Official Title: A Phase I, Single Center, Open-Label, Partially Randomized, Two Part Study to Investigate the Absorption, Metabolism, and Excretion of [^{14}C]-GDC-9545 Following a Single Oral Dose (Part 1) and to Evaluate the Absolute Bioavailability of Oral Capsule Formulations of GDC-9545 F12 and F18 and the Relative Bioavailability of F18 Compared to F12 (Part 2) in Healthy Female Subjects of Non-Childbearing Potential

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REPORTING AND ANALYSIS PLAN

A Phase I, Single Center, Open-Label, Partially Randomized, Two Part Study to Investigate the Absorption, Metabolism and Excretion of [^{14}C]-GDC-9545 Following a Single Oral Dose (Part 1) and to Evaluate the Absolute Bioavailability of the Oral Capsule Formulation of GDC-9545 F12 and F18 and the Relative Bioavailability of F18 Compared to F12 (Part 2) in Healthy Female Subjects of Non-Childbearing Potential

Quotient Study Number: QSC204283
Sponsor Study Number: GP42662
Investigational Product: GDC-9545

Sponsor:
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Date

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01/21/2021

[redacted]

Signed by: [redacted] Date

Study Biostatistician (Genentech, Inc.)

1 Table of Contents

2 List of Abbreviations

^{14}C	carbon-14
ADaM	analysis data model
AE	adverse event
ATC	anatomical therapeutic chemical
AUC	area under the curve
BLQ	below the limit of quantification
BMI	body mass index
BP	blood pressure
CDISC	Clinical Data Interchange Standards Consortium
CHMP	Committee for Medicinal Products for Human Use
CI	confidence interval
COVID-19	Coronavirus disease 2019
CSR	clinical study report
CV%	Coefficient of variation
CVw%	Intra-subject variability
D	'substantial' decrease from baseline for vital signs parameters
DP	decimal place
ECG	electrocardiogram
F	absolute bioavailability
Frel	relative bioavailability
GMR	geometric mean ratio
h	hour
H	flag used for value that is above normal reference range
HR	heart rate

I	‘substantial’ increase from baseline for vital signs parameters increase in QTcF interval from baseline
ICH	International Council for Harmonisation
IMP	investigational medicinal product
IV	intravenous
L	flag used for value that is below normal reference range
LLOQ	lower limit of quantification
LOCF	last observation carried forward
LOD	limit of detection
Max	maximum
MBq	megabecquerel
MedDRA	Medical Dictionary for Regulatory Activities
µCi	microcurie
Min	minimum
n	number of subjects with an observation
N	number of subjects in the dataset
NA	not applicable
NC	not calculated
ND	not detected
NMT	no more than
NR	not reportable
NS	no sample
PI	principal investigator
PK	pharmacokinetic
PT	preferred term

QC	quality control
RAP	reporting analysis plan
SAE	serious adverse event
SD	standard deviation
SDTM	study data tabulation model
SF	significant figure
SI	substantial increase in QTcF interval from baseline
SOC	system organ class
SOP	standard operating procedure
TFL	tables, figures and listings
TR	total radioactivity
WB	whole blood
WHO	World Health Organisation

3 Introduction

This document details the following for Quotient Sciences (Quotient) Study QSC204283 (GP42662):

- criteria to be used for the definition of the populations and analysis sets relating to safety, pharmacokinetic (PK) and mass balance data
- handling of missing data
- proposed tables, figures and listings for demographic, dosing, PK, mass balance and safety data
- methods for PK parameter estimation and the formal statistical analysis

This document has been compiled according to the Quotient standard operating procedure (SOP) “Production of Reporting and Analysis Plans” and has been written based on information contained in the final study protocol version 3.0 dated 19 Jan 2021.

3.1 Responsibilities

The Data Sciences Department at Quotient will be responsible for the production of the following items using Quotient SOPs: Clinical Data Interchange Standards Consortium (CDISC) study data tabulation model (SDTM) and analysis data model (ADaM) datasets, PK parameter estimation and output, mass balance parameter estimation and output; including all summary tables, figures and data listings (TFLs), and formal statistical analysis; and the clinical study report (CSR).

Quotient will provide three sets of TFLs during the study:

- after database close but prior to database lock for Genentech, Inc.
- post database lock TFLs (draft) for Genentech, Inc review and
- post-review TFLs (final) for inclusion into the CSR

Quotient will be responsible for the quality control (QC) of all deliverables prior to the client review (Section 13.2).

Metabolite profiling will be the responsibility of Genentech, Inc., and will be the subject of a separate Analytical Work Plan. These aspects will be reported separately from the Clinical Study Report as a standalone document.

3.2 Definitions

3.2.1 Subject Definitions

During the clinical phase of the study, an evaluable subject is defined as a subject;

- Part 1: who has provided mass balance and PK samples for up to 480 hours (up to Day 21) or until they have met the mass balance discharge criteria (i.e., cumulative recovery of radioactivity exceeds 90% of the administered dose; OR radioactivity in urine and feces is less than 1% of the administered dose over a 24 hour period on 2 consecutive PK sample collection days, as determined by quick counts).
- Part 2: who has received an investigational medicinal product (IMP) and has sufficient drug concentration measurements up to 168 hours after dosing for

evaluation of defined PK parameters for each treatment, and have completed all planned safety assessments up to 168 hours after dosing for each treatment.

These will be monitored during the clinical phase to identify any requirement for replacement subjects (i.e. Part 2). This definition will not be used during the reporting phase including the identification of analysis populations and datasets.

An enrolled subject is defined as a subject who signed the informed consent, qualified per the inclusion/exclusion criteria and were allocated a unique identification number (Part 1) or were randomized (Part 2).

3.2.2 Definition of Treatments

Throughout the reporting of the study, IMP will be referred to as treatments will be reported as detailed in Table 1 below:

Table 1 Study Treatments

Part	Treatment	Description	Label for Reporting Purposes
1	A	[^{14}C]-GDC-9545 capsule, 30 mg ([NMT 4.6 MBq[124 µCi]) in fasted state	[14C]-GDC-9545 Cap
2	B	GDC-9545 IV administration of 30 mg as a solution for infusion, 3 mg/mL (10 mL), over 30 min in fasted state	GDC-9545 IV
	C	GDC-9545/F12 capsule, 30 mg in fasted state	GDC-9545/F12 Cap
	D	GDC-9545/F18 capsule, 30 mg in fasted state	GDC-9545/F18 Cap

3.2.3 Definition of Visits

For clinical data, visits will be referred to as Day throughout this document and will be referred to Screening, Day -1 (Admission) and Day 1 through to Day 42 (Part 1) and Day 1 through to Day 8 of the respective treatment period and follow up (14 to 16 days after final dose) [Part 2]. Time points within these days are detailed in the schedule of activities in Appendix 1 and 2, for Part 1 and Part 2 respectively.

Baseline is defined as nominally the last measurement recorded prior to the first dose of IMP for Part 1 and last measurement recorded prior to receiving IMP for each dosing period in Part 2.

4 Objectives

4.1 Primary Objectives

The primary objectives of this study are:

- To determine the mass balance and routes of elimination of [^{14}C]-GDC-9545 following a single oral dose of [^{14}C]-GDC-9545 capsule, 30 mg containing not more than (NMT) 4.6 megabecquerel (MBq; 124 microcurie [µCi]) (Part 1)
- To assess the PK of GDC-9545 and total drug-derived material in plasma following a single oral dose of [^{14}C]-GDC-9545 capsule, 30 mg (NMT 4.6 MBq [124 µCi]) (Part 1)

- To determine the absolute bioavailability of an oral GDC-9545/F12 capsule, 30 mg and an oral GDC-9545/F18 capsule, 30 mg (Part 2)
- To determine the relative bioavailability of GDC-9545/F18 capsule, 30 mg compared to the GDC-9545/F12 capsule, 30 mg (Part 2)

4.2 Secondary Objectives

The secondary objectives of this study are:

- To characterize and identify metabolites of [^{14}C]-GDC-9545 in plasma, urine, and feces (Part 1)[a]
- To characterize the PK of GDC-9545 following oral and IV administration (Part 2)
- To evaluate the safety and tolerability of single doses of GDC-9545 (Parts 1 and 2)

4.3 Study Endpoints

4.3.1 Primary Endpoints

The primary endpoints of this study are:

- Mass balance recovery of total radioactivity (TR) in all excreta (urine and feces): $CumA_e$ and $CumF_e$ (Part 1)
- Determination of routes and rates of elimination of [^{14}C]-GDC-9545 by A_e, $CumA_e$, F_e and $CumF_e$ by interval for all excreta (urine and feces) (Part 1)
- Calculation of PK parameters as appropriate for GDC-9545 (plasma only) and TR (plasma and whole blood) (Part 1)
- Assessment of the concentrations of TR in whole blood and plasma (Part 1)
- Evaluation of whole blood:plasma concentration ratios for TR (Part 1)
- Absolute bioavailability assessment based on the PK parameter $AUC_{0\text{-inf}}$ for GDC-9545 (Part 2)
- Relative bioavailability assessment based on the PK parameters C_{max} and $AUC_{0\text{-inf}}$ for GDC-9545 (Part 2)

4.3.2 Secondary Endpoints

The secondary endpoints of this study are:

- Characterization of abundant metabolites by liquid chromatography-high resolution mass spectrometry (Part 1)[a]
- Calculation of PK parameters as appropriate for GDC-9545 in plasma only (Part 2)
- Incidence and severity of adverse events (AEs) [Parts 1 and 2]
- Incidence of abnormalities in laboratory safety tests, 12-lead ECGs and vital sign measurements (Parts 1 and 2)

Note the objective and endpoint with [a] are related to metabolite profiling and identification hence will be reported separately from the CSR.

5 Study Design

5.1 Brief Description

5.1.1 Part 1

Part 1 is an open-label, single-treatment design to evaluate the mass balance and routes of elimination of [^{14}C]-GDC-9545. It is planned to enroll 6 subjects to ensure data in a minimum of 4 evaluable subjects

Each subject will receive a single oral dose of [^{14}C]-GDC-9545 capsule, 30 mg (NMT 4.6 MBq [124 µCi]) with approximately 240 mL water in the fasted state (Treatment A).

Subjects will undergo preliminary screening procedures for the study up to 28 days (Day -28 to Day -2) before [^{14}C]-GDC-9545 administration on Day 1. Subjects will be admitted in the morning on the day prior to [^{14}C]-GDC-9545 administration (Day -1) and will be dosed in the morning of Day 1 following an overnight fast of a minimum of 10 hours.

It is planned that subjects will remain resident in the clinical unit until 480 hours post-dose (Day 21) when they will be discharged from the clinical unit.

It is planned that subjects will be released as a group when all subjects have achieved the following mass balance discharge criteria:

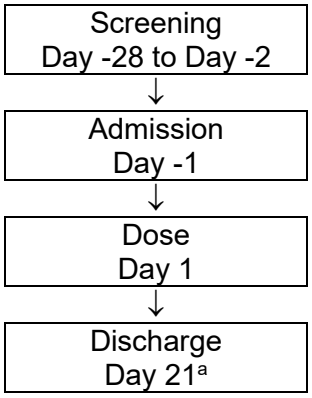
- Cumulative recovery of radioactivity exceeds 90% of the administered dose; OR
- Radioactivity in urine and feces is less than 1% of the administered dose over a 24 hour period on 2 consecutive PK sample collection days, as determined by quick counts

This may result in the subjects being discharged as a group prior to completion of the planned residency period. Once the mass balance discharge criteria have been achieved, collection of all samples (blood, urine, and feces) will be stopped and the subjects will undergo discharge assessments. If the mass balance discharge criteria have not been met by all subjects by Day 21, subjects will be discharged from the clinical unit and those who have not met discharge criteria will return for outpatient visits every 7 days for a 24-hour sample collection interval (i.e., subjects will be resident in the clinical unit for 24 hours during each return visit) until the mass balance discharge criteria are met (the maximum number of 24-hour return visits will not exceed 3). During the period of weekly collection, mass balance cumulative recovery will be estimated by means of interpolation.

If additional residency is not considered appropriate or necessary, then home collections of urine and/or feces may be requested at the discretion of the Investigator for individual subjects.

Figure 1 presents an overview of the study design for Part 1.

Figure 1 Overview of Part 1 Design



[a] Subjects may be discharged as a group earlier if the mass balance discharge criteria have been achieved. If the criteria have not been met by Day 21, subjects will be discharged from the clinical unit and those who have not met the discharge criteria will return for outpatient visits every 7 days for a 24-hour sample collection interval until the mass balance discharge criteria are met (the maximum number of 24-hour return visits will not exceed 3). If additional residency is not considered appropriate or necessary, then home collections of urine and/or feces may be requested at the discretion of the Investigator for individual subjects.

5.1.2 Part 2

Part 2 is a randomized, open-label, three-treatment, two-sequence crossover design conducted over three periods. It is planned to enroll 10 subjects to ensure data in a minimum of 8 evaluable subjects.

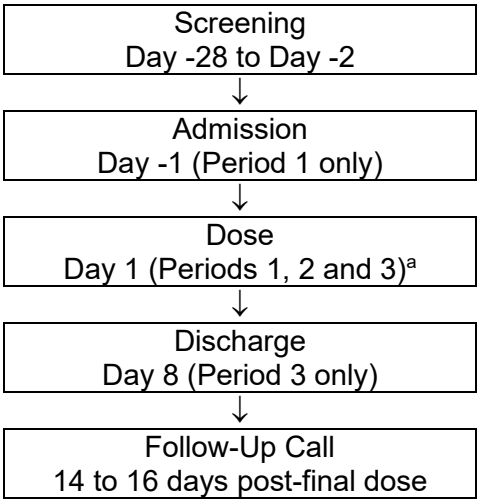
Subjects will undergo preliminary screening procedures for the study up to 28 days (Day -28 to Day -2) before GDC-9545 administration on Day 1 of Period 1. Subjects will be admitted in the morning on the day prior to the first GDC-9545 administration (Day -1 of Period 1). Subjects will be resident in the clinical unit from the morning of Day -1 in Period 1 until Day 8 in Period 3 (i.e., for 28 to 29 consecutive nights that will cover all 3 treatment periods).

Subjects will be randomly allocated to one of two treatment sequences (BCD and BDC; see Section 5.4.2) on the morning of Period 1. For each treatment period, subjects will be dosed in the morning of Day 1 following an overnight fast of a minimum of 10 hours. The treatment descriptions are given in Table 1.

For Treatment B (see Table 1), to assess tolerability of the IV administration, the first subject will be dosed as a sentinel; then, at least 4 hours later, the second subject will be dosed only if there are no acute safety findings for the first subject. If the first two subjects tolerated the IV dose, in the opinion of the Principal Investigator (PI) and Medical Monitor per the criteria in protocol Section 6.8.1**Error! Reference source not found.**, the remaining subjects will be dosed. The third subject will be dosed at least 20 hours after the second subject (i.e., at least 24 hours after the first subject). All subsequent dosing of the IV formulation will be staggered by at least 15 minutes.

