the primary objectives these datasets will be double programmed per the QC Plan.

8.2.5 ADaM Datasets and Metadata

The analysis datasets will be generated in accordance with Clinical Data Interchange Standard Consortium (CDISC) Analysis Data Model (ADaM) Version 2.1.

ADaM compliant datasets will be delivered to the sponsor. A define.xml file version 2 with the corresponding metadata will be included. Analysis results metadata are excluded.

8.3 Software

The statistical analysis and reporting will be done using SAS® for Windows™ Version 9.4 or higher (SAS Institute, Inc.).

PK parameter calculations will primarily be done using Phoenix® WinNonlin® (WNL) Version 6.3 or higher (Pharsight, Inc.). Additional PK computations may be performed in SAS®.

8.4 Statistical Methods

8.4.1 Statistical Outlier Determination

No statistical outlier analysis is planned.

8.4.2 Predetermined Covariates and Prognostic Factors

There are no predetermined covariates or prognostic factors.

8.4.3 Hypothesis Testing

No formal hypothesis testing will be done.

9.0 Analysis Sets

Analyses	Enrolled	Safety	PK	PD
Disposition	✓			
Demographics and Baseline Characteristics		✓		
Safety Assessments		✓		
PK Concentrations			✓	
PK Parameters			✓	
PD Concentrations				✓

9.1 Enrolled

The Enrolled analysis set will consist of all subjects who signed informed consent. This analysis set will be used for disposition summaries.

9.2 Safety

The Safety analysis set will consist of subjects who receive at least one dose of study drug. This set will be used for disposition summaries, baseline characteristic summaries, and safety summaries.

9.3 Pharmacokinetic

The PK analysis set will consist of all subjects who receive at least 1 dose of BMS-986251 and have sufficient concentration-time data to calculate a valid Cmax and AUC(0-T).

9.4 Pharmacodynamic

All subjects who receive at least 1 dose of BMS-986251 or placebo and have any available data for the PD assessments.

10.0 Subject Disposition

The number of subjects in each analysis set will be presented. The number and percentage of subjects who withdrew from the study prematurely and a breakdown of the corresponding reasons for withdrawal will also be presented. Percentages will be based on the total number of subjects in the analysis set.

11.0 Protocol Deviations

Protocol deviations will be collected and entered into the Clinical Trial Management System (CTMS) per clinical monitoring Standard Operating Procedures. From CTMS, protocol deviations will be pulled into SDTM. All protocol deviation data will be listed by subject.

12.0 Demographic and Baseline Characteristics

12.1 Demographics

Subject demographics will be summarized descriptively for all subjects by analysis set and treatment group. The summary will include the subjects' age (in years), sex, race, ethnicity, weight (in kg), height (in cm), and body mass index (BMI) (in kg/m^2). Any measurements will be included from assessments performed during the Screening Visit. Demographics will be summarized for the Safety, PK and PD analysis sets.

All demographic data, as collected during the screening visit and Day -1, will be listed by subject.

12.2 Medical History

Medical history will be listed by subject. Medical history data will be coded according to the latest Medical Dictionary for Regulatory Activities (MedDRA) version 21.0.

12.3 Other Baseline Characteristics

Substance use (tobacco and alcohol) will be listed.

The results of drug and alcohol screen at screening and at pre-treatment will be listed.

The results of pregnancy tests at screening and at pre-treatment will be listed, the results for follicle stimulating hormone (FSH) tests at screening will be listed.

The results of serology, including hepatitis B surface antigen (HBsAg), anti-hepatitis C virus (HCV) antibodies or anti-human immunodeficiency virus (HIV) 1 and 2 antibodies will be listed.

The results of Quantiferon Gold test® for tuberculosis (TB) at screening will be listed.

Non-compliance to in- or exclusion criteria (if any) will be listed.

13.0 Prior and Concomitant Medications

Prior and concomitant medications, categorized by medication group and subgroup according to the World Health Organization (WHO) Drug Dictionary Version 2018MAR01+HD (Enhanced+Herbal) B3, will be listed by subject. Medications with an end date prior to the first dose of study drug will be considered prior medications and will be identified in the listing. If a partial date allows a medication to be considered concomitant it will be categorized as such.

14.0 Treatment Compliance and Exposure

The number of subjects receiving each dose of study drug will be summarized.

All study drug administration data will be listed by subject. If applicable, date and time and food and fluid intake and comments will be listed.

15.0 Pharmacokinetic Analyses

The PK summaries described in this section will be created using the PK analysis set.

15.1 Pharmacokinetic Variables

15.1.1 Plasma Variables

15.1.1.1 Concentrations

- Plasma concentration of BMS-986251

15.1.1.2 Parameters

PK Parameters for BMS-986251 as defined Table 4.