Figure 2 presents an overview of the study design for Part 2.

Figure 2 Overview of Part 2 Design



[a] Subjects will receive Treatments B in Period 1, and C and D in Periods 2 and 3 in a randomized manner. There will be a minimum washout of 10 days between each IMP administration.

5.2 Criteria for In-Study Decisions

No interim analyses are planned for Part 1.

The following in-study decision will be made during Part 2 of this study:

- Progression from sentinel group to main group where sentinel dosing is used for Treatment B

For Treatment B, to assess tolerability of the IV administration, the first subject will be dosed as a sentinel; then, at least 4 hours later, the second subject will be dosed only if there are no acute safety findings for the first subject. If the first two subjects tolerated the IV dose, in the opinion of the Principal Investigator and Medical Monitor, the remaining subjects will be dosed. The third subject will be dosed at least 20 hours after the second subject (i.e., at least 24 hours after the first subject). All subsequent dosing of the IV formulation will be staggered by at least 15 minutes.

The decision to proceed with the main group will be made by the Investigator, based on safety data until up to 24 hours post-dose for the two sentinel subjects. The Investigator will inform the Sponsor of any safety concerns.

The decision to proceed to the next dose level will be based on safety and tolerability data. The following data are required:

- Adverse events
- ECGs
- Vital signs

5.3 Study Sample Size

For Part 1, it is planned to enroll 6 subjects to ensure data in a minimum of 4 evaluable subjects. For Part 2, it is planned to enroll 10 subjects to ensure data in a minimum of 8 evaluable subjects. No replacement subjects are to be used in Part 1 of this study. Up to 4 replacement subjects are permitted in Part 2 of this study to ensure there are 8 evaluable subjects.

The study is exploratory and no formal sample size calculation has been made. Based on experience from previous studies of a similar design, a sample size of 6 subjects for Part 1 and 10 subjects for Part 2 is considered appropriate to meet the objectives of the study.

5.4 Randomization (including Replacement Subjects)

5.4.1 Part 1

Part 1 is non-randomized; therefore a randomization schedule will not be produced.

Eligible subjects will be assigned a unique identification number on the morning of dosing (Period 1, Day 1) according to the code [redacted] to [redacted] for Part 1, using the lowest number available.

All subjects in Part 1 will receive Treatment A in Period 1 (see Table 1).

5.4.2 Part 2

Using a computer-generated randomization schedule, subject numbers will be allocated to one of two treatment sequences (Table 2) in Part 2. The allocation will be balanced with 5 subjects assigned to each of the treatment sequences. The treatment descriptions are given in Table 1.

Table 2 Part 2 Treatment Sequences

Treatment Sequence	Period 1	Period 2	Period 3
BCD	B	C	D
BDC	B	D	C

Eligible subjects will be assigned a unique identification number on the morning of dosing in Period 1 according to the code [redacted] to [redacted] for Part 2, using the lowest number available. Replacement subjects will be allocated subject numbers [redacted] to [redacted] where the last 2 digits are the same as those of the original subject (e.g., if Subject [redacted] withdraws the replacement will have Subject Number [redacted]). Replacement subjects will be assigned to the same treatment sequence as the subject they replaced and will receive any treatments that the replaced subject did not receive in addition to any treatments that are required to make the required comparison of interest.

5.5 Blinding Issues

This is an open-label study and therefore blinding is not required.

6 Populations and Analysis Sets

6.1 Safety Population and Safety Analysis Set

The safety population will be defined separately for each study part including all subjects who have received at least one dose of IMP of the respective part.

The safety analysis set will be defined separately for each study part and will be defined on a treatment basis and will include all relevant data from the subjects included in the safety population who have received that treatment.

The safety population will be confirmed by Quotient with approval from Genentech after database lock and will be summarized for the populations table and to determine the subjects to be included in the safety analysis set.

The safety analysis set will be confirmed by Quotient with approval from Genentech at the same time as the safety population and will be summarized for the analysis of demographic and baseline characteristics, and all safety data.

All enrolled subjects will be used for the safety data listings.

6.2 Mass Balance Population and Mass Balance Analysis Set

In Part 1, the mass balance population will include all subjects who have received a dose of IMP and who have evaluable total radioactivity concentration (urinary and fecal) data and who have no protocol deviations that affect the mass balance analysis. Such protocol deviations would include anything that affects the accurate measurement of the amount of urine or feces collected or any adverse events that may affect the mass balance analysis, for example:

- Spillage of urine and/or feces
- Missing collections
- Adverse events that may affect the mass balance analysis*

*for example, if vomiting is observed, this will be assessed on a case by case basis to determine the potential impact on the mass balance recovery

The mass balance population will be confirmed by Quotient with approval from Genentech once all urinary and fecal data have been received and will be summarized for the populations table and to determine the subjects to be included in the mass balance analysis set

The mass balance analysis set will include all relevant data from the subjects included in the mass balance population who have received Treatment A.

If required, a mass balance analysis subset or subsets will also be documented by Quotient, with approval from Genentech, at the same time as the mass balance population and analysis set, if additional subjects are required to be excluded from the summary tables and figures (for example to exclude subjects who have incomplete collections for one matrix).

All enrolled subjects will be used for the mass balance data listings and individual figures. The mass balance population will be used for the populations table. The mass balance analysis set and/or the mass balance analysis subset(s), if defined, will be used for the provision of mass balance summary tables and figures and will be documented as the same time as the mass balance population.

The mass balance population is applicable to Part 1 only.

6.3 Pharmacokinetic Population and Pharmacokinetic Analysis Sets

The PK population will be defined separately for study parts 1 and 2 and will include all subjects who have received at least one dose of IMP in each study part and who satisfy the following criteria for at least 1 profile:

- No missing samples or invalid post-dose analytical results at critical time points e.g. around Cmax
- No relevant protocol deviations which may impact the study objectives with respect to the PK endpoints
- For Part 1 & 2 oral doses: no relevant AEs, such as vomiting, which suggest that the whole dose was not available for absorption for a particular subject
- For Part 2 intravenous dose: no relevant AEs, which suggest that the whole dose was not fully delivered for a particular subject

The PK analysis set will be defined on a per-treatment basis and will include all relevant data from the subjects included in the PK population who have received that treatment.

Individual subjects (i.e. on a per treatment basis) will be excluded from the PK analysis set where deemed appropriate such as if the subject's data for the treatment affected did not meet the bullet point criteria above for at least one individual profile (i.e. analyte), or other study emergent point related to PK analysis or interpretation.

Individual subject profiles (i.e. on a per analyte basis) will be flagged and excluded from the PK summary statistics, where deemed appropriate such as if the profile in the treatment affected did not meet the bullet point criteria above, or other study emergent point related to PK analysis or interpretation.

The PK population and analysis set will be confirmed by Quotient with approval from Genentech following derivation of all PK parameter estimates.

If required, a PK analysis subset(s) will also be documented by Quotient, with approval from Genentech, at the same time as the PK population and analysis set, if additional subjects are required to be excluded from the summary tables and figures or statistical analysis.

All enrolled subjects will be used for the PK data listings. The PK population will be used for the populations table. The PK analysis set and/or the PK analysis subset(s), if defined, will be used for the provision of PK summary tables, figures and formal statistical analysis and will be documented as the same time as the PK population.

7 Subject Disposition, Demographics and Baseline Characteristics

No formal statistical testing will be performed on subject disposition, or on demographic or baseline data. Summaries of subject disposition and analyses populations will be based on all enrolled subjects of the respectively study part and summaries of all other data described in this section will be based on the safety analysis set of the respectively study part unless otherwise stated. Separate tables and listings will be produced for each study part.

7.1 Screening Failures

Data for subjects who have failed screening will be databased but will not be cleaned and therefore will not be included in the SDTM or ADaM datasets or any of the tables, figures or data listings or the CSR.

7.2 Subject Disposition and Withdrawals

The number and percentage of subjects enrolled, dosed, completed and discontinued will be presented by; overall in Part 1 and sequence and overall in Part 2. If all subjects in Part 2 receive all treatments then this will be presented by overall only. If any subjects discontinued from the study early then the number of subjects for each reason for discontinuation will be presented by; overall (Part 1) and sequence and overall (Part 2). However, if none of the subjects discontinued from the study early, then the reasons for discontinuation will not be populated in the summary table. A subject may be discontinued from the study early for 1 reason only.

Subject disposition and withdrawal data will be listed including details of informed consent.

Protocol deviations and any violations of the inclusion/exclusion criteria will also be listed.

7.3 Analysis Populations

A summary table will be produced detailing the number and percentage of subjects in each safety, mass balance (Part 1 only) and PK population by; overall in Part 1 and sequence and overall in Part 2. If all subjects in Part 2 receive all treatments then this will be presented by overall only. The reasons for exclusion from each population will also be included in the summary table. However, if none of the subjects were excluded from a population, then the reasons for exclusion will not be populated in the summary table. A subject may be excluded from a population for more than 1 reason. The denominator for the percentage the number of subjects enrolled (Part 1) and the number of subjects enrolled in the respective sequence (Part 2).

Details of subjects included and excluded in the different analysis populations will be listed.

7.4 Analysis Sets and Subsets

A summary tables for each study part will be produced detailing the number and percentage of subjects in each of the safety/mass balance (Part 1 only)/PK analysis sets and safety/mass balance (Part 1)/PK analysis subsets (if applicable) for each treatment

(Part 2 only) and overall. The table will be based on the relevant population the analysis set/subset is derived from (i.e., the safety/mas balance/PK population). Separate tables will be presented for the safety (analysis set only), mass balance and PK (analysis set and analysis subsets to be included in the same table, if applicable). The reasons for exclusion from each analysis set/subset will also be included in the summary. However, if none of the subjects were excluded from a population, then the reasons for exclusion will not be populated in the summary table. A subject may be excluded from a population for more than 1 reason. The denominator for the percentage is the number of subjects in each population.

Details of subjects included and excluded in the different analysis sets/subsets (where appropriate) will be listed.

7.5 Demographic Characteristics and Lifestyle Details

Demographic data (date of birth, ethnicity, race, sex, height [cm], weight [kg] and body mass index [BMI; kg/m^2]) will be recorded at screening. Age will be calculated using the following formula:

$$\text{Age (years)} = \frac{\text{Date of Informed Consent} - \text{Date of Birth}}{365.25}$$

and will be rounded down to the nearest year (using the SAS Software floor function).

Summary statistics (n, mean, SD, median, minimum and maximum) will be presented for age, height, weight and BMI at screening by; overall in Part 1 and sequence and overall in Part 2. The number and percentage of subjects will be presented by; overall in Part 1 and sequence and overall in Part 2 for ethnicity, race and sex. If all subjects in Part 2 receive all treatments then this will be presented by overall only, unless a sequence effect is observed in the formal statistical analyses described below. The denominator for the percentage is all subjects in the safety analysis set for the respective study part. If any values are missing, a “missing” row will be presented on the table.

Lifestyle details (i.e., smoking history [does the subject smoke, use e-cigarettes or use nicotine replacement products?] and alcohol consumption) will be summarized by; overall in Part 1 and sequence and overall in Part 2 as a categorical variable. If all subjects in Part 2 receive all treatments then this will be presented by overall only.

Demographic and lifestyle data for all enrolled subjects will be listed.

7.6 Medical/Surgical History

Medical/surgical history will be recorded for each subject at the screening visit and updated on admission will be coded using the Medical Dictionary for Regulatory Activities (MedDRA v23.1). All medical/surgical history data will be listed by subject, MedDRA system organ class (SOC) and preferred term (PT).

7.7 Prior and Concomitant Medication

Medications (product name) will be coded using the World Health Organization (WHO) Drug Dictionary Global Drug Reference: 2020 September B3 version using the following Anatomical Therapeutic Chemical (ATC) classification codes

- product name
- preferred name
- drug code
- therapeutic subgroup (ATC 2nd level code)
- chemical subgroup (ATC 4th level code)

Prior medications are defined as medications that start and stop prior to the first dose of IMP. All other medications will be defined as concomitant medications including those that start prior to the first dose of IMP and continue thereafter. Any medications with an unknown start or stop date will be assumed to be concomitant medications unless a partial start or stop date indicates otherwise.

All medications, including coded terms, and the underlying indication for which the medication was given, will be listed. All medications, including coded terms, will be listed One combined data listing of prior and concomitant medications will be provided. All prior medications as defined above will be flagged with a "#" symbol. Within this flagged group medications that started after screening and stopped before dosing of IMP will also be flagged using a "*" symbol.

7.8 Other Baseline Characteristics

All other baseline characteristics, as listed below, at screening and on admission (unless otherwise stated) will be listed by subject for all enrolled subjects of the respectively study part:

- urine drug screen
- alcohol breath test
- carbon monoxide breath test
- virology (screening only)
- urine/serum pregnancy test (serum pregnancy test at screening and urine pregnancy test at admission)
- follicle stimulating hormone (post-menopausal subjects at screening only)
- estradiol (post-menopausal subjects at screening only)
- creatinine clearance (screening only)

8 Efficacy

Not applicable.

9 Mass Balance and Pharmacokinetics

9.1 Mass Balance Parameter Estimation and Reporting

Pharmaron will provide the following concentration and weight data on a per subject basis for each collection interval as specified in the clinical protocol in Part 1:

- Total radioactivity concentration for urine and feces (mass unit equivalents/g)
- Weight of urine (g)
- Feces weight (g) i.e. not fecal homogenate weight

Quotient Data Sciences will be responsible for the calculation of excretion and recovery of total radioactivity in urine and feces and combined urine and feces inclusion into the clinical study report.

9.1.1 Definition of Mass Balance Parameters

A list of mass balance parameter definitions is provided in Table 3.

Table 3 Mass Balance Parameters and Reporting Specifications

Parameter	Definition	Units	DP or SF	No. of DP/SF
Ae(urine)	amount of total radioactivity excreted in urine	Mass unit equiv	SF	3
Fe(urine)	amount of total radioactivity excreted in urine expressed as a percentage of the radioactive dose administered	%	DP	2
CumAe(urine)	cumulative amount of total radioactivity excreted in urine	Mass unit equiv	SF	3
CumFe (urine)	cumulative amount of total radioactivity excreted in urine expressed as a percentage of the radioactive dose administered	%	DP	2
Ae(feces)	amount of total radioactivity eliminated in feces	Mass unit equiv	SF	3
Fe(feces)	amount of total radioactivity eliminated in feces expressed as a percentage of the radioactive dose administered	%	DP	2
CumAe(feces)	cumulative amount of total radioactivity eliminated in feces	Mass unit equiv	SF	3
CumFe(feces)	cumulative amount of total radioactivity eliminated in feces expressed as a percentage of the radioactive dose administered	%	DP	2
Ae(total)	amount of total radioactivity excreted in urine and feces combined	Mass unit equiv	SF	3
Fe (total)	amount of total radioactivity excreted in urine and feces combined expressed as a percentage of the radioactive dose administered	%	DP	2
CumAe(total)	cumulative amount of total radioactivity excreted in urine and feces combined	Mass unit equiv	SF	3
CumFe (total)	cumulative amount of total radioactivity excreted in urine and feces combined expressed as a percentage of the radioactive dose administered	%	DP	2

Dose will be used in the calculation of mass balance parameters as per Table 4.