Table 4 Plasma BMS-986251 PK Parameters- Part A (SAD Part)

Parameter	SAD Part	MAD Part Day 1*	Description	SAS Programming Notes
Cmax	X	X	Maximum plasma concentration. Observed peak analyte concentration obtained directly from the experimental data without interpolation, expressed in concentration units	Cmax from WNL
Tmax	X	X	Time to maximum plasma concentration. First observed time to reach peak analyte concentration obtained directly from the experimental data without interpolation, expressed in time units.	Tmax from WNL
AUC(0-T)	X	X	Area under the concentration-time curve (time 0 to time of last quantifiable concentration).	AUClast from WNL
AUC(INF)	X	X	Area under the plasma concentration-time curve (time 0 to infinity). A valid half-life is required to retain this parameter.	AUCINF_obs from WNL If T-HALF is present.
AUC%Extrap	X	X	Percentage of the AUC(INF) that is extrapolated.	AUC_%Extrap_obs from WNL– Listed only
T-HALF	X	X	Terminal phase half-life expressed in time units. A valid Lz is required to retain.	HL_Lambda_z from WNL
Lz	X	X	Terminal phase rate constant calculated by the WinNonlin generated best fit linear regression of the terminal log-linear portion of the concentration vs. time curve. Linear regression of at least 3 points and an adjusted R2 > 0.80 are required to retain.	Lambda_z from WNL.
CL/F	X	X	Apparent clearance	CL_F_obs from WNL
Vd/F	X	X	Apparent volume of distribution at terminal phase	Vz_F_obs from WNL
Adj R^2	X	X	Adjusted R^2 value of terminal elimination phase	Rsq_adjusted from WNL – Listed only

Parameter	SAD Part	MAD Part Day 1*	Description	SAS Programming Notes
Lz_Start	X	X	The time point starting the log-linear elimination phase defining their terminal half-life	Lambda_z_lower from WNL – Listed only
Lz_End	X	X	The time point ending the log-linear elimination phase defining the terminal half-life	Lambda_z_upper from WNL – Listed only
Lz_N	X	X	Number of time points in the log-linear elimination phase defining the terminal half-life	No_points_lambda_z from WNL – Listed only

Note: AUCs will be calculated using linear up / log down, expressed in units of concentration x time.

* There are only 2 subjects in cohort B1 who have been dosed till Day 10. PK parameters will be calculated for Part B (MAD part) Day 1 if feasible.

15.1.2 Urine Variables

15.1.2.1 Amounts Excreted

- Amount of BMS-986251 excreted in urine (Ae)
  - Calculated as the urine volume times the urine concentration for each interval.

15.1.2.2 Parameters

- PK Parameters for BMS-986251 as defined in Table 5.

Table 5 Urine Parameter –SAD Part

Parameter	Description	SAS Programming Notes
Ae(0-T)	Total amount of drug excreted unchanged into urine to time t obtained by adding the amounts excreted over each collection interval.	Summation i = 1 to n of (Concentration (ng/mL) ti-1-ti*volume(mL)ti-1-ti) Parameter will be missing if data is missing for any prior individual time interval.
Ae	Total amount of drug excreted unchanged into urine to last time obtained by adding the amounts excreted over each collection interval.	Summation i= 1 to n of (Concentration (ng/mL) t_{i-1}-t_i*volume(mL)t_{i-1}-t_i) Parameter will be missing if data is missing for any individual time interval.
Fe	Fraction (%) of the administered dose excreted unchanged into urine	Ae/XXmg (dose)*100
CLr	Renal clearance	Ae(0-T)/AUC(0-T)

15.2 Pharmacokinetic Summaries

15.2.1 Pharmacokinetic Concentrations

Plasma concentrations for BMS-986251 below the limit of quantification (BLQ) will be set to zero in the computation of mean concentration values. Descriptive statistics (n, mean, SD, geometric mean, %CV, median, min, and max) will be used to summarize the plasma concentrations by treatment at each scheduled time point. If over 50% of the subjects in a given cell have values BLQ, then the descriptive statistics will not be presented and will instead display as BLQ for the mean and minimum. With the exceptions of n and maximum, all other statistics will be missing.

Linear and semi-logarithmic plots of the arithmetic mean plasma concentrations + SD by scheduled sampling times will be provided for Part A, the treatments will be presented in one plot. These plots will show time in hours. The plots will match the summary table results and will not have an observation at a given time point if more than half of the subjects have values BLQ. Linear plots will be presented to 24 hours and to the last scheduled time point. Semi-log plots will be presented to the last scheduled time point. The linear and semi-logarithmic plots will be presented side-by-side on a single page.

Linear and semi-logarithmic plots of the individual plasma concentrations by actual sampling times will be provided by subject. These plots will show time in hours. Individual plots will use the BLQ handling procedure described below for “Pharmacokinetic Parameters”. Linear plots will be presented to 24 hours and semi-log plots will be presented to the last scheduled time point.

Linear and semi-logarithmic spaghetti plots of the individual plasma concentrations by actual sampling times will be provided by treatment. These plots will show time in hours. Spaghetti plots will use the BLQ handling procedure described below for “Pharmacokinetic Parameters”. Linear plots will be presented to 24 hours and semi-log plots will be presented to the last scheduled time point.

All individual subject plasma concentration data will be listed, including time deviations and comments.

15.2.2 Pharmacokinetic Parameters

PK parameters for BMS-986251 will be estimated using non-compartmental methods with WinNonlin®.The plasma PK parameters will be estimated from the concentration-time profiles. In estimating the PK parameters, BLQ values at the beginning of the profile will be set to zero. BLQ values that occur after the first quantifiable point will be considered missing. Values that are embedded between BLQs, or quantifiable values occurring after two or more BLQs, will be set to missing at the discretion of the pharmacokineticist. Actual sampling times, rather than scheduled sampling times, will be used in all computations involving sampling times. If the actual time or dose time is missing, the scheduled time may be substituted in order to calculate the PK parameter.

Descriptive statistics (n, mean, SD, geometric mean, %CV, median, min, and max) will be used to summarize the calculated PK parameters by treatment. For Tmax, only n, median, min and max will be presented.

The points to be included in the Lz range will be from the WinNonlin best fit generated profiles. At least 3 points will be required to be used. The Cmax data point will not be included.

15.2.3 Statistical Analyses

15.2.3.1 Dose-proportionality

The pharmacokinetic parameters Cmax, AUC(0-T), and AUC(INF) for BMS-986251 from the Part A groups will be compared across each dose level to assess dose proportionality. Dose proportionality will be assessed by estimating the slope of the linear regressions of natural logarithmic transformed AUC(0-T), AUC(INF), and Cmax on log(dose).

Statistical analyses will be done using a power model (Gough et al, 1995) with mixed effects of the following general form,

$$\ln(PK) = \ln(\beta 0) + \beta 1 \cdot \ln(Dose) + \varepsilon,$$

where

PK is the pharmacokinetic parameter tested (e.g., Cmax or AUC)

ln(β0) is the y-intercept,

β1 is the slope (a value of β1 1 indicates linearity), and

ε is an error term

The estimate of β1 and 90% CI will be reported along with the associated p-value and the dose range for proportionality. A significant difference from unity (1) and lack of proportionality will be defined as $p < 0.05$.

Plots of AUC(0-T), AUC(INF) and Cmax versus dose on the linear scale and the equation line will be provided to assess dose proportionality.

15.2.4 Urine Pharmacokinetics

If applicable, descriptive statistics (n, mean, SD, geometric mean, %CV, median, min, and max) will be used to summarize the urine concentrations, amounts excreted and derived PK parameters for BMS-986251 in SAD part and treatment at each scheduled time interval and cumulative.

All available derived urine PK parameters will be included in the PK data set and reported, but only subjects with adequate PK profiles will be included in the summary statistics and statistical analysis.

All available individual subject urine BMS-986251 concentrations, amount excreted data, urine parameters will be listed.

16.1 Pharmacodynamic Analysis

The following PD assessment is planned in this study:

- ex-vivo inhibition (I) of IL-17 secretion in in stimulated and unstimulated whole blood

16.1 Pharmacodynamic Variables

16.1.1 IL-17 Inhibition in Whole Blood Variables

- The IL-17 concentrations in stimulated whole blood
- The IL-17 concentrations in unstimulated whole blood
- Percentage of IL-17 inhibition in stimulated whole blood

16.1.2 IL-17 Inhibition PD Parameters

Table 6 IL-17 PD Parameters (in whole blood)

Parameter	Description	SAS Programming Notes
Imax	Maximum observed inhibition	In SAS
tImax	Time of maximum observed inhibition	In SAS
tI>50%*	Time of inhibition above 50%	
tI>90%*	Time of inhibition above 90%	

*if feasible

16.2 Pharmacodynamic Summaries

16.2.1 IL-17 Inhibition in Whole Blood

Individual data of IL-17 concentration in stimulated and unstimulated whole blood will be listed. Descriptive statistics (n, mean, SD, geometric mean, %CV, median, min, and max) of the IL-17 whole blood concentration will be summarize by treatment and time point. Levels of BLQ will be set to 0.

Percentage of IL-17 inhibition is calculated as:

[(stimulated concentration at baseline – unstimulated concentration at baseline) - (stimulated concentration at Rx time point – unstimulated concentration at Rx time point)] / (stimulated concentration at baseline – unstimulated concentration at baseline) *100%.

Baseline is defined as the average concentration of pre-dose (T=-18.00 hr and T=0.00 hr). Percentage of IL-17 inhibition will be listed and summarized by treatment and time point. Linear plots of the arithmetic mean of percentage of IL-17 inhibition + SD in the whole blood by scheduled sampling times will be provided for SAD part. Linear plots of the combined individual percentage of IL-17 inhibition in the whole blood by scheduled sampling times will be provided by dose of BMS-986251 and placebo.

Mean plots of percentage of IL-17 inhibition versus mean BMS-986251 plasma concentration will be provided by treatment.

16.2.2 Pharmacodynamic Parameters

Descriptive statistics (n, mean, SD, geometric mean, %CV, median, min, and max) will be used to summarize the calculated PD parameters by treatment. For tImax, tI>50%, and tI>90%, only n, median, min and max will be presented.

16.2.3 Evaluation of PK/PD correlation

PK/PD correlation will be evaluated by scatter Plot of IL-17 Inhibition versus BMS-986251 plasma concentration.

17.0 Safety Analyses

The safety summaries described in this section will be created using the Safety analysis set. Changes will not be provided if collections are not made during treatment periods.