Table 4 Mass Balance Dose Specifications

Radioactive dose level for mass balance analysis	Actual
Rounded dose level	As provided by Pharmaron

9.1.2 Rules for Mass Balance Parameter Estimation

The following will be calculated for total radioactivity in urine, feces and urine and feces combined by Quotient Data Sciences (note that the amount excreted in pre-dose samples will not be included in the calculation of the cumulative amount excreted or in the calculation of the cumulative percentage of the radioactive dose excreted):

- The amount excreted in urine i.e. Ae(urine) and the amount excreted in feces i.e. Ae(feces) will be calculated for each collection interval using the following formula (where matrix is either urine or feces):

*Ae(<matrix>) = concentration * weight*

- The total amount excreted in urine and feces combined, i.e. Ae(total), will be calculated for each collection interval using the following formula:

Ae(total) = Ae(urine) + Ae(feces)

- The cumulative amount excreted in urine i.e. CumAe(urine) and the cumulative amount excreted in feces i.e. CumAe(feces) will be calculated by the incremental summation of the Ae(<matrix>) across all collection intervals (where matrix is either urine or feces). The amount excreted in the pre-dose sample should not be included in the calculation of the cumulative amount excreted.

- The cumulative amount excreted in urine and feces combined i.e. CumAe(total) will be calculated across all collection intervals using the following formula:

CumAe(total) = CumAe(urine) + CumAe(feces)

- The % amount of the total radioactive excreted in urine i.e. Fe(urine) and the % amount of the total radioactive dose excreted in feces i.e. Fe(feces) will be calculated for each collection interval using the following formula (where matrix is either urine or feces):

*Fe(<matrix>) = 100 * Ae(<matrix>) / Total Radioactive Dose Administered*

- The % amount of the total radioactive dose excreted in urine and feces combined will be calculated for each collection interval using the following formula:

Fe(total) = Fe(urine) + Fe(feces)

- The cumulative % amount of the total radioactive dose excreted in urine i.e. CumFe(urine) and the cumulative % amount of the total radioactive dose excreted in feces i.e. CumFe(feces) will be calculated by the incremental summation of the Fe(<matrix>) across all collection intervals (where matrix is either urine or feces).

The % amount of the total radioactive dose excreted in the pre-dose sample should not be included in the calculation of the cumulative % of dose excreted.

- The cumulative % amount of the total radioactive dose excreted in urine and feces combined will be calculated for each collection interval using the following formula:

CumFe(total) = CumFe(urine) + CumFe(feces)

- Following Day 21, where urine/fecal collections are no longer continuous and spot sampling days (i.e. 24 h) commence, additional interpolation of Ae will be calculated to estimate amount excreted on non-collection days (i.e. over the entire interpolation interval), as follows:

$$A_e\ (interval) = (\frac{A_e\ 24h\ [Day\ x\ +\ Day\ y]}{2}) * \ duration\ of\ interval\ (days)$$

where Day x and Day y are the actual amounts excreted for the preceding and proceeding days of the interpolation interval and the interval is considered to be from Day X+1 to Day Y-1.

Home collections of urine and/or feces may be requested at the discretion of the investigator for individual subjects. For amount excreted and cumulative excretion this will be calculated for all time points including home collection, if applicable

For urine and feces, where a subject has failed to void over a particular collection interval the Amount Eliminated (Ae) will be set to zero.

If part of a void over a particular collection interval is missing due to spillage or accidental discarding, the Ae will still be calculated providing other samples have be collected within the interval. Where no other samples are collected within the interval the data will be set to missing for the purposes of the calculation of Ae, CumAe and CumFe. In both scenarios the data will be flagged to highlight a missing void.

Imputation of non-numerical values reported in the urine and fecal data (i.e. concentrations that are not detected [ND]) will be entered as zero for calculation of parameters such as mean and SD.

When converting urine collection weights to urine volume (if required), the following conversion factor will be used:

1.02 g of urine = 1 mL of urine

This will be calculated in SAS as follows:

Urine weight (g) / 1.02 = Urine volume (mL)

If total radioactivity concentrations in urine have been provided in mass unit/g units the following conversion (if required) will be performed using SAS:

*Concentration (mass units/g) * 1.02 = Concentration (mass units/mL)*

The radioactivity associated with toilet paper may be determined with the approval of Genentech. The results will be reported for each subject as a single value for the whole collection period and included in the calculation of total amount excreted and % of dose recovered. Accidental sources of elimination, e.g., emesis, will be collected and sent for total radioactivity analysis. This will be reported on a case by case basis and details will be included in the documentation of the mass balance population.

9.1.3 Mass Balance Summary Tables

Summary statistics (i.e. n, mean, SD, CV%, minimum, median and maximum) will be presented for amount excreted (Ae) and recovery (Fe) by collection period (including interpolated periods which will be marked with a #) for the following:

- Urine [i.e. Ae(urine) and Fe(urine)] for total radioactivity
- Feces [i.e. Ae(feces) and Fe(feces)] for total radioactivity
- Urine and feces combined [i.e. Ae(total) and Fe(total)] for total radioactivity

In addition, summary statistics (i.e. n, mean, SD, CV%, minimum, median and maximum) will be presented for the cumulative excretion and cumulative recovery by collection period (including interpolated periods which will be marked with a #) for each of the following:

- Urine [i.e. CumAe(urine) and CumFe(urine)] for total radioactivity
- Feces [i.e. CumAe(feces) and CumFe(feces)] for total radioactivity
- Urine and feces combined [i.e. CumAe(total) and CumFe(total)] for total radioactivity

Imputation of non-numerical values reported in the urine and fecal data set (i.e. concentrations that are ND) will be entered as zero for calculation of statistics such as mean and SD.

Finally, summary statistics (i.e. n, mean, SD, CV%, minimum, median and maximum) will be presented for the cumulative excretion and cumulative recovery for the study as a whole for each of the following:

- Urine [i.e. CumAe(urine) and CumFe(urine)] for total radioactivity
- Feces [i.e. CumAe(feces) and CumFe(feces)] for total radioactivity
- Urine and feces combined [i.e. CumAe(total) and CumFe(total)] for total radioactivity

If any subject withdraws prior to the end of a study visit or if subjects have differing collection intervals [(e.g. Day 10 for some subjects and Day 14 for others)] then a last observation carried forward (LOCF) approach will be used whilst calculating cumulative Ae and Fe (i.e. CumAe and CumFe), where the last observed value will be carried forward to the subsequent time point. The number of subjects included at each collection interval will therefore remain the same regardless of subject withdrawals. The LOCF approach will be used for all summary tables detailed above.

9.1.4 Mass Balance Figures

Mean mass balance figures will be presented for the mass balance analysis set.

Mean cumulative excretion (i.e. CumAe) and cumulative recovery (i.e. CumFe) vs time curves will be produced on a linear/linear scale and will include ± SD bars. These plots will be produced for CumAe and CumFe, respectively, with urine, feces and total overlaid:

- Urine [i.e. CumAe(urine) and CumFe(urine)] for total radioactivity
- Feces [i.e. CumAe(feces) and CumFe (feces)] for total radioactivity
- Urine and feces combined [i.e. CumAe(total) and CumFe(total)] for total radioactivity

A legend identifying each profile (i.e. urine, feces and total) will be displayed on the mean plots. Figures will be produced using the LOCF imputation strategy (see Section 9.1.3**Error! Reference source not found.** figures as required). figures as required).

Spaghetti plots of individual cumulative excretion for CumAe(urine), CumAe(feces) and CumAe(total) against actual collection period after dosing will be produced on a linear/linear scale for total radioactivity. In addition, spaghetti plots of individual cumulative recovery for CumFe(urine), CumFe(feces) and CumFe(total) against actual collection period after dosing will be produced on a linear/linear scale for total radioactivity. Each subject's profile will be represented on these plots with a different letter or symbol and a legend will be included on the plots to define the letters/symbols used. All enrolled subjects will be used for the provision of spaghetti plots.

9.1.5 Mass Balance Listings

The sample collection data (e.g. collection intervals) for all urine and fecal samples will be listed. In addition, all total radioactivity concentrations, urine and fecal weights and all mass balance parameters will be listed on a per subject basis. The LOCF approach will be used for all cumulative mass balance parameters. Where LOCF values appear in the listings they will be flagged. In addition, where values were calculated for interpolated days these will be flagged.

9.1.6 Statistical Analysis of Mass Balance Parameters

No formal statistical analysis is required for the mass balance data in this study. Descriptive statistics are considered adequate for a study of this type.

9.2 Pharmacokinetic Parameter Estimation and Reporting

The PK parameters will be estimated where possible and appropriate for each subject profile by non-compartmental analysis methods using Phoenix WinNonlin software (v8.0 or a more recent version, Certara USA, Inc., USA) for:

- GDC-9545 in plasma and total radioactivity in plasma and whole blood in Part 1
- GDC-9545 in plasma in Part 2

Additional parameters may be calculated if required, depending on the data.

9.2.1 Definition of Pharmacokinetic Parameters

Plasma and whole blood PK parameter definitions are provided in Table 5.

Table 5 Plasma and Whole Blood Pharmacokinetic Parameter Definitions and Rounding Specifications

Parameter	Definition	Unit	DP or SF	No. of DP/SF
Cmax	Maximum observed concentration	ng/mL	SF	3
tmax	Time of maximum observed concentration	h	DP	2
AUC(0-t)	Area under the curve from time 0 to the time of last measurable concentration	ng.h/mL	SF	3
AUC(0-inf)	Area under the curve from time 0 extrapolated to infinity	ng.h/mL	SF	3
%AUCextrap	Area under the curve (AUC) from time of the last measurable concentration to infinity as a percentage of the area under the curve extrapolated to infinity	%	DP	2
t1/2	Terminal elimination half-life	h	DP	2
lambda-z	First order rate constant associated with the terminal (log-linear) portion of the curve	1/h	DP	4
CL	Total body clearance calculated after a single intravenous administration	L/h	SF	3
CL/F	Total body clearance calculated after a single extravascular administration where F (fraction of dose bioavailable) is unknown	L/h	SF	3
Vz	Volume of distribution based on the terminal phase calculated using AUC(0inf) after a single intravenous administration	L	SF	3
Vz/F	Apparent volume of distribution based on the terminal phase calculated using AUC(0-inf) after a single extravascular administration where F (fraction of dose bioavailable) is unknown	L	SF	3
F	Absolute bioavailability calculated using AUC(0-inf)	%	DP	2
Frel Cmax	Relative bioavailability based on Cmax	%	DP	2
Frel AUC(0-t)	Relative bioavailability based on AUC(0-t)	%	DP	2
Frel AUC(0-inf)	Relative bioavailability based on AUC(0inf)	%	DP	2
WB:P AUC(0-inf)	Total radioactivity blood to plasma concentration ratio based on AUC(0-inf)	N/A	DP	2
lambda-z lower*	Lower limit on time for values to be included in the calculation of lambda-z	h	DP	2
lambda-z upper*	Upper limit on time for values to be included in the calculation of lambda-z	h	DP	2

DP=decimal places
SF=significant figures
*=these values should be listed but omitted from the descriptive statistics
NA=not applicable

Total radioactivity blood to plasma concentration ratios will also be determined (Part 1 only).

Dose will be used in the calculation of relevant PK parameters as per Table 6.

Table 6 Pharmacokinetic Parameter Dose Specifications

Dose Route	Nominal/Actual	Precision
IV (Part 2, Treatment B only)	Actual	As received from Pharmaron
Oral	Nominal	As per protocol

Absolute bioavailability (F) will be calculated in Part 2 for individual subjects as follows:

$$F = \left\{\frac{\text{AUC [GDC} - 9545](\text{oral})}{\text{AUC [GDC} - 9545](\text{IV})} \times \frac{\text{Dose(IV)}}{\text{Dose(oral)}}\right\} \times 100$$

F will be calculated using AUC(0-inf). If for any reason the AUC(0-inf) is not calculable then an alternative or additional AUC over a partial area may be used to calculate F for all subjects.

The following comparisons will be made:

- GDC-9545/F12 capsule, 30 mg versus GDC-9545 intravenous infusion (absolute bioavailability)
- GDC-9545/F18 capsule, 30 mg versus GDC-9545 intravenous infusion (absolute bioavailability)

Relative bioavailability (Frel) will be calculated in Part 2 for individual subjects as follows: (Frel) will be calculated in Part 2 for individual subjects as follows:

$$\text{Frel} = \left\{\frac{\text{AUC or Cmax (test)}}{\text{AUC or Cmax (reference)}}\right\} \times 100$$

Frel will be calculated using Cmax, AUC(0-t) and AUC(0-inf). If for any reason the AUC(0-inf) is not calculable then an alternative or additional AUC over a partial area may be used to calculate Frel for all subjects.

The following comparison will be made:

- GDC-9545/F18 capsule, 30 mg (test) versus GDC-9545/F12 capsule, 30 mg (reference) [relative bioavailability]

Ratio of GDC-9545 AUC(0-inf) over total radioactivity AUC(0-inf) will be calculated in Part 1 for individual subjects as follows:

$$\frac{\text{AUC}(0-\text{inf})[\text{GDC} - 9545]}{\text{AUC}(0-\text{inf})[\text{Total radioactivity}]}$$

Total radioactivity blood to plasma ratios based on AUC(0-inf) will be calculated in Part 1 for individual subjects as follows:

$$\frac{\text{AUC}(0-\text{inf})[\text{whole blood total radioactivity}]}{\text{AUC}(0-\text{inf})[\text{plasma total radioactivity}]}$$

If for any reason the AUC(0-inf) is not calculable then an alternative or additional AUC over a partial area may be used to calculate ratio of plasma total radioactivity over whole blood total radioactivity.

Total radioactivity blood to plasma ratios will be determined using SAS by the Lead Statistical Programmer (or designee) at the time points defined in the protocol. If either the blood or plasma concentration values are BLQ at any given timepoint the ratio will not be calculated.

When converting blood collection weights to blood volume (if required) for the calculation of the whole blood:plasma ratio, the following conversion factor will be used:

1.06 g of blood = 1 mL of blood

This will be calculated in SAS as follows:

Blood weight (g) / 1.06 = Blood volume (mL)

Alternatively, where total radioactivity concentrations in blood have been provided in mass unit/g units the following conversion will be performed using SAS:

*Concentration (mass units/g) * 1.06 = Concentration (mass units/mL)*

9.2.2 Rules for Pharmacokinetic Parameter Estimation using WinNonlin

The imputation of non-numerical (e.g. below the limit of quantification [BLQ] or below the level of detection [LOD]) or negative values (e.g. pre-dose sampling times) reported in the input data set will be performed as follows for calculation of PK parameters:

- Pre-dose sample times will be entered as zero
- Values that are BLQ* obtained prior to Cmax will be entered as zero
- Values that are BLQ* after Cmax will be treated as missing but where BLQ concentrations are defined as parameters these will be reported as BLQ
- Values that are BLQ* after Cmax may be imputed as zero for the calculation of partial AUCs, in cases where lambda-z cannot be determined
- Values that are measurable after at least 2 consecutive BLQ* values after Cmax will be treated as missing for the calculation of PK parameters
- Values that are reported as “No Result” or “Not Reportable” (NR), “Not Calculated” (NC) or “No Sample” (NS) etc. will be generally be considered missing

* values that are reported as below the LOD will be treated in the same way as samples reported as BLQ.

Missing or unusual concentration values in the input data may be queried to ascertain any underlying cause. Exclusion of missing or unusual concentration values, or repeat bioanalysis of samples, will only be performed if a definitive root cause can be established and approval from Genentech has been obtained. Any exclusions of concentration values or repeat analysis of samples will be documented appropriately.

Plasma and whole blood PK parameters will be estimated using standard Phoenix WinNonlin methods, details of which may be found in the documentation accompanying the WinNonlin software package. The rules specified in Table 7 will be applied:

Table 7 Pharmacokinetic Parameter Estimation Details

Sampling times	Actual for oral doses Actual (relative to start of infusion) for IV doses
Calculation method	Linear up log down
Number of points used for lambda-z	At least 3, not including Cmax
Minimum requirements for AUC	At least 3 consecutive measurable concentrations

Prior to PK parameter estimation the bioanalytical data of GDC-9545 for Part 1 may be corrected to account for the proportion of administered ^{14}C material not measured due to the use of a ^{12}C LC-MS/MS analysis method. Data correction will only be performed if the ^{14}C contribution exceeds 1% of the dose administered. GDC-9545 bioanalytical data will be multiplied by the determined data correction factor in SAS.

Where possible, the terminal elimination rate constant (lambda-z) will be calculated for all subject profiles. The value of lambda-z will be determined by the slope of the regression line of the natural log transformed concentrations vs time.

The WinNonlin determined choice of data points for determination of lambda-z will be reviewed by the pharmacokineticist who may adjust the selection in order to provide a more appropriate fit. The choice of data points for determination of lambda-z for each profile will be confirmed following a documented peer review.

9.2.3 Pharmacokinetic Parameter Reporting Specifications

The following parameters will be reported for each study part, treatment, analyte and matrix as applicable, according to the rounding specifications provided in Table 5:

Part 1 - following oral administration of ^{14}C-GDC-9545 (plasma GDC-9545):

- Cmax, Tmax, AUC(0-t), AUC(0-inf), AUCextrap, T1/2, lambda-z, CL/F, Vz/F, lambda-z lower, lambda-z upper

Part 1 - following oral administration of ^{14}C-GDC-9545 (total radioactivity in plasma and whole blood):

- Cmax, Tmax, AUC(0-t), AUC(0-inf), AUCextrap, T1/2, lambdaz, WB:P AUC(0inf) [whole blood only], lambdaz lower, lambdaz upper

Part 2 - following IV administration (plasma GDC-9545):

- Cmax, Tmax, AUC(0-t), AUC(0-inf), AUCextrap, T1/2, lambda-z, CL, Vz, lambdaz lower, lambdaz upper

Part 2 - following oral administrations (plasma GDC-9545):

- Cmax, Tmax, AUC(0-t), AUC(0-inf), AUCextrap, T1/2, lambda-z, CL/F, Vz/F, F, Frel Cmax, Frel AUC(0-t), Frel AUC(0-inf) , lambdaz lower, lambdaz upper

The flags/footnotes given in Table 8 will be applied to the PK parameters where relevant and will be shown in PK parameter listings. Additional flags may be applied based on emerging data.

Table 8 Pharmacokinetic parameter Flags and Footnotes

Flag	Footnote
a	Adjusted rsq of regression (the goodness of fit statistic for the elimination phase) was <0.9
b	Period used for regression analysis was less than 2-fold the calculated half-life
c	Extrapolated portion of AUC(0-inf) >20%
d	Insufficient post-Cmax data points for estimation of lambda-z
e	Entire profile BLQ, no PK parameters could be calculated
f	Fewer than 3 consecutive measurable concentrations, AUCs not calculated
g	Measurable pre-dose values were observed, however were considered less than 5 % of Cmax

In the event that the adjusted rsq of regression was <0.9 (“a” flag) then lambda-z and parameter estimates derived using lambda-z and AUC(0inf) will be deemed unreliable and will be flagged and listed but excluded from the summary statistics and statistical analysis (Part 2 only).

In the event that the time period used for regression analysis was less than 2-fold the calculated half-life (“b” flag) T1/2 will be flagged, listed, and included in summary statistics.

In the event that the extrapolated portion of AUC(0-inf) >20% (“c” flag), then AUC(0-inf) and parameter estimates derived using AUC(0inf) will be deemed unreliable and will be flagged and listed but excluded from the summary statistics and statistical analysis (Part 2 only).

In the event that there are insufficient post-Cmax data points for estimation of lambda-z (“d” flag) then lambda-z and parameter estimates derived using lambda-z and AUC(0inf) will be reported as ‘NC’.

In the event that there are fewer than 3 consecutive measurable concentrations (“f” flag) then all AUC parameter estimates will be reported as NC.

In the event that measurable pre-dose values less than 5% of Cmax were observed (“g” flag), all parameter estimates for the profiles affected will be listed, flagged and included in summary statistics and formal statistical analysis (Part 2 only).

Note: in the event that measurable pre-dose concentrations greater than 5% of Cmax are observed, requirements for additional flags and further action will be agreed with Genentech and documented at the same time as the PK population.

9.2.4 Bioanalytical and Pharmacokinetic Summary Tables

Summary statistics (i.e. n, mean, SD, CV%, median, minimum, maximum, geometric mean, geometric SD and geometric CV%) of concentration data will be calculated for the following analytes/matrices by treatment. The number of BLQ values (n#) per time point will also be presented. Geometric statistics will not be calculated for Day 1, pre-dose concentrations.

- Plasma concentrations of GDC-9545 by time point
- Plasma concentrations of total radioactivity by time point (Part 1 only)
- Whole blood concentrations of total radioactivity by time point (Part 1 only)
- Whole blood:plasma concentration ratio of total radioactivity by time point (Part 1 only)

Summary statistics (i.e. n, mean, SD, CV%, median, minimum and maximum) of plasma and whole blood PK parameters will be calculated for GDC-9545 (plasma only) and total radioactivity (where applicable) by treatment. Geometric mean, geometric SD and geometric CV% will be presented for all plasma and whole blood PK parameters except Tmax.

Non-measurable values reported in the plasma and whole blood concentration data (i.e. values that are BLQ), will be entered as zero for the determination of summary statistics with the exception of geometric means, geometric SD and geometric CV%, where BLQ values will be imputed as half the lower limit of quantification (LLOQ) value. This also applies to any concentrations that are defined as PK parameters. Data recorded as NR, NS or NC will be handled as missing (i.e. no assumption will be made about the actual concentration).

9.2.5 Bioanalytical and Pharmacokinetic Figures

Mean, spaghetti and individual plasma and whole blood concentration vs time plots will be produced on both the linear/linear scale and on log10/linear scale.

For all plots on a linear/linear scale, post-dose concentration values reported as BLQ will be set to zero, up to the point at which all concentrations fall below BLQ, after which they will be presented as missing.

For all plots on a log 10/linear scale, post-dose concentration values reported as BLQ will be set to half the BLQ value, up to the point at which all concentrations fall below BLQ, after which they will be presented as missing.

Where curves from multiple treatment regimens or subjects are overlaid on the same plot, symbols will be used to identify different subjects/ treatment regimens and a legend will be included on the plots to define the symbols used.

Mean plasma and whole blood concentration vs time plots (using nominal times) will be produced for:

- Whole blood and plasma concentrations of total radioactivity on same plot (Part 1)
- Plasma concentrations of GDC-9545 and total radioactivity on the same plot (Part 1)

- Plasma concentrations of GDC-9545 for the oral dose(s) and IV dose on the same plot (Part 2)

These will be produced as follows:

- Linear/linear scale using arithmetic mean concentrations (error bars ± arithmetic SD)
- Log10/linear scale using geometric mean concentrations (error bars x/÷ geometric SD)

Separate concentration vs time spaghetti plots (using actual sampling time after dosing) will be produced for each treatment and analyte (where applicable) with each plot displaying 1 line per subject.

Individual concentration vs time plots (using actual sampling times after dosing) will be produced separately for each individual subject with all treatments and analytes/matrices (where applicable) on the same plot.

9.2.6 Bioanalytical and Pharmacokinetic Listings

The sample collection data (e.g. collection times) for PK samples will be listed. In addition, all concentration data and PK parameters will be listed on a per subject basis. Any flags used will be included as a footnote with the appropriate definition.

9.2.7 Statistical Analysis of Pharmacokinetic Parameters

No formal statistical analysis will be carried out on Part 1 data.

Part 2

Absolute Bioavailability

Formal statistical analysis will be performed on the PK parameter AUC(0-inf). AUC(0inf) will undergo a natural logarithmic transformation and will be analyzed using mixed effect modelling techniques. The model will include terms for treatment and sequence fitted as fixed effects and subject nested within sequence as a random effect (i.e., assuming a compound symmetry covariance structure). The following treatment comparisons (test versus reference) are of interest:

- GDC-9545/F12 Capsule (test) compared to GDC-9545 IV dose (reference)
- GDC-9545/F18 Capsule (test) compared to GDC-9545 IV dose (reference)

Only subjects who received and have reliable estimates of AUC(0-inf) for at least the reference IV dose and one of the test capsules will be included in the statistical analysis.

If the number of subjects with reliable estimates of AUC(0-inf) for any comparison falls below the planned number of evaluable subjects, then consideration will be given as to whether formal statistical analysis will be performed or if an alternative AUC parameter will be used.

The adjusted means including differences from the comparisons and their associated 90% CIs obtained from the model will be back transformed on the log scale to obtain

adjusted geometric means, adjusted geometric mean ratios (GMRs) and 90% CIs of the ratios. GMRs and 90% CIs for each comparison will be presented.

In addition, intra-subject variability values (denoted as CVw in the results table) will also be presented.

The intra-subject variability values will be calculated for all treatments combined and are obtained from the residual term from the SAS Software output. These values are calculated as follows:

$$CVw = 100 \times (\exp(\text{Mean Square Error}) - 1)^{1/2}$$

The statistical analysis will be performed using actual treatment received. The model will be fitted using the SAS Software procedure PROC MIXED, the method will specified as Restricted Maximum Likelihood and the denominator degrees of freedom for the fixed effects will be calculated using Kenward and Roger's method [1]. The following is an example of the SAS Software code that will be used:

```
PROC MIXED DATA=<input dataset name> METHOD=REML ORDER=INTERNAL;
           CLASS SUBJIDN TRTAN TRTSEQPN;
           MODEL LVAR = TRTAN TRTSEQPN / OUTP=PRED DDFM=KR;
           RANDOM SUBJIDN(TRTSEQPN);
           ESTIMATE <relevant pairwise treatment comparisons> / CL ALPHA=0.10;
           LSMEANS TRTAN / ALPHA=0.10;
           ODS OUTPUT LSMEANS=MEANS ESTIMATES=EST COVPARMS=CVW;
RUN;
```

where

- LVAR is the natural log transformed PK parameter of interest
- SUBJIDN is the numeric subject identifier variable
- TRTSEQPN is the numeric sequence variable for the planned sequence received
- TRTAN is the numeric treatment variable for the actual treatment received

Relative Bioavailability

Formal statistical analysis will be performed on the PK parameters Cmax, AUC(0-t) and AUC(0-inf). The PK parameters will undergo a natural logarithmic transformation and will be analyzed using mixed effect modelling techniques. The model will include terms for treatment, sequence and period fitted as fixed effects and subject nested within sequence as a random effect (i.e., assuming a compound symmetry covariance structure). The null hypothesis is that there is no difference between GDC-9545/F18 (test) and GDC-9545/F12 (reference).

Only subjects with parameters for both treatments will be included in the statistical analysis.

The adjusted means including differences from the comparisons and their associated 90% CIs obtained from the model will be back transformed on the log scale to obtain adjusted geometric mean ratios (GMRs) and 90% CIs of the ratios. GMRs and 90% CIs for each comparison will be presented.

In addition, p-values associated with the treatment comparison and CVw values will also be presented. The intra-subject variability values will be calculated for both treatments combined using the formula shown above (i.e. absolute bioavailability).

The fixed effects table from the model with F-statistic and p-value for the relevant effects will be presented in a separate table.

The statistical analysis will be performed using actual treatment received and planned sequence. The model will be fitted using the SAS Software procedure PROC MIXED, the method will specified as Restricted Maximum Likelihood and the denominator degrees of freedom for the fixed effects will be calculated using Kenward and Roger's method [1]. The following is an example of the SAS Software code that will be used:

```
PROC MIXED DATA=<input dataset name> METHOD=REML ORDER=INTERNAL;
           CLASS SUBJIDN TRTAN APERIODN TRTSEQPN;
           MODEL LVAR = TRTAN APERIODN TRTSEQPN/ OUTP=PRED DDFM=KR;
           RANDOM SUBJIDN(TRTSEQPN);
           ESTIMATE <relevant pairwise treatment comparisons> / CL ALPHA=0.10;
           LSMEANS TRTAN / ALPHA=0.10;
           ODS OUTPUT LSMEANS=MEANS ESTIMATES=EST COVPARMS=CVW;
RUN;
```

where

- LVAR is the natural log transformed PK parameter of interest
- SUBJIDN is the numeric subject identifier variable
- APERIODN is the numeric period variable
- TRTAN is the numeric treatment variable for the actual treatment received
- TRTSEQPN is the numeric sequence variable for the planned sequence received

If there are any deviations from the planned treatment or sequence, then the analysis models specified above or methods of analysis may be re-evaluated, as appropriate. Details of any deviations from the planned analysis will be documented in the CSR.

For each analysis, distributional assumptions underlying the statistical analyses will be assessed by visual inspection of residual plots. Normality will be examined by normal probability plots, while homogeneity of variance will be assessed by plotting the residuals against the predicted values for the model. If the distributional assumptions for the parametric approach are not satisfied, then additional sensitivity analyses may be performed including the removal of potential outliers or the use of non-parametric methods to assess the robustness of the original analysis. This will be documented in the CSR together with the reasoning supporting the most appropriate action taken, if applicable. In general terms the results of the original analysis will always be presented in the CSR.

10 Safety Assessments

Safety data summaries will be presented by actual treatment and the respectively safety analysis set will be used throughout.

Separate summary tables and listings will be produced for each study part.

10.1 Extent of Exposure and Treatment Compliance

The total dose given (as measured in mg) and the TR dose (as measured in MBq and microcurie [µCi]) will be summarized (i.e., n, mean, SD, median, minimum and maximum) in Part 1.