17.1 Safety Variables

The following safety variables will be summarized:

- Treatment-Emergent Adverse Events (TEAE)
- Clinical Laboratory Evaluations
  - Clinical Chemistry
  - Hematology
  - Urinalysis
  - Coagulation
- Vital Signs
  - Systolic Blood Pressure (SBP)
  - Diastolic Blood Pressure (DBP)
  - Heart rate
  - Oral body temperature
  - Respiratory rate
- Electrocardiograms (ECG)
  - Heart Rate
  - PR Interval
  - QRS-Duration

  - QT Interval
  - QTc (Frederica) Interval
  - T-Wave Assessment
  - U-Wave Assessment
- Physical Examination
- Taste questionnaire

17.1.1 Adverse Events

An AE is defined as any new untoward medical occurrence or worsening of a preexisting medical condition in a clinical investigation participant that does not necessarily have a causal relationship with treatment. AE summaries will include only TEAEs. TEAEs are those which occur after the first dose of study drug. All TEAE summaries will be presented alphabetically by system organ class, with preferred terms sorted in decreasing order of frequency within each system organ class based on MedDRA version 21.0.

TEAEs occurring following dosing in a specific period but before dosing in the following period will be attributed to that specific period. If the time is missing for an AE on a dosing day then the AE will be attributed to the treatment given on that day.

The following missing data will be imputed (for calculations only) as defined:

- Missing AE start and / or end times for the calculation of onset and duration will be assumed to be at 00:01 for a start time and 23:59 for end times
- Missing AE severity or relationship will be left as missing
- Missing AE start times for the determination of treatment emergence will be assumed to occur after treatment unless partial date documents the AE as happening prior to treatment
- Missing AE start times for the determination of treatment assignment will be assumed to occur after treatment on the recorded date one minute after dosing
- Missing AE start date will be assumed to be after treatment for the determination of TEAE, but will not be attributed to a specific treatment in studies with multiple treatments.

A summary of the number and percentage of subjects reporting TEAEs, serious AEs (SAEs), who discontinue study drug due to a TEAE, and will be presented by treatment and overall.

A summary of the number and percentage of subjects reporting each TEAE will be presented by treatment and overall. Counting will be done by subject only, not by event; subjects will only be counted once within each body system or preferred term.

A summary of the number and percentage of subjects reporting each TEAE will be presented by relationship to study drug (as recorded on the eCRF) and by treatment and overall. Subjects with multiple events within a particular system organ class (SOC) or preferred term will be counted as related unless no events were related in that SOC/preferred term.

A summary of the number and percentage of subjects reporting each TEAE will be presented by severity (as recorded on eCRF) and by treatment and overall. Subjects with multiple events within a particular system organ class or preferred term will be counted under the category of their most severe event within that system organ class or preferred term.

All AEs (including non-treatment-emergent events) recorded on the eCRF will be listed by subject.

A separate listing of AEs leading to study drug discontinuation will be provided.

17.1.2 Deaths and Serious Adverse Events

A listing of deaths and other SAEs will be provided for all subjects.

17.1.3 Laboratory Data

Clinical laboratory data will be presented using units from the study data tabulation model (SDTM) Controlled Terminology.

A descriptive statistics summary of continuous laboratory results for clinical chemistry, hematology and derived changes from baseline will be provided by treatment and scheduled time point.

Shift tables describing the change in clinical laboratory values from baseline to each post-dose scheduled time point (number and percentage of subjects) will also be provided by treatment. The following categories will be used: low, normal, and high.

All laboratory data will be listed by subject, including laboratory variables not listed in the protocol.

A separate listing of out-of-range values will also be provided. Normal ranges will be used directly from the clinical laboratory and will be included in the listings for reference.

17.1.4 Vital Signs

A descriptive statistics summary of vital signs and derived changes from baseline will be provided by treatment and scheduled time point.

If considered informative by the data obtained, plots of the mean change from baseline for the vital signs parameters versus time since dosing will be presented by part and treatment.

All vital signs data will be listed by subject.

17.1.5 Electrocardiograms

The observed measurements for all ECG parameters and the corresponding abnormalities will be listed for all time points. The means of triplicate measurements for continuous parameters and the change from baseline of the mean triplicate measurements at each scheduled time point will be listed by subject.

Descriptive statistics will be provided to summarize mean ECG parameters (observed and changes from baseline) by treatment and scheduled time.

QTC prolongation potential will be by scatter Plot of change from baseline of QTcF versus BMS-986251 plasma concentration.

Appendix 1: Glossary of Abbreviations

Glossary of Abbreviations:	
AE	Adverse event
ADaM	Analysis data model
BA	Bioavailability
BMI	Body mass index
BMS	Bristol-Myers Squibb Research and Development
BLQ	Below the limit of quantification
CDISC	Clinical Data Interchange Standard Consortium
CSR	Clinical study report
CTMS	Clinical Trial Management System
CV	Coefficient of variation
DBP	Diastolic blood pressure
ECG	Electrocardiogram
eCRF	Electronic case report form
EDS	Early Development Services
FE	Food effect
FSH	Follicle stimulating hormone
HBsAg	Hepatitis B surface antigen
HCV	Hhepatitis C virus
HIV	Human immunodeficiency virus
I	Inhibition
ICH	The International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
IL	Interleukin
LLOQ	Lower limit of quantification
MAD	Multiple ascending dose
Max	Maximum
MedDRA	Medical Dictionary for Regulatory Activities
Min	Minimum
PD	Pharmacodynamic
PK	Pharmacokinetic
Pso	Psoriasis
QC('d)	Quality control(led)
QD	Once daily