The number and percentage of subjects dosed with IMP will be summarized for each treatment and overall in Part 2.

Dosing details (including the date and time of all IMP administrations and any comments) will be listed for all enrolled subjects. Any recorded deviations from the planned dosing treatment will be listed as protocol deviations.

10.2 Meal Details

Meal details as recorded on the eCRF will be listed for all enrolled subjects of the respectively study part. Any recorded deviations from the planned meal times will be listed as protocol deviations.

10.3 Adverse Events

Throughout the study, all adverse events (AE) will be evaluated by the PI and noted in the AE section of the eCRF. An AE is any untoward medical occurrence in a clinical investigation subject administered a pharmaceutical product, regardless of causal attribution. Adverse events that occur before dosing which is not considered serious will not be included in the database and hence, will not be reported.

AEs will be coded using the Medical Dictionary for Regulatory Activities (MedDRA v23.1 or more recent version), and reported by SOC and PT.

For Part 2, AEs will be assigned to the treatment of the period in which the AE first occurred. Where the severity of an AE intensifies or symptoms change in a subsequent period, this will be defined as a new AE and included under the treatment associated with the subsequent period. Adverse events that occur during the washout period will be assigned to the treatment the subject received during the period immediately before the washout period.

An IMP-related AE is any AE where a causal relationship with the IMP is at least a reasonable possibility. When considering their relationship to IMP, AEs will be classified as follows

- “YES” (i.e., there is a plausible temporal relationship between the onset of the adverse event and administration of the study drug, and the adverse event cannot be readily explained by the subject's clinical state, intercurrent illness, or concomitant therapies; and/or the adverse event follows a known pattern of response to the study drug; and/or the adverse event abates or resolves upon discontinuation of the study drug or dose reduction and, if applicable, reappears upon re-challenge.)
- “NO” (i.e., evidence exists that the adverse event has an etiology other than the study drug [e.g., pre-existing medical condition, underlying disease, intercurrent illness, or concomitant medication]; and/or the adverse event has no plausible temporal relationship to administration of the study drug [e.g., cancer diagnosed 2 days after first dose of study drug]).

The severity of AEs will be assessed according to the National Cancer Institute Common Terminology Criteria for Adverse Events (NCI CTCAE, v5.0) grading scale when considering their initial and maximum severity separately. All summary tables will be based on maximum severity but relevant listings will include both initial and maximum severity: The same grading scale for events listed in NCI CTAE and those not specifically listed in NCI CTCAE will be used, see below:

Grade	Severity
1	Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; or intervention not indicated
2	Moderate; minimal, local, or non-invasive intervention indicated; or limiting age appropriate instrumental activities of daily living[a]
3	Severe or medically significant, but not immediately life threatening; hospitalization or prolongation of hospitalization indicated; disabling; or limiting self-care activities of daily living[b, c]
4	Life-threatening consequences or urgent intervention indicated[d]
5	Death related to AE[d]

[a] Instrumental activities of daily living refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.
[b] Examples of self-care activities of daily living include bathing, dressing and undressing, feeding oneself, using the toilet, and taking medications, as performed by subjects who are not bedridden.
[c] If an event is assessed as a "significant medical event," it must be reported as a serious AE.
[d] Grade 4 and 5 events must be reported as serious AEs.

If the severity or relationship to IMP of a AE is missing, the severity/relationship will be tabulated as “missing” in the summary tables.

Where the start date of an AE is missing and the stop date is on or after the day of first dose of IMP or both the start and stop dates are missing then a “worst-case” scenario will be assumed, i.e., the AE is assumed to have occurred post-dose. If a partial start date/time is available, then the event will be considered to have occurred post-dose unless the partial information suggests otherwise.

10.3.1 Summary Tables for Adverse Events

Any AEs which occurred pre-dose will be excluded from the summary tables but will be listed.

Descriptive statistical methods will be used to summarize the AE data.

AEs with the following preferred terms will be combined and presented together:

- “sinus bradycardia” and “bradycardia”
- “neutropenia” and “neutrophil count decreased”
- “thrombocytopenia” and “platelet count decreased”
- “thrombocytosis” and “platelet count increased”
- “leukopenia” and “leukocyte count decreased”
- “leukocytosis” and “leukocyte count increase”

The number and percentage of subjects reporting each AE will be summarized for both SOC and PT. For summaries by SOC and PT, with the exception of AEs by severity and relationship to IMP, the number of subjects and the number of events will be summarized. For summaries by severity and relationship only the number of subjects will be summarized.

For counts of subjects experiencing events the following will apply:

- a subject experiencing AEs in more than one body system, within a study part/period, will be counted once in the total number of subjects with AEs in that study part/period;
- a subject with more than 1 AE in the same SOC, within a study part/period, counts only once at the SOC level;
- a subject with more than 1 AE in the same PT, within a study part/period, counts only once at the PT level;
- a subject with either or both PT for the combined preferred terms, within a study part/period, counts only once at the combined PT level.

For event counts, all events are included.

When it is necessary to calculate percentages, the denominator will be the total number of subjects in the safety analysis set for that treatment or study part/period and the numerator will be the total number of subjects reporting a AE within the relevant category.

Summaries presented for SOC and PT will be presented in descending order of frequency overall i.e., most frequently reported SOC in the study part and then by most frequently reported PT in the study part within each SOC.

10.3.1.1 Overall Summary of Adverse Events

The following will be summarized by treatment and overall (Part 2 only) for the safety analysis set:

- number and percentage of subjects reporting at least 1 AE
- number and percentage of subjects reporting at least 1 Grade 3 AE
- number and percentage of subjects reporting at least 1 Grade 4 AE
- number and percentage of subjects reporting at least 1 IMP-related AE
- number and percentage of subjects reporting at least 1 AE of special interest
- number and percentage of subjects reporting at least 1 serious AE
- number and percentage of subjects reporting at least 1 AE leading to IMP withdrawal
- number and percentage of subjects reporting at least 1 Grade 5 AE

- total number of AEs
- total number of Grade 3 AEs
- total number of Grade 4 AEs
- total number of IMP-related AEs
- total number of AEs of special interest
- total number of serious AEs
- total number of AEs leading to IMP withdrawal
- total number of Grade 5 AEs

10.3.1.2 Summary of Adverse Events

All subjects reporting AEs will be summarized by treatment. Counts will be given for number of subjects and number of events. Subjects experiencing more than 1 AE within a treatment will be counted only once for number of subjects but will be counted more than once for number of events.

Additionally, subjects reporting AEs will be summarized for SOC and PT treatment. Counts will be given for number of subjects and number of events. For programming purposes counts of number of subjects will be by maximum severity i.e., subjects experiencing more than 1 episode of a AE within a treatment will be counted only once within each SOC and PT using the most severe episode.

10.3.1.3 Summary of Adverse Events by Severity

All subjects reporting AEs will be summarized by severity and treatment. Counts will be given for number of subjects, not number of events. Counts will be given by maximum severity (i.e., subjects experiencing more than 1 AE within a treatment will be counted only once using the most severe episode).

Additionally, subjects reporting AEs will be summarized for SOC and PT by maximum severity and treatment. Counts will be given for total number of subjects, not for events. Counts by maximum severity will be given (i.e., subjects experiencing more than 1 AE within a treatment will be counted only once within each SOC and PT using the most severe episode).

10.3.1.4 Summary of Adverse Events by Relationship to IMP

All subjects reporting AEs will be summarized by relationship to IMP and treatment. Counts will be given for number of subjects, not number of events. Counts will be given by the closest relationship to IMP (i.e., subjects experiencing more than 1 AE within a treatment will be counted only once using the most closely related event).

Additionally, subjects reporting AEs will be summarized for SOC and PT by closest relationship to IMP and treatment. Counts will be given for total number of subjects, not for events. Counts by closest relationship will be given (i.e., subjects experiencing more than 1 AE within a treatment will be counted only once within each SOC and PT using the most closely related event).

10.3.1.5 Summary of Adverse Events of Special Interest

All subjects reporting AEs of special interest will be summarized by treatment. Counts will be given for number of subjects and number of events. Subjects experiencing more than one AE of special interest within a treatment will be counted only once for number of subjects but will be counted more than once for number of events.

Additionally, subjects reporting AEs of special interest will be summarized for SOC and PT by treatment. Counts will be given for number of subjects and number of events. For programming purposes counts of number of subjects will be by maximum severity i.e., subjects experiencing more than one episode of an AE of special interest within a treatment will be counted only once within each SOC and PT using the most severe episode.

10.3.1.6 Summary of Serious Adverse Events

All subjects reporting serious adverse events (SAEs) will be summarized by treatment. Counts will be given for number of subjects and number of events. Subjects experiencing more than one SAE within a treatment will be counted only once for number of subjects but will be counted more than once for number of events.

Additionally, subjects reporting SAEs will be summarized for SOC and PT by treatment. Counts will be given for number of subjects and number of events. For programming purposes counts of number of subjects will be by maximum severity i.e., subjects experiencing more than one episode of a SAE within a treatment will be counted only once within each SOC and PT using the most severe episode.

10.3.2 Listings for Adverse Events

A separate data listing of all post-dose AEs will be provided including the SOC and PT. In addition, listings of all AEs of special interest and SAEs (including pre-dose SAE if applicable) will be provided.

In addition to the data recorded in the database, the listing will include derived onset and duration in days for TEAEs only. The onset will be calculated respective of last dose prior to TEAE and as follows:

$$Onset\ (days)\ = Start\ Date\ of\ TEAE - (Date\ of\ First\ Dose\ or\ Date\ of\ Last\ Dose)\ + 1$$

The duration will be calculated as follows:

$$Duration\ (days)\ = End\ Date\ of\ TEAE - Start\ Date\ of\ TEAE + 1$$

Should the TEAE be ongoing or the end date of TEAE be missing, the end date of TEAE will be taken to be the date of last study contact for the subject concerned and the value will be presented as " > X days". For the calculation of onset and duration will be set to NC where the start date of TEAE is missing.

10.4 Laboratory Evaluations

The details of sample collection for laboratory safety analysis are described in the study protocol.

Where a value is provided by the safety laboratory as either above or below the limit of detection (LOD) this will be set to the respective LOD itself for descriptive summaries. The individual listings will show these as <X or >X, where X represents the lower or upper LOD.

10.4.1 Summary Tables for Laboratory Evaluations

Hematology and coagulation, and clinical chemistry data will be summarized (n, mean, SD, median, minimum and maximum) for each laboratory parameter at each time point, including changes from baseline (Day -1, Period 1) at each postbaseline time point by treatment.

Shift tables from baseline to each scheduled postbaseline time point (with respect to the number and percentage of subjects with values below, within or above the reference range) will be presented by treatment. Percentages will be based on the number of subjects with measurements at baseline and the relevant postbaseline time point.

Reference ranges for each laboratory parameter will be presented for the relevant parameter in each summary table.

10.4.2 Listings for Laboratory Evaluations

The sample collection data (e.g., collection times) for laboratory analysis and urinalysis data will be listed.

All individual subject data, for planned hematology and coagulation, clinical chemistry and urinalysis data including derivations, such as change from baseline, will be listed. If applicable, data from unscheduled laboratory tests will also be listed and flagged with a "#" to indicate it will not be used in the summary statistics. In these listings, individual data will be flagged with an "H" or an "L" for values that are higher or lower than their reference ranges, respectively.

Separate listings of all hematology and coagulation, clinical chemistry and urinalysis values outside their reference ranges by subject will also be provided. References ranges will be supplied by the safety laboratory for hematology and clinical chemistry and per the eCRF for urinalysis (i.e., a positive or negative result) with the exception of the following reference ranges for urinalysis:

- pH: 5.0 to 8.0
- Specific gravity: 1.005 to 1.035

10.5 Vital Signs

The details of measurement of supine vital signs are described in the study protocol.

10.5.1 Summary Tables for Vital Signs

Vital signs data (i.e., systolic and diastolic blood pressure [BP], pulse rate and oral temperature), including change from baseline (Day 1, Pre-dose of each treatment period) will be summarized (i.e., n, mean, SD, median, minimum and maximum) at each postbaseline time point by treatment.

In addition, the number of subjects with 'substantial' increases ("INC") or decreases ("DEC") or no substantial change ("NONE") from baseline in systolic BP (>±20 mmHg), diastolic BP (>±10 mmHg) and pulse rate (>±15 bpm) will be summarized.

10.5.2 Listings for Vital Signs

All individual vital signs data (i.e., systolic and diastolic BP, pulse rate and oral temperature) data will be listed, including change from baseline. Individual data will be flagged with an "H" or an "L" for values that are higher or lower than their reference ranges, respectively, and subjects with 'substantial' increases or decreases from baseline (as defined in Section 10.5.1) in systolic BP, diastolic BP and pulse rate will be flagged with an "I" (increase) or "D" (decrease), respectively. If applicable, data from

unscheduled vital signs assessments will also be listed and flagged with a "#" to indicate it will not be used in the summary statistics.

In addition, a separate listing of all vital signs data outside their reference ranges by subject will also be provided.

The reference ranges (from Quotient SOP "The Interpretation of the Electrocardiogram, Vital Signs and Clinical Laboratory Data During Phase I / II Clinical Trials" defined in Table 9 will be used.

Table 9 Vital Signs Reference Ranges

Parameter	Split	Lower limit	Upper limit
Systolic BP	18-45 years	90 mmHg	140 mmHg
Systolic BP	>45 years	90 mmHg	160 mmHg
Diastolic BP	NA	50 mmHg	90 mmHg
Pulse rate	NA	51 bpm	100 bpm
Oral Body Temperature	NA	35.5ºC	37.5ºC

NA=Not applicable

10.6 ECGs

The details of measurement of supine ECG parameters (i.e., ventricular rate, RR interval, uncorrected QT interval, QTcF interval, PR interval, QRS interval, QRS axis, rhythm and interpretation) are described in the study protocol. ECG parameters will be reported in the order given above i.e., both summary tables and data listings.

10.6.1 Summary Tables for ECGs

ECG data, including change from baseline (Day 1, Pre-dose of each treatment period), will be summarized (i.e., mean, SD, median, minimum, maximum and n) at each postbaseline time point by treatment.

The number and percentage of subjects with normal and prolonged QT intervals corrected for heart rate using Fridericia's correction (i.e., QTcF) and increases in QTcF intervals from baseline within the categories defined in Table 10 (based on the International Council on Harmonization [ICH] E14 guideline [2]) will be summarized by time point. Percentages will be based on the number of subjects with measurements at the relevant time point.

Table 10 ICH E14 Ranges for QTcF Intervals

Parameter	ICH E14 Range
QTcF interval	≤450 msec (normal) 451-480 msec 481-500 msec >500 msec
Increase in QTcF interval from baseline	<30 msec 30-60 msec >60 msec

10.6.2 Listings for ECGs

All ECG measurements, including derivations such as change from baseline will be listed.

All ECG measurements will be flagged with an “H” or an “L” for values that are higher or lower than their reference ranges, respectively. If applicable, data from unscheduled ECG assessments will also be listed and flagged with a “#” to indicate it will not be used in the summary statistics.

In addition, subjects with increase in QTcF interval from baseline (30-60 msec) and with ‘substantial increases’ (>60 msec) will be flagged with ‘I’ and ‘SI’, respectively.

A separate listing of all ECG parameters outside their reference range by subject will also be provided.

The reference ranges taken from the exclusion criteria of the protocol for ventricular rate and from Quotient SOP “The Interpretation of the Electrocardiogram, Vital Signs and Clinical Laboratory Data During Phase I / II Clinical Trials” for all other ECG parameters, as defined in Table 11, will be used, apart from the reference range for RR interval (msec) which is calculated by the following formula:

$$\text{RR interval} = \frac{60000}{\text{heart rate}}$$

Table 11 ECG Reference Ranges

Parameter	Split	Lower limit	Upper limit
Ventricular Rate (HR)	NA	51 bpm	100 bpm
RR Interval	NA	600 msec	1176 msec
QT Interval	NA	200 msec	500 msec
QTcF Interval	Females	NA	470 msec
PR Interval	NA	120 msec	220 msec
QRS Duration	NA	NA	120 msec
QRS Axis	NA	-30º	100º
Rhythm	NA	Sinus rhythm, Sinus bradycardia (rate dependent), Sinus arrhythmia	

HR=heart rate
NA=Not applicable

10.7 Physical Examination

All physical examination details and comments on any physical examination findings will be listed.

11 Interim Statistical Analyses

No interim statistical analysis is planned for this study.

12 Changes in the Conduct of the Study or Planned Analysis

12.1 Changes in the Conduct of the Study

No changes in the conduct of the study had been reported at the time this document was written.

12.2 Changes to the Planned Analyses

For the formal statistical analysis of:

- Absolute bioavailability the fixed effect period has been replaced with sequence as a fixed effect in the mixed effects model since period and treatment are confounded as Treatment B is always given in period 1.
- Relative bioavailability an additional fixed effect (i.e. sequence) has been included in the mixed effects model as the two treatments are given in a randomized manner.

12.3 Any Other Relevant Changes

Not applicable.

13 Overall Considerations

13.1 Statistical Programming and Analysis

The Data Sciences Department at Quotient will perform the statistical programming and analysis to produce all analysis datasets, summary tables, figures and data listings using the statistical SAS Software v9.4.

In general terms, categorical data will be presented using counts and percentages, while continuous variables will be presented using the n, mean, median, SD, minimum and maximum. For PK data additional statistics including CV%, geometric mean, geometric SD and geometric CV% will be presented, as appropriate.

The geometric mean is obtained by applying a natural log transformation to the raw data, calculating the arithmetic mean of the transformed values and then back transforming the arithmetic mean.

The following formula will be used to calculate the geometric SD:

$$\text{geometric SD} = \exp\{SD[\log(\text{raw data})]\}$$

i.e., a natural log transformation is applied to the raw data, the arithmetic SD of the transformed values is calculated, and then the arithmetic SD of the transformed values is back transformed.

The following formula will be used to calculate the geometric CV%:

$$\text{geometric CV\%} = 100 \times (\exp\{SD[(\log(\text{raw data})]\}^2 - 1)^{1/2}$$

i.e., a natural log transformation is applied to the raw data, the arithmetic SD of the transformed values is calculated. This value is then squared. The square value is back transformed and a value of 1 is subtracted from the back transformed value. A square root is then applied and the resulting value is multiplied by 100.

In general summary statistics and statistical analysis results will be presented as detailed in Table 12, unless otherwise stated:

Table 12 Reporting Conventions for Summary Statistics and Statistical Analysis

Data Type	Statistic	Number of decimal places for reporting (i)
Frequency	Counts (n)	None
	Percentages (%)	1 decimal place
Summary statistic	n	None
	Mean	i + 1 decimal places
	Median	i + 1 decimal places
	SD	i + 1 decimal places
	Min	i decimal places
	Max	i decimal places
	CV%	1 decimal place
	Geometric n	None
	Geometric Mean	i + 1 decimal place
	Geometric SD	i + 1 decimal places
	Geometric CV%	1 decimal place
Statistical analysis	Ratios (%)	2 decimal places
	Confidence intervals (%)	2 decimal places
	p-values	if <0.001: presented as <0.001
		if ≥0.001 and <0.099: presented to 3 decimal places
		all other p-values will be presented to 2 decimal places

i refers to the number of decimal places reported in the eCRF or other appropriate source data for the original data. Where bioanalytical or PK data are received rounded in significant figures rather than decimal places, summary statistics will be supplied to the same precision.

Details of how the individual PK parameters will be presented are detailed in Section 9.2 Where data requires rounding, values ending with 1 to 4 will be rounded down and values ending with 5 to 9 will be rounded up.

All data listings will be based on all enrolled subjects i.e., subjects who signed informed consent and have met the inclusion/exclusion criteria and were assigned a unique identification number (Part 1) or randomized (Part 2). Details of age and sex will be included on all data listings.

All statistical tests relating to PK parameters will be 2-sided and will be performed using a 10% significance level, leading to 90% (2-sided) confidence intervals (CIs).

If any baseline measurements are found to be missing then consideration will be given to imputation using the preceding time point (e.g., Screening, Admission, if applicable). Unscheduled assessment may be used if appropriate. Details of any such imputations will be documented as part of the safety analysis set.

There will be no other imputations for the safety data with regard to missing values or study discontinuation (i.e., subjects who do not complete the study). Imputation for mass balance parameter estimation using SAS Software is described in Section 9.1.2, for PK parameter estimation using WinNonlin is described in Section 9.2.2.

If partial dates are available for smoking history, prior medications or medical/surgical history, there will be no date imputations. The data listings will only show the date information for the date part that is available, e.g., if only the year part of the date is available then YYYY will be presented in the listing. If the full date information is missing, then this will be presented as missing on the data listing.

Separate summary tables, figures and data listings will be produced for Part 1 and Part 2 of the study, respectively. The different parts will be identified by a subtitle indicating the relevant part. The text in the remainder of this document refers to both parts, unless specified otherwise.

If all or part of this study is conducted during the Coronavirus disease 2019 [COVID-19] pandemic and there is evidence that data relating to primary and/or key secondary endpoints may have been affected in a way that may bias results, then sensitivity analyses may be conducted. Requirements for any sensitivity analyses will be documented at the same time as the related population (i.e. safety, mass balance or PK Concentration) and details of any sensitivity analyses which were carried out would be fully documented in the CSR.

13.2 Quality Control of Summary Tables, Figures and Listings and Statistical Analysis

Isolated data errors detected as a result of the QC checks that are deemed significant (i.e., errors that would impact the interpretation of the results in relation to the study objectives) will be corrected as per the data management plan. Systematic data errors will be investigated further. The data will be corrected if necessary, and the appropriate table, figure, and/or listing re-generated and then rechecked.

In addition to QC checks, a documented peer review will be performed of all SAS Software generated report standard summary tables, figures and data listings, including a review of SAS Software code and program log files.

13.2.1 Quality Control - Summary Tables

Manual QC methods (i.e., comparison of results in the table to results calculated by a calculator or spreadsheet) will be used for all analyses and summary tables. All summary tables will be QC'd as follows:

- where tables are presented by treatment/sequence (i.e., no time points), QC will alternate between treatment/sequence to avoid the same treatment/sequence being QC'd every time however, all summary statistics for that treatment/sequence will be checked
- where tables are presented by treatment and time point, QC will alternate between treatment and time point to avoid the same treatment and time point being QC'd every time, however a single treatment at 1 time point in each table will be checked
- where tables are produced using a macro for multiple parameters, a minimum of 3 tables, using different treatments or combinations of treatments and time point as appropriate, will be QC'd
- for AEs, the treatment details will be 100% QC'd against the treatment allocation list/randomization schedule for all subjects
- AE summary tables will be 100% checked using the relevant data listing

13.2.2 Quality Control - Figures

All figures will be QC'd manually using the corresponding/appropriate summary table or data listing, as follows:

- across all figures, QC will alternate between treatments to avoid the same treatment being QC'd every time
- where a figure presents data from more than 1 treatment, only 1 treatment will be QC'd; however, all data points for that treatment will be checked
- where figures are produced using a macro for individual subjects and/or multiple parameters, a minimum of 3 figures will be QC'd
- mean figures will be QC'd using the corresponding summary table
- figures showing individual data will be QC'd using the corresponding data listing

13.2.3 Quality Control - Data Listings

All data listings will be subjected to a 100% manual check against the eCRF or other appropriate source data for a minimum of 2 subjects (1 from each study part). If appropriate, the subjects checked will include at least 1 subject who withdrew early from the study.

The study treatment allocation details on the dosing data listing will be 100% QC checked against the study randomization schedule.

13.2.4 Quality Control - Statistical Analysis

QC of statistical analyses will be performed by peer review of program code, log and output. This will be performed by a statistician at Quotient who is not responsible for performing the statistical analysis.

14 SAS Data Transfer

Study data in ADaM dataset format will be transferred to Genentech at the following milestones:

- Pre database close
- Pre database lock
- Post database lock

Data will be provided in SAS dataset format, each dataset will be contained in a respective SAS transport (XPT) file and conform to CDISC ADaM format (SDTM IG 1.1)

The following standards and versions for creation and validation of the Clinical Data Interchange Standards Consortium (CDISC) Standardized Datasets will be used:

- Study Data Tabulation Model (SDTM) Version: 1.4
- SDTM Implementation Guide Version: 3.2
- ADaM: Model 2.1
- Implementation Guide 1.1
- OpenCDISC Version: 2.2.0
- CDISC SDTM Controlled Terminology Version: "2020-03-27 or latest available"
- SDRG (Standard Data Review Guide): 1.2 or latest available (end of study transfer only)
- ADRG (Standard Data Review Guide): 1.1 or latest available (end of study transfer only)

- Define.xml: 2.0> (end of study transfer only)
- SAS v9.4
- Pinnacle 21

A define.xml will be provided to Genentech for ADaM datasets. This will be accompanied by a Data Reviewers Guide (in pdf format) and linked to the ADaM define.xml. Datasets will be provided in SAS transport file format (XPT), each dataset will be in an individual transport file. The define.xml will be issued on finalization of the CSR.

15 Programming Conventions

Quotient standards for layout of tables, figures and data listings and programming conventions will be used as follows:

- courier new, font size 8
- landscape
- US letter size paper

Tables and listings will be produced as MS Word 2016 documents and figures will be produced as PDF files. Listings will be sorted by subject ID number and period.

The mock tables (Section 20) presented are a representation of Quotient reporting standards. However, these are provided for illustrative purposes only. The numbering and titles of all tables, figures and listings and the formatting, labelling, footnotes and cosmetic appearance of output may be modified or additional labelling/footnotes may need to be added during analysis and reporting, for clarification purposes. Any such changes will not be regarded as changes to planned analyses.

16 Reference List

[1] Brown, Prescott, Repeated Measures data. In Brown H and Prescott R, 3rd edition. Applied Mixed Models in Medicine. Chichester, UK: John Wiley &Sons Ltd., 2015: 242-243

[2] International Council for Harmonisation (ICH) Topic E14, The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs Guidelines approved by the Committee for Medicinal Products for Human Use (CHMP) in May 2005 which came into force November 2005.

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TABLE 14.1.1.1
Subject Disposition by Reason
Summary Statistics: All Enrolled Subjects
Part 1

	[14C]-GDC-9545 Cap (N=XX) n (%)
Subjects enrolled (1)	xx (xx.x)
Subjects dosed	xx (xx.x)
Subjects completed	xx (xx.x)
Subjects discontinued	xx (xx.x)
Reason for discontinuation	
REASON 1	xx (xx.x)
REASON 2	xx (xx.x)
REASON 3	xx (xx.x)
…	…
<All categories on source>	xx (xx.x)

Note: The data in this table are presented in listing x.x
All subjects were planned to receive a single oral dose of [14C]-GDC-9545 capsule, 30mg (NMT 4.6 MBq [124 µCi]) in Part 1
(1) An enrolled subject is defined as a subject who signed the informed consent, qualified per the inclusion/exclusion criteria and was allocated a unique identification number
A subject may be discontinued for one reason only
Percentages are based on the number of subjects enrolled

PROGRAM PATH: X:\~\QSCXXXXXX\~\TFLS\PRODUCTION\TAB-XX DDMMMYYYY HH:MM

(Programming note: This table will be continued for all reasons for discontinuation as recorded on the eCRF. If none of the subjects discontinued from the study early then reasons for discontinuation will not be populated in the summary table)

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TABLE 14.1.1.2.1
Analysis Populations
Summary Statistics: All Enrolled Subjects
Part 1

	[14C]-GDC-9545 Cap (N=XX) n (%)
Subjects in Safety Population	xx (xx.x)
Reasons for exclusion from Safety Population	
<All categories on source listing>	xx (xx.x)
	…
Subjects in Mass Balance Population	xx (xx.x)
Reasons for exclusion from Mass Balance Population	
<All categories on source listing>	xx (xx.x)
	…
Subjects in PK Population	xx (xx.x)
Reasons for exclusion from PK Population	
<All categories on source listing>	xx (xx.x)
	…

Note: The data in this table are presented in listing x.x
All subjects were planned to receive a single oral dose of [14C]-GDC-9545 capsule, 30mg (NMT 4.6 MBq [124 µCi]) in Part 1
A subject may be excluded for more than 1 reason
Percentages are based on the number of subjects enrolled

PROGRAM PATH: X:\~\QSCXXXXXX\~\TFLS\PRODUCTION\TAB-XX DDMMMYYYY HH:MM

(Programming note: This table will be continued for all reasons for exclusion. If none of the subjects were excluded from a population, then reasons for exclusion will not be populated in the summary table)

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TABLE 14.1.1.2.2
Safety Analysis Set
Summary Statistics: Safety Population
Part 1

	[14C]-GDC-9545 Cap (N=XX) n (%)
Subjects in Safety Analysis Set	xx (xx.x)
Reasons for exclusion from Safety Analysis Set	
<All categories from source>	xx (xx.x)
	…

Note: The data in this table are presented in listing x.x
All subjects were planned to receive a single oral dose of [14C]-GDC-9545 capsule, 30mg (NMT 4.6 MBq [124 µCi]) in Part 1
A subject may be excluded for more than 1 reason

PROGRAM PATH: X:\~\QSCXXXXXX\~\TFLS\PRODUCTION\TAB-XX DDMMMYYYY HH:MM

(Programming note: This table will be continued for all reasons for exclusion. If none of the subjects were excluded from the safety analysis set, then reasons for exclusion will not be populated in the summary table. Similar tables will be produced for
• Mass Balance Analysis Set, i.e. Table [14.1.1.2.3] and
• PK Analysis Set, i.e. Table [14.1.1.2.4]
Each analysis set will be a subset of their respective populations and percentages will be based on number of subjects in each population)