SAD	Single ascending dose
SAP	Statistical analysis plan
SAE	Serious adverse event
SBP	Systolic blood pressure
SD	Standard deviation
SDTM	Study data tabulation model
SOC	System organ class
tbd	To be determined
TB	Tuberculosis
TBNK	T, B, and natural killer cells
TEAE	Treatment-emergent adverse event
TFL(s)	Tables, figures and listings
WHO	World Health Organization
WNL	WinNonlin

Appendix 2: Schedule of Assessments from Protocol

Table 7 Study Procedural Outline Part A – SAD Healthy Subjects (IM024 005)

		Period 1 Period 2 (Cohort for Bioavailability and Food Effect Assessment only) Period 3 (Cohort for Bioavailability and Food Effect Assessment only)																			
Visit	**Screening**	**Pre-Treatment**	**Treatment**																		**Follow-up[1]**
Study Days	**-21 to -1**	**-1**	**1**											**2**		**3**	**4**	**5**	**6**	**7**	**9**	**11**
Time Post-Dosing (hrs)			**Pre-dose**	**0**	**0.5**	**1**	**1.5**	**2**	**3**	**4**	**6**	**8**	**12**	**24**	**36**	**48**	**72**	**96**	**120**	**144**	**192**	**240**
Confinement		X																				
Discharge[2]																				X		
Ambulant visit	X																				X	X
Informed consent and medical history	X																					
Demographics	X																					
Physical examination	X																					X
Genotyping(CYPs, transporters)[3]				X																		
Vital signs	X		X			X		X		X		X		X		X	X	X	X	X	X	X
Body weight and height (including BMI calculation)[4]	X	X																				X
Eligibility check	X	X	X																			
12-lead ECG (triplicate)	X		X			X		X				X		X		X		X		X		X

[1] For relative bioavailability/food effect cohort follow-up assessments on Day 11 of Period 3 only. At the Day 11 visit in Period 1 and 2 only blood sampling for PK and PD (Period 1 only), vital signs, and drug and alcohol screen will be performed.

[2] Discharge from the clinical research unit.

[3] Mandatory whole blood collection for analysis of DNA variants in ADME-related genes (http://pharmaadme.org/Appendix 6). For relative bioavailability/food effect cohort sample will be collected in Period 1 only. Sample may be taken at any time post-dose during Day 1.

[4] Height will only be measured at screening. BMI will also only be calculated at screening.

		Period 1 Period 2 (Cohort for Bioavailability and Food Effect Assessment only) Period 3 (Cohort for Bioavailability and Food Effect Assessment only)																				
Visit	**Screening**	**Pre-Treatment**	**Treatment**																			**Follow-up[1]**
Study Days	**-21 to -1**	**-1**	**1**											**2**		**3**	**4**	**5**	**6**	**7**	**9**	**11**
Time Post-Dosing (hrs)			**Pre-dose**	**0**	**0.5**	**1**	**1.5**	**2**	**3**	**4**	**6**	**8**	**12**	**24**	**36**	**48**	**72**	**96**	**120**	**144**	**192**	**240**
Holter monitoring[5] [6]			X[7]						X													
Clinical laboratory, hematology incl. reticulocytes	X	X												X			X			X		X
Drug and alcohol screen	X	X																			X	X
HBsAg, anti-HCV, and anti-HIV 1/2 tests	X																					
Quantiferon Gold test	X																					
FSH (females only)	X																					
Pregnancy test (females only)	X	X																				X
Overnight fast (10 hours)		X																				
Standardized lunch, snacks, dinner[8]									X													
High-fat breakfast[9]			X																			
Randomization			X																			
Study drug administration				X																		
Taste questionnaire				X[10]																		

[5] For bioavailability/food effect cohort in fasted Period 1 only
[6] Including a 15 minute supine period prior to every PK sample
[7] In triplicate in 3 supine periods
[8] In Period 1 with Holter monitoring only.
[9] In Period 3 of bioavailability/food effect cohort only
[10] To be completed immediately after drug administration (within first 10 seconds) and after approximately 1 minute (before drinking the provided glass of water)

		Period 1 Period 2 (Cohort for Bioavailability and Food Effect Assessment only) Period 3 (Cohort for Bioavailability and Food Effect Assessment only)																				
Visit	**Screening**	**Pre-Treatment**	**Treatment**																			**Follow-up[1]**
Study Days	**-21 to -1**	**-1**	**1**											**2**		**3**	**4**	**5**	**6**	**7**	**9**	**11**
Time Post-Dosing (hrs)			**Pre-dose**	**0**	**0.5**	**1**	**1.5**	**2**	**3**	**4**	**6**	**8**	**12**	**24**	**36**	**48**	**72**	**96**	**120**	**144**	**192**	**240**
Previous and concomitant medications	X	X																				
PK sampling blood[11]			X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Urine collection for parent drug and metabolites		X						X					X		X		X	X	X	X	X	X
Sampling for ex-vivo IL-17 inhibition in whole blood[12]		X	X			X		X		X			X	X		X		X		X		
Adverse events		X												X								
Serious adverse events	X																					