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TABLE 14.1.2.1
Subject Disposition by Reason
Summary Statistics: All Enrolled Subjects
Part 2

	Treatment Sequence		
	BCD (N=X) n (%)	BDC (N=X) n (%)	Overall (N=X) n (%)
Subjects enrolled (1)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subjects dosed	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subjects completed	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subjects discontinued	xx (xx.x)	xx (xx.x)	xx (xx.x)
Reason for discontinuation			
REASON 1	xx (xx.x)	xx (xx.x)	xx (xx.x)
REASON 2	xx (xx.x)	xx (xx.x)	xx (xx.x)
REASON 3	xx (xx.x)	xx (xx.x)	xx (xx.x)
…	…	…	…
<All categories on source>	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: The data in this table are presented in listing x.x
All subjects were to receive GDC-9545 IV administration 30 mg as a solution for infusion, 3 mg/mL (10 mL)[B] in Period 1 and GDC-9545/F12 capsule 30 mg [C] and GDC-9545/F18 capsule 30 mg [D] in a randomized manner in Period 2 and 3 in Part 2
(1) An enrolled subject signed the informed consent, qualified per the inclusion/exclusion criteria and was randomized
A subject may be discontinued for 1 reason only

PROGRAM PATH: X:\~\QSCXXXXXX\~\TFLS\PRODUCTION\TAB-XX DDMMMYYYY HH:MM

(Programming note: This table will be continued for all reasons for discontinuation as recorded on the source. If none of the subjects discontinued from the study early then reasons for discontinuation will not be populated in the summary table)
(Programming note: Percentages are based on the number of subjects enrolled in the respective sequence)

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TABLE 14.1.2.2.1
Analysis Populations
Summary Statistics: All Enrolled Subjects
Part 2

	Treatment Sequence		
	BCD (N=X) n (%)	BDC (N=X) n (%)	Overall (N=X) n (%)
Subjects in safety population	xx (xx.x)	xx (xx.x)	xx (xx.x)
Reason for exclusion from safety population			
<All categories on source listing>	xx (xx.x)	xx (xx.x)	xx (xx.x)
	…	…	…
Subjects in PK population	xx (xx.x)	xx (xx.x)	xx (xx.x)
Reason for exclusion from PK population			
<All categories on source listing>	xx (xx.x)	xx (xx.x)	xx (xx.x)
	…	…	…

Note: The data in this table are presented in listing x.x
All subjects were to receive GDC-9545 IV administration 30 mg as a solution for infusion, 3 mg/mL (10 mL)[B] in Period 1 and GDC-9545/F12 capsule 30 mg [C] and GDC-9545/F18 capsule 30 mg [D] in a randomized manner in Period 2 and 3 in Part 2
A subject may be excluded for more than 1 reason

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(Programming note: Percentages are based on the number of subjects enrolled in the respective sequence)
(Programming note: If all subjects in Part 2 receive all treatments then this will be presented by overall only)

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TABLE 14.1.2.2.2
Safety Analysis Set
Summary Statistics: Safety Population
Part 2

	GDC-9545 IV (N=X) n (%)	GDC-9545/F12 Cap (N=X) n (%)	GDC-9545/F18 Cap (N=X) n (%)
Subjects in safety analysis set	xx (xx.x)	xx (xx.x)	xx (xx.x)
Reasons for exclusion from safety analysis set			
<All categories from source>	xx (xx.x)	xx (xx.x)	xx (xx.x)
	…	…	…

Note: The data in this table are presented in listing x.x
All subjects were to receive GDC-9545 IV administration 30 mg as a solution for infusion, 3 mg/mL (10 mL)[B] in Period 1 and GDC-9545/F12 capsule 30 mg [C] and GDC-9545/F18 capsule 30 mg [D] in a randomized manner in Period 2 and 3 in Part 2
A subject may be excluded for more than 1 reason

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(Programming note: A similar table will be produced for the PK Analysis Set (and Subset[s], if required), i.e. Table [14.1.2.2.3]
Each analysis set/subset will be a subset of their respective population and percentages
will be based on number of subjects in each population)

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TABLE 14.1.1.3
Demographic and Baseline Characteristics
Summary Statistics: Safety Analysis Set
Part 1

		[14C]-GDC-9545 Cap (N=XX)
Age (years)	n	xx
	Mean	xx.xx
	SD	xx.xx
	Median	xx.xx
	Min	xx.x
	Max	xx.x
Ethnicity n(%)	<All categories on source>	xx (xx.x)
Race n(%)	<All categories on source>	xx (xx.x)
Sex n(%)	Females	xx (xx.x)
Height (cm)	…	…
Weight (kg)	…	…
BMI (kg/m^2)	…	…

Note: The data in this table are presented in listing x.x
All subjects were planned to receive a single oral dose of [14C]-GDC-9545 capsule, 30mg (NMT 4.6 MBq [124 µCi]) in Part 1

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(Programming note: This table will continue for all categories of ethnicity and race. Height, Weight and BMI will be summarized using the same descriptive statistics as Age. If any values are missing, then a 'missing' row will be presented in the table)

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TABLE 14.1.1.4
Lifestyle Details: Smoking History and Alcohol Consumption
Summary Statistics: Safety Analysis Set

		[14C]-GDC-9545 Cap (N=XX) n (%)
Does the subject smoke (1)	NO	xx (xx.x)
	PREVIOUSLY	xx (xx.x)
Alcohol Consumption (2)	NONE	xx (xx.x)
	YES: NOT EXCESSIVE	xx (xx.x)

Note: The data in this table are presented in listing x.x
All subjects were planned to receive a single oral dose of [14C]-GDC-9545 capsule, 30mg (NMT 4.6 MBq [124 µCi]) in Part 1
(1) Anyone who smoked or used e-cigarettes or nicotine replacement products in the last 12 months is excluded from the study
(2) Anyone who excessively consumes alcohol (>14 units/week) is excluded from the study
1 unit = 1/2 pint beer, 25 mL of 40% spirit, 1.5 to 2 units = 125 mL glass of wine depending on type

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TABLE 14.1.2.3
Demographic and Baseline Characteristics
Summary Statistics: Safety Analysis Set
Part 2

		Treatment Sequence		
		BCD (N=X)	BDC (N=X)	Overall (N=X)
Age (years)	n	xx	xx	xx
	Mean	xx.xx	xx.xx	xx.xx
	SD	xx.xx	xx.xx	xx.xx
	Median	xx.xx	xx.xx	xx.xx
	Min	xx.x	xx.x	xx.x
	Max	xx.x	xx.x	xx.x
Ethnicity n(%)	<All categories on source>	xx (xx.x)	xx (xx.x)	xx (xx.x)
Race n(%)	<All categories on source>	xx (xx.x)	xx (xx.x)	xx (xx.x)
Sex n(%)				
	Female	xx (xx.x)	xx (xx.x)	xx (xx.x)
Height (cm)	…	…	…	…
Weight (kg)	…	…	…	…
BMI (kg/m^2)	…	…	…	…

Note: The data in this table are presented in listing x.x
All subjects were to receive GDC-9545 IV administration 30 mg as a solution for infusion, 3 mg/mL (10 mL)[B] in Period 1 and GDC-9545/F12 capsule 30 mg [C] and GDC-9545/F18 capsule 30 mg [D] in a randomized manner in Period 2 and 3 in Part 2

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(Programming note: This table will continue for all categories of ethnicity and race
Height, Weight and BMI will be assessed using the same descriptive statistics as Age
If any values are missing, then a "missing" row will be included in the table, as applicable)

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TABLE 14.1.2.4
Lifestyle Details: Smoking History and Alcohol Consumption
Summary Statistics: Safety Analysis Set
Part 2

		Treatment Sequence		
		BCD (N=X) n (%)	BDC (N=X) n (%)	Overall (N=X) n (%)
Does the subject smoke? (1)	NO	xx (xx.x)	xx (xx.x)	xx (xx.x)
	PREVIOUSLY	xx (xx.x)	xx (xx.x)	xx (xx.x)
Alcohol Consumption (2)	NONE	xx (xx.x)	xx (xx.x)	xx (xx.x)
	YES: NOT EXCESSIVE	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: The data in this table are presented in listing x.x
All subjects were to receive GDC-9545 IV administration 30 mg as a solution for infusion, 3 mg/mL (10 mL)[B] in Period 1 and GDC-9545/F12 capsule 30 mg [C] and GDC-9545/F18 capsule 30 mg [D] in a randomized manner in Period 2 and 3 in Part 2
(1) Anyone who smoked or used e-cigarettes or nicotine replacement products in the last 12 months is excluded from the study
(2) Anyone who excessively consumes alcohol (>14 units/week) is excluded from the study
1 unit = 1/2 pint beer, 25 mL of 40% spirit, 1.5 to 2 units = 125 mL glass of wine depending on type

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TABLE 14.1.1.5
Extent of Exposure
Summary Statistics: Safety Analysis Set
Part 1

	[14C]-GDC-9545 Cap (N=XX)		
	mg	MBq	µCi
n	xx	xx	xx
Mean	xx.xx	xx.xx	xx.xx
SD	xx.xx	xx.xx	xx.xx
Median	xx.xx	xx.xx	xx.xx
Min	xx.x	xx.x	xx.x
Max	xx.x	xx.x	xx.x

Note: The data in this table are presented in listing x.x
All subjects were planned to receive a single oral dose of [14C]-GDC-9545 capsule, 30mg (NMT 4.6 MBq [124 µCi]) in Part 1

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TABLE 14.1.2.5
Extent of Exposure
Summary Statistics: Safety Analysis Set
Part 2

Treatment	Subjects Dosed (N=X) n (%)
GDC-9545 IV	xx (xx.x)
GDC-9545/F12 Cap	xx (xx.x)
GDC-9545/F18 Cap	xx (xx.x)
Overall	xx (xx.x)

Note: The data in this table are presented in listing x.x
All subjects were to receive GDC-9545 IV administration 30 mg as a solution for infusion, 3 mg/mL (10 mL)[B] in Period 1 and GDC-9545/F12 capsule 30 mg [C] and GDC-9545/F18 capsule 30 mg [D] in a randomized manner in Period 2 and 3 in Part 2

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TABLE 14.2.1.1.1
Excretion: Total Radioactivity
Ae(Urine) by Collection Period <(units)>
Summary Statistics: Mass Balance Analysis Set
Part 1

[14C]-GDC-9545 Cap (N=XX)

Collection Period	n	Mean	SD	CV%	Median	Min	Max
ADMISSION - 0 H	xx	xx.xx	xx.xx	xx.x	xx.xx	xx.x	xx.x
TIME0 - TIME1	xx	xx.xx	xx.xx	xx.x	xx.xx	xx.x	xx.x
TIME1 - TIME2	xx	xx.xx	xx.xx	xx.x	xx.xx	xx.x	xx.x
TIME2 - TIME3#	xx	xx.xx	xx.xx	xx.x	xx.xx	xx.x	xx.x
…	…	…	…	…	…	…	…
<All other time intervals>	xx	xx.xx	xx.xx	xx.x	xx.xx	xx.x	xx.x

Note: The data in this table are presented in listing x.x
All subjects were planned to receive a single oral dose of [14C]-GDC-9545 capsule, 30mg (NMT 4.6 MBq [124 µCi]) in Part 1
Where a subject has failed to void or has a ND concentration over a particular collection interval, the amount excreted (Ae) has been set to zero
represents an interpolated period

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(Programming Note: This table will be continued for all collection periods. Similar tables will be produced for
- Fe(Urine) (Recovery), i.e. Table [14.2.1.1.3]
- Ae(Feces), i.e. Table [14.2.1.2.1]
- Fe(Feces) (Recovery), i.e. Table [14.2.1.2.3]
- Combined (Ae[total]), i.e. Table [14.2.1.3.1] and
- Combined (Fe[total]) (Recovery), i.e. Table [14.2.1.3.3])

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TABLE 14.2.1.1.2
Excretion: Total Radioactivity
Cumulative Ae(Urine) by Collection Period <(units)>
Summary Statistics: Mass Balance Analysis Set
Part 1

[14C]-GDC-9545 Cap (N=XX)

Collection Period	n	Mean	SD	CV%	Median	Min	Max
ADMISSION - 0 H	xx	xx.xx	xx.xx	xx.x	xx.xx	xx.x	xx.x
TIME0 - TIME1	xx	xx.xx	xx.xx	xx.x	xx.xx	xx.x	xx.x
TIME0 - TIME2	xx	xx.xx	xx.xx	xx.x	xx.xx	xx.x	xx.x
TIME0 - TIME3	xx	xx.xx	xx.xx	xx.x	xx.xx	xx.x	xx.x
…	…	…	…	…	…	…	…
<All other time intervals>	xx	xx.xx	xx.xx	xx.x	xx.xx	xx.x	xx.x

Note: The data in this table are presented in listing x.x
All subjects were planned to receive a single oral dose of [14C]-GDC-9545 capsule, 30mg (NMT 4.6 MBq [124 µCi]) in Part 1

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(Programming note: This table will be continued for all collection periods. Similar tables will be produced for
- Cumulative Fe(Urine) (Recovery), i.e. Table [14.2.1.1.4]
- Cumulative Ae(Feces), i.e. Table [14.2.1.2.2]
- Cumulative Fe(Feces) (Recovery), i.e. Table [14.2.1.2.4]
- Combined Cumulative (Ae[total]), i.e. Table [14.2.1.3.2] and
- Combined Cumulative (Fe[total]) (Recovery), i.e. Table [14.2.1.3.4])

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TABLE 14.2.1.4
Excretion and Recovery: Total Radioactivity
Cumulative Excretion and Recovery Parameters
Summary Statistics: Mass Balance Analysis Set
Part 1

[14C]-GDC-9545 Cap (N=XX)

	Urine		Feces		Total	
	CumAe (units)	CumFe (%)	CumAe (units)	CumFe (%)	CumAe (units)	CumFe (%)
n	xx	xx	xx	xx	xx	xx
Mean	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
CV%	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Min	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Max	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x

Note: The data in this table are presented in listing x.x
All subjects were planned to receive a single oral dose of [14C]-GDC-9545 capsule, 30mg (NMT 4.6 MBq [124 µCi]) in Part 1
CumAe represents the cumulative excretion. CumFe represents the cumulative recovery as a percentage of the radioactive dose administered

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TABLE 14.2.1.5.1
Plasma Pharmacokinetic Concentrations: GDC-9545 <(units)>
Summary Statistics: PK Analysis Set
Part 1

[14C]-GDC-9545 Cap (N=XX)