BMI = body mass index; CYP = cytochrome P450; ECG = electrocardiogram; FSH = follicle stimulating hormone; HBsAg = hepatitis B surface antigen; HCV = hepatitis C virus; HIV = human immunodeficiency virus; hrs = hours; IL-17 = interleukin 17; PK = pharmacokinetic

[11] Including a 15 minute supine period prior to every PK sample during Holter monitoring
[12] Period 1 only

Table 7 Study Procedural Outline Part B – MAD Healthy Subjects (IM024 005)

Visit	Screening	Pre-Treatment	Treatment																		Follow-up
Study Days	-21 to -1	-1	1 14[13]											2-13			15	16	18	20	24
Time Post-Daily Dose (hrs)[14]			Pre-dose	0	0.5	1	1.5	2	3	4	6	8	12	Pre-dose	0	4	24	48	96	144	240
Confinement		X																			
Discharge[15]																		X			
Ambulant visit	X																		X	X	X
Informed consent and medical history	X																				
Demographics	X																				
Physical examination	X																				X
Genotyping(CYPs, transporters)[16]				X																	
Vital signs	X		X			X		X		X		X		X		X	X	X	X	X	X
Body weight and height (including BMI calculation)[17]	X	X																			X
Eligibility check	X	X	X[18]																		
12-lead ECG (triplicate)	X		X			X		X				X				X[19]					X

[13] Schedule for Day 1 (first day of dosing) and Day 14 (last day of dosing).
[14] Time is given relative to dosing on the relevant study day. In the CRF, time "0" will be the time of first dosing and all other time points will be relative to time "0".
[15] Discharge from the clinical research unit.
[16] Mandatory whole blood collection for analysis of DNA variants in ADME-related genes (http://pharmaadme.org/Appendix 6). Sample may be taken at any time post-dose during Day 1; no sample to be taken on Day 14.
[17] Height will only be measured at screening. BMI will also only be calculated at screening.
[18] Not on Day 14.
[19] Days 2, 4, 6, 8, 10, and 12 only.

Visit	Screening	Pre-Treatment	Treatment																	Follow-up
Study Days	**-21 to -1**	**-1**	**1 14[13]**											**2-13**			**15**	**16**	**18**	**20**	**24**
Time Post-Daily Dose (hrs)[14]			**Pre-dose**	**0**	**0.5**	**1**	**1.5**	**2**	**3**	**4**	**6**	**8**	**12**	**Pre-dose**	**0**	**4**	**24**	**48**	**96**	**144**	**240**
Clinical laboratory, hematology incl. reticulocytes	X	X	X[20]											X[21]				X			X
Holter monitoring [22] [23]			X[24]	X																	
Drug and alcohol screen	X	X																	X		X
HBsAg, anti-HCV, and anti-HIV 1/2 tests	X																				
Quantiferon Gold test	X																				
FSH (females only)	X																				
Pregnancy test (females only)	X	X																			X
Randomization			X[25]																		
Overnight fast (10 hours)		X																			
Standardized lunch, snacks, dinner				X																	
Study drug administration				X											X						
Taste questionnaire				X[26]																	
Previous and concomitant medications	X	X																			

[20] Day 14 only.
[21] Days 3, 7, and 10 only.
[22] Including a 15 minute supine period prior to every PK sample.
[23] If upcoming preclinical safety results indicate the need for a dedicated TQTc study, Holter monitoring for this study will be simplified and not plan for concentration-effect modeling.
[24] In triplicate in 3 supine periods.
[25] On Day 1 only.
[26] On Day 1 only. To be completed immediately after drug administration (within first 10 seconds) and after approximately 1 minute (before drinking the provided glass of water).

Visit	Screening	Pre-Treatment	Treatment																	Follow-up
Study Days	**-21 to -1**	**-1**	**1 14[13]**											**2-13**			**15**	**16**	**18**	**20**	**24**
Time Post-Daily Dose (hrs)[14]			**Pre-dose**	**0**	**0.5**	**1**	**1.5**	**2**	**3**	**4**	**6**	**8**	**12**	**Pre-dose**	**0**	**4**	**24**	**48**	**96**	**144**	**240**
PK sampling blood[27]			X		X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X
Urine collection for parent drug and metabolites		X		X[28]																	
Sampling for ex-vivo IL-17 inhibition in whole blood		X	X			X		X		X			X	X[29]				X		X	X
Sampling for IL-17, IL-22, β-defensin, and erythropoietin			X														X				X
Sampling for T, B, and NK cells (TBNK), γδ T cells, T cell subsets.			X														X				X
Adverse events				X																	
Serious adverse events	X																				

[27] Including a 15 minute supine period prior to every PK sample during Holter monitoring.
[28] 24-hours urine collection on Day 14 only
[29] Pre-dose at Days 2, 4 and 7 only.

Appendix 3: Pharmacokinetic Sampling Schedule from Protocol

Table 8 Pharmacokinetic Sampling Schedule; Part A

Sample Collection Time		Time (relative to dosing) hour:min	Blood Sample	Urine Sample
Study Day	Time (event)		PK Blood Sample	Collection Interval
-1	NA	NA		X
1	0 h (pre-dose)	00:00	X	
1	0.5 h	00:30	X	X (0-12 h)
1	1 h	01:00	X	
1	1.5 h	01:30	X	
1	2 h	02:00	X	
1	3 h	03:00	X	
1	4 h	04:00	X	
1	6 h	06:00	X	
1	8 h	08:00	X	
1	12 h	12:00	X	X (12-24 h)
2	24 h	24:00	X	
2	36 h	36:00	X	X (24-48 h)
3	48 h	48:00	X	
4	72 h	72:00	X	X (48-72 h)
5	96 h	96:00	X	X (72-96 h)
6	120 h	120:00	X	X (96-120 h)
7	144 h	144:00	X	X (120-144 h)
9	192 h	192:00	X	
11	240 h	240:00	X	

Table 9 Pharmacokinetic Sampling Schedule; Part B

Sample Collection Time		Time (relative to dosing) hour:min	Blood Sample	Urine Sample
Study Day	Time (event)		PK Blood Sample	Collection Interval
-1	NA	NA		X
1	0 h (pre-dose)	00:00	X	
1	0.5 h	00:30	X	
1	1 h	01:00	X	
1	1.5 h	01:30	X	
1	2 h	02:00	X	
1	3 h	03:00	X	
1	4 h	04:00	X	
1	6 h	06:00	X	
1	8 h	08:00	X	
1	12 h	12:00	X	
2-13	0 h (pre-dose)	0:00	X	
2-13	4 h	4:00	X	
14	0 h (pre-dose)	0:00	X	X (0-24 h on Day 14)
14	0.5 h	00:30	X	
14	1 h	01:00	X	
14	1.5 h	01:30	X	
14	2 h	02:00	X	
14	3 h	03:00	X	
14	4 h	04:00	X	
14	6 h	06:00	X	
14	8 h	08:00	X	
14	12 h	12:00	X	
15	24 h	24:00	X	
16	48 h	48:00	X	
18	96 h	96:00	X	
20	144 h	144:00	X	
24	240 h	240:00	X	

Table 10 Pharmacodynamic Sampling Schedule; Part A

Sample Collection Time		Time (relative to dosing) hour:min	Blood Samples
Study Day	Time (event)		Ex-vivo IL-17 Inhibition in Whole Blood
-1	Admission	NA	X
1	0 h (pre-dose)	00:00	X
1	1 h	01:00	X
1	2 h	02:00	X
1	4 h	04:00	X
1	12 h	12:00	X
2	24 h	24:00	X
3	48 h	48:00	X
5	96 h	96:00	X
7	144 h	144:00	X
11	240 h	240:00	X

h = hour; IL-17 = interleukin-17; min = minute; NA = not applicable.

Table 11 Pharmacodynamic Sampling Schedule; Part B

Sample Collection Time		Time (relative to dosing) hour:min	Blood Sample		
Study Day	Time (event)		Ex-vivo IL-17 inhibition in whole blood	IL-17, IL-22, β-defensin, and erythropoietin concentrations	T, B, and NK cells (TBNK), γδ T cells, T cell subsets
-1	Admission	NA	X		
1	0 h (pre-dose)	00:00	X	X	X
1	1 h	01:00	X		
1	2 h	02:00	X		
1	4 h	04:00	X		
1	12 h	12:00	X		
2	0 h (pre-dose)	0:00	X		
4	0 h (pre-dose)	0:00	X		

Sample Collection Time		Time (relative to dosing) hour:min	Blood Sample		
Study Day	Time (event)		Ex-vivo IL-17 inhibition in whole blood	IL-17, IL-22, β-defensin, and erythropoietin concentrations	T, B, and NK cells (TBNK), γδ T cells, T cell subsets
7	0 h (pre-dose)	0:00	X		
14	0 h (pre-dose)	0:00	X		
14	1 h	01:00	X		
14	2 h	02:00	X		
14	4 h	04:00	X		
14	12 h	12:00	X		
15	24 h	24:00		X	X
16	48 h	48:00	X		
20	144 h	144:00	X		
24	240 h	240:00	X	X	X

h = hour; IL-17 = interleukin-17; IL-22 = interleukin-22; min = minute; NA = not applicable; NK = natural killer.