	Arithmetic (1)								Geometric (2)		
Time Point	n	n#	Mean	SD	CV%	Median	Min	Max	Mean	SD	CV%
PRE-DOSE	xx	xx	xx.xx	xx.xx	xx.x	xx.xx	xx.x	xx.x	NC	NC	NC
TIME POINT 1	xx	xx	xx.xx	xx.xx	xx.x	xx.xx	xx.x	xx.x	xx.xx	xx.x	xx.x
TIME POINT 2	xx	xx	xx.xx	xx.xx	xx.x	xx.xx	xx.x	xx.x	xx.xx	xx.x	xx.x
TIME POINT 3	xx	xx	xx.xx	xx.xx	xx.x	xx.xx	xx.x	xx.x	xx.xx	xx.x	xx.x
…	…	…	…	…	…	…	…	…	…	…	…
<All other time points>	xx	xx	xx.xx	xx.xx	xx.x	xx.xx	xx.x	xx.x	xx.xx	xx.x	xx.x

Note: The data in this table are presented in listing x.x
All subjects were planned to receive a single oral dose of [14C]-GDC-9545 capsule, 30mg (NMT 4.6 MBq [124 µCi]) in Part 1
n# indicates the number of subjects with a BLQ value recorded at the time point indicated
(1) For arithmetic summary statistics, concentration values reported as < BLQ> have been set to zero
(2) For calculation of geometric summary statistics, values reported as < BLQ> have been set to ½ × <LLOQ>, except for pre-dose values which will not be summarized. The < LLOQ> value was <value, units>

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(Programming note: This table will be continued for all time points. Similar tables will be produced for
- Plasma Pharmacokinetic Concentrations: Total Radioactivity, i.e. Table [14.2.1.5.2]
- Whole Blood Pharmacokinetic Concentration, i.e. Table [14.2.1.5.3]) and
- Whole Blood: Plasma Concentration Ratio, i.e. Table [14.2.1.5.4])

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TABLE 14.2.2.5.1
Plasma Pharmacokinetic Concentrations: GDC-9545 <(units)>
Summary Statistics: <PK Analysis Set/PK Analysis Subset>
Part 2

		Arithmetic (1)							Geometric (2)		
Treatment	Time Point	n	n#	Mean	SD	CV%	Median	Min	Max	Mean	SD	CV%
GDC-9545 IV (N=X)	PRE-DOSE	xx	xx	xx.xx	xx.xx	xx.x	xx.xx	xx.x	xx.x	NC	NC	NC
	TIME POINT 1	xx	xx	xx.xx	xx.xx	xx.x	xx.xx	xx.x	xx.x	xx.xx	xx.xx	xx.x
	TIME POINT 2	xx	xx	xx.xx	xx.xx	xx.x	xx.xx	xx.x	xx.x	xx.xx	xx.xx	xx.x
	TIME POINT 3	xx	xx	xx.xx	xx.xx	xx.x	xx.xx	xx.x	xx.x	xx.xx	xx.xx	xx.x
	…	…	…	…	…	…	…	…	…	…	…	…
	<All other time points>	xx	xx	xx.xx	xx.xx	xx.x	xx.xx	xx.x	xx.x	xx.xx	xx.xx	xx.x
GDC-9545/ F12 Cap (N=X)	PRE-DOSE	xx	xx	xx.xx	xx.xx	xx.x	xx.xx	xx.x	xx.x	NC	NC	NC
	TIME POINT 1	xx	xx	xx.xx	xx.xx	xx.x	xx.xx	xx.x	xx.x	xx.xx	xx.xx	xx.x
	TIME POINT 2	xx	xx	xx.xx	xx.xx	xx.x	xx.xx	xx.x	xx.x	xx.xx	xx.xx	xx.x
	TIME POINT 3	xx	xx	xx.xx	xx.xx	xx.x	xx.xx	xx.x	xx.x	xx.xx	xx.xx	xx.x
	…	…	…	…	…	…	…	…	…	…	…	…
	<All other time points>	xx	xx	xx.xx	xx.xx	xx.x	xx.xx	xx.x	xx.x	xx.xx	xx.xx	xx.x
…	…	…	…	…	…	…	…	…	…	…	…	…

Note: The data in this table are presented in listing x.x
All subjects were to receive GDC-9545 IV administration 30 mg as a solution for infusion, 3 mg/mL (10 mL)[B] in Period 1 and GDC-9545/F12 capsule 30 mg [C] and GDC-9545/F18 capsule 30 mg [D] in a randomized manner in Period 2 and 3 in Part 2
n# indicates the number of subjects with a BLQ value recorded at the time point indicated
(1) For arithmetic summary statistics, concentration values reported as BLQ have been set to zero
(2) For calculation of geometric summary statistics, values reported as BLQ have been set to ½ × LLOQ, except for pre-dose values which will not be summarized. The LLOQ value was <value, units>

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(Programming note: This table will be continued for each treatment and all time points)

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TABLE 14.2.1.6.1
Plasma Pharmacokinetic Parameters: GDC-9545
Summary Statistics: PK Analysis Set
Part 1

[14C]-GDC-9545 Cap (N=XX)

Statistic	Parameter 1 (units)	Parameter 2 (units)	Parameter 3 (units)	.....	All Other PK Parameters (units)
n	xx	xx	xx	…	xx
Mean	xx.xx	xx.xx	xx.xx	…	xx.xx
SD	xx.xx	xx.xx	xx.xx	…	xx.xx
CV%	xx.x	xx.x	xx.x	…	xx.x
Median	xx.xx	xx.xx	xx.xx	…	xx.xx
Min	xx.x	xx.x	xx.x	…	xx.x
Max	xx.x	xx.x	xx.x	…	xx.x
Geometric Mean	xx.xx	xx.xx	xx.xx	…	xx.xx
Geometric SD	xx.xx	xx.xx	xx.xx	…	xx.xx
Geometric CV%	xx.x	xx.x	xx.x	…	xx.x

Note: The data in this table are presented in listing x.x
All subjects were planned to receive a single oral dose of [14C]-GDC-9545 capsule, 30mg (NMT 4.6 MBq [124 µCi]) in Part 1
<For concentration parameters, BLQ values will be set to 0 for arithmetic statistics and to ½ × LLOQ for geometric statistics>

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(Programming note: A similar table will be produced for
• Plasma Pharmacokinetic Parameters: Total Radioactivity, i.e. Table [14.2.1.6.2]) and
• Whole Blood Pharmacokinetic Parameters: Total Radioactivity, i.e. Table [14.2.1.6.3])

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TABLE 14.2.2.6.1
Plasma Pharmacokinetic Parameters: GDC-9545
Summary Statistics: <PK Analysis Set/PK Analysis Subset>
Part 2

Treatment	Statistic	Parameter 1 (units)	Parameter 2 (units)	Parameter 3 (units)	.....	All Other PK Parameters (units)
GDC-9545 IV (N=X)	n	xx	xx	xx	…	xx
	Mean	xx.xx	xx.xx	xx.xx	…	xx.xx
	SD	xx.xx	xx.xx	xx.xx	…	xx.xx
	CV%	xx.x	xx.x	xx.x	…	xx.x
	Median	xx.xx	xx.xx	xx.xx	…	xx.xx
	Min	xx.x	xx.x	xx.x	…	xx.x
	Max	xx.x	xx.x	xx.x	…	xx.x
	Geometric Mean	xx.xx	xx.xx	xx.xx	…	xx.xx
	Geometric SD	xx.xx	xx.xx	xx.xx	…	xx.xx
	Geometric CV%	xx.x	xx.x	xx.x	…	xx.x
GDC-9545/F12 Cap (N=X)	…	…	…	…	…	…
…	…	…	…	…	…	…

Note: The data in this table are presented in listing x.x
All subjects were to receive GDC-9545 IV administration 30 mg as a solution for infusion, 3 mg/mL (10 mL)[B] in Period 1 and GDC-9545/F12 capsule 30 mg [C] and GDC-9545/F18 capsule 30 mg [D] in a randomized manner in Period 2 and 3 in Part 2
For concentration parameters, BLQ values will be set to 0 for arithmetic statistics and to ½ × LLOQ for geometric statistics
The LLOQ value was <value, units>

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(Programming note: This table will be continued for each treatment and parameter)

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TABLE 14.2.2.7.1
Plasma Pharmacokinetic Parameters: GDC-9545
Statistical Analysis Results - Assessment of Absolute Bioavailability: <PK Analysis Set/PK Analysis Subset>
Part 2

		Test		Reference				
Comparison	Parameter	n	Adj Geo Mean (1)	n	Adj Geo Mean (1)	Ratio (%) (2)	90% CI (3)	CVw (%) (4)
GDC-9545/F12 Cap vs GDC-9545 IV	AUC(0-inf) (units)	xx	xx.xx	xx	xx.xx	xx.xx	(xx.xx, xx.xx)	xx.xxx
GDC-9545/F18 Cap vs GDC-9545 IV	AUC(0-inf) (units)	xx	xx.xx	xx	xx.xx	xx.xx	(xx.xx, xx.xx)	xx.xxx

Note: The data in this table are presented in listing x.x
All subjects were to receive GDC-9545 IV administration 30 mg as a solution for infusion, 3 mg/mL (10 mL)[B] in Period 1 and GDC-9545/F12 capsule 30 mg [C] and GDC-9545/F18 capsule 30 mg [D] in a randomized manner in Period 2 and 3 in Part 2
Results obtained from mixed effects model of natural log transformed PK parameters including terms for treatment and sequence fitted as fixed effects and subject within sequence fitted as a random effect
(1) Adj geo mean = adjusted geometric mean from model (2) Ratio of adj geo means with comparison presented as test/reference (3) CI = confidence interval for ratio of adj geo means (4) CVw = Intra-subject variability

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(Programming note: A similar table will be produced for Relative Bioavailability, Table [14.2.2.7.2], with the inclusion of a column for p-value)

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TABLE 14.2.2.7.3
Plasma Pharmacokinetic Parameters: GDC-9545
Statistical Analysis Results - Fixed Effects Table for Assessment of Relative Bioavailability: <PK Analysis Set/PK Analysis Subset>
Part 2

Parameter	Effect (1)	df (2)	F-Statistic (3)	p-value (4)
AUC(0-inf) (units)	TREATMENT	xx,xx	x.xx	0.xxx
	PERIOD	xx,xx	x.xx	0.xxx
	SEQUENCE	xx,xx	x.xx	0.xxx

Note: The table accompanies the statistical analysis results given in Tablet 14.2.2.7.1
All subjects were to receive GDC-9545 IV administration 30 mg as a solution for infusion, 3 mg/mL (10 mL)[B] in Period 1 and GDC-9545/F12 capsule 30 mg [C] and GDC-9545/F18 capsule 30 mg [D] in a randomized manner in Period 2 and 3 in Part 2
Results obtained from mixed effects model of natural log transformed PK parameters including terms for treatment, period and sequence fitted as fixed effects and subject nested within sequence fitted as a random effect
(1) Fixed effects from the model (2) degrees of freedom for the fixed effects (3) F-statistic from the model for the relevant fixed effect (4) p-value (2-sided test with null hypothesis of no difference) for the relevant fixed effect

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(Programming note: A similar table will be produced to accompany the relative bioavailability: Table [14.2.2.7.4])

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TABLE 14.3.1.1
Overall Summary of Adverse Events
Summary Statistics: Safety Analysis Set
Part 1

Event	[14C]-GDC-9545 Cap (N=XX) n(%)	Total Number of Events
AEs	xx (xx.x)	xx
Grade 3 AEs (1)	xx (xx.x)	xx
Grade 4 AEs (2)	xx (xx.x)	xx
IMP related AEs	xx (xx.x)	xx
AEs of Special Interest	xx (xx.x)	xx
Serious AEs	xx (xx.x)	xx
AEs leading to IMP withdrawal	xx (xx.x)	xx
Grade 5 (3)	xx (xx.x)	xx

Note: The data in this table are presented in listing x.x
All subjects were planned to receive a single oral dose of [14C]-GDC-9545 capsule, 30mg (NMT 4.6 MBq [124 µCi]) in Part 1
AEs are coded using MedDRA vXX.X
(1) NCI CTCAE Grade 3: Severe or medically significant but not immediately life threatening, (2) NCI CTCAE Grade 4: Life-Threatening consequences or urgent intervention indicated, (3) NCCI CTCAE Grade 5: Death related to AE
Serious AEs are those AEs which are graded as NCI CTCAE Grade 4 or 5

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TABLE 14.3.1.2
Adverse Events
By MedDRA System Organ Class and Preferred Term
Summary Statistics: Safety Analysis Set
Part 1

System Organ Class Preferred Term	[14C]-GDC-9545 Cap (N=XX) n(%)	Total Number of Events
AEs	xx (xx.x)	xx
SYSTEM ORGAN CLASS 1	xx (xx.x)	xx
PREFERRED TERM 1	xx (xx.x)	xx
PREFERRED TERM 2	xx (xx.x)	xx
etc	…	…
SYSTEM ORGAN CLASS 2	xx (xx.x)	xx
PREFERRED TERM 1	xx (xx.x)	xx
PREFERRED TERM 2	xx (xx.x)	xx
etc	…	…
…	…	…

Note: The data in this table are presented in listing x.x
All subjects were planned to receive a single oral dose of [14C]-GDC-9545 capsule, 30mg (NMT 4.6 MBq [124 µCi]) in Part 1
AEs are coded using MedDRA vXX.X and are presented in descending order of frequency
Subjects experiencing more than 1 episode of a AE are counted only once within each SOC and PT
Counts of number of subjects are by maximum severity, i.e. subjects experiencing more than 1 episode of a AE are counted only once within each SOC and PT using the most severe episode

PROGRAM PATH: X:\~\QSCXXXXXX\~\TFLS\PRODUCTION\TAB-XX DDMMMYYYY HH:MM

(Programming note: This table will be continued for all SOC and PT)
(Programming note: Similar tables will be produced for AEs of Special Interest, i.e. Table 14.3.1.5 and SAEs, i.e. Table 14.3.1.6.)

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TABLE 14.3.1.3
Adverse Events
By MedDRA System Organ Class, Preferred Term and Severity
Summary Statistics: Safety Analysis Set
Part 1

System Organ Class Preferred Term	[14C]-GDC-9545 Cap (N=XX) Mild n(%)	Moderate n(%)	Severe n(%)	Life-threatening n(%)	Death n(%)
AEs	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
SYSTEM ORGAN CLASS 1	xx (xx.x)	xx (xx.x)	xx (xx.x	xx (xx.x)	xx (xx.x)
PREFERRED TERM 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
PREFERRED TERM 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc	…	…	…		
SYSTEM ORGAN CLASS 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
PREFERRED TERM 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
PREFERRED TERM 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc	…	…	…		
…	…	…	…		

Note: The data in this table are presented in listing x.x
All subjects were planned to receive a single oral dose of [14C]-GDC-9545 capsule, 30mg (NMT 4.6 MBq [124 µCi]) in Part 1
AEs are coded using MedDRA vXX.X and are presented in descending order of frequency
Counts are given for total number of subjects, not for events
Counts of number of subjects are by maximum severity, i.e. subjects experiencing more than 1 episode of a AE are counted only once within each SOC and PT using the most severe episode

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(Programming note: This table will be continued for all SOC and PT)

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TABLE 14.3.1.4
Adverse Events
By MedDRA System Organ Class