Appendix 4: List of Tables, Figures, and Listings

List of Tables and Figures:		
Output	**Title**	**Analysis Set**
Section 14.1 – Disposition and Demographic Data		
Table 14.1.1	Summary of Analysis Sets	All sets
Table 14.1.2	Summary of Subject Disposition	All sets
Table 14.1.3	Summary of Demographics	All sets
Table 14.1.4	Summary of Dosing	Safety
Section 14.2 – Pharmacokinetic Data		
Table 14.2.1.1	Summary of BMS-986251 Plasma Concentration	PK
Table 14.2.1.2	Summary of Plasma Pharmacokinetic Parameters	PK
Table 14.2.1.3	Summary Analysis of Dose Proportionality	PK
Figure 14.2.1.4	Plot of Arithmetic Mean (+SD) BMS-986251 Plasma Concentrations versus Time on Linear and Semi-logarithmic Scales - SAD Part	PK
Figure 14.2.1.5	Plot of Individual BMS-986251 Plasma Concentrations Versus Time on Linear and Semi-logarithmic Scales by Subject	PK
Figure 14.2.1.6	Spaghetti Plot of Individual BMS-986251 Plasma Concentrations Versus Time on Linear and Semi-logarithmic Scales by Treatment	PK
Figure 14.2.1.7	Plot of Dose Proportionality: AUC(0-T), AUC(INF) and Cmax versus Dose (Log scale)	PK
Table 14.2.2.1	Individual Values and Descriptive Statistics of BMS-986251 Excretion Parameters in Urine	PK
Section 14.3 – Pharmacodynamic Data		
Table 14.3.1	Individual Values and Descriptive Statistics of IL-17 Concentrations in Whole Blood	PD
Table 14.3.2	Individual Values and Descriptive Statistics of IL-17 Inhibition	PD
Table 14.3.3	Individual Values and Descriptive Statistics of IL-17 Inhibition Pharmacodynamic Parameters	PD
Figure 14.3.4	Arithmetic Mean +/- SD IL-17 Inhibition Versus Time (Linear Scale) –SAD Part	PD
Figure 14.3.5	Combined Individual IL-17 Inhibition Versus Time (Linear Scale)	PD
Figure 14.3.6	Scatter Plot of IL-17 Inhibition Versus BMS-986251 Plasma Concentration	PD
Section 14.4 – Safety Data		
Table 14.4.1.1	Summary of Adverse Events	Safety

Table 14.4.1.2	Summary of Treatment Emergent Adverse Events by System Organ Class and Preferred Term	Safety
Table 14.4.1.3	Summary of Treatment Emergent Adverse Events by System Organ Class, Preferred Term and Relationship to Study Drug	Safety
Table 14.4.1.4	Summary of Treatment Emergent Adverse Events System Organ Class, Preferred Term and Severity	Safety
Table 14.4.2.1	Listing of Deaths and Other Serious Adverse Events	All Subjects
Table 14.4.3	Not part of TFL – Reserved for Narratives in CSR	
Table 14.4.4.1	Listing of Abnormal Laboratory Values	All Subjects
Table 14.4.4.2	Summary of Safety Laboratory Results	Safety
Table 14.4.4.3	Shift Summary of Laboratory Results by Reference Range and Time Point	Safety
Table 14.4.4.4	Summary of Vital Signs	Safety
Figure 14.4.4.5	Plots of mean change from baseline of Vital Signs	Safety
Table 14.4.4.6	Summary of 12-Lead Electrocardiograms	Safety

List of End of Text Listings:	
Output	**Title**
Section 16.2.1 – Disposition	
Listing 16.2.1.1	Subject Disposition
Listing 16.2.1.2	Tuberculosis Screening
Section 16.2.2 – Protocol Deviations	
Listing 16.2.2	Important Protocol Deviations
Section 16.2.3 – Excluded Subjects	
Listing 16.2.3	Analysis Sets
Section 16.2.4 – Demographics and Baseline Characteristics	
Listing 16.2.4.1	Subject Demographics
Listing 16.2.4.2	Medical History
Listing 16.2.4.3	Prior and Concomitant Medications
Listing 16.2.4.4	Tobacco and Alcohol Use
Section 16.2.5 - Compliance	
Listing 16.2.5.1	Study Drug Administration
Section 16.2.6 – Response Data	
Listing 16.2.6.1	Plasma BMS-986251 Concentrations
Listing 16.2.6.2	Plasma Pharmacokinetic Parameters
Listing 16.2.6.3	Urine BMS-986251 Concentrations and Amounts Excreted

Listing 16.2.6.4	Urine Pharmacokinetic Parameters
Listing 16.2.6.5	IL-17 Concentrations in Stimulated and Unstimulated Whole Blood
Listing 16.2.6.6	IL-17 Inhibition in Whole Blood
Listing 16.2.6.7	IL-17 Inhibition in Whole Blood Pharmacokinetic Parameters
Section 16.2.7 – Adverse Events Data	
Listing 16.2.7.1	Adverse Events
Listing 16.2.7.2	Adverse Events Leading to Study Drug Discontinuation
Section 16.2.8 – Laboratory Data	
Listing 16.2.8.1	Clinical Laboratory Results – Chemistry
Listing 16.2.8.2	Clinical Laboratory Results – Hematology
Listing 16.2.8.3	Clinical Laboratory Results – Urinalysis
Listing 16.2.8.4	Clinical Laboratory Results – Serology
Listing 16.2.8.5	Clinical Laboratory Results – Pregnancy
Listing 16.2.8.6	Clinical Laboratory Results – Drug and Alcohol Screen
Listing 16.2.8.7	Clinical Laboratory Results – Comments
Section 16.2.9– Other Safety Data	
Listing 16.2.9.1	Vital Signs
Listing 16.2.9.2	12-Lead Electrocardiograms
Figure 16.2.9.3	Scatter Plots of ΔQTcF Versus BMS-986251 Plasma Concentration
Listing 16.2.9.4	Physical Examinations
Listing 16.2.9.5	Taste Questionnaire

Other Appendix Outputs:	
Output	**Title**
Appendix 16.1.7	Randomization
Appendix 16.1.9.2	Statistical Appendices

Appendix 5: Shells for Tables, Figures and Listings

Shells are provided in a separate document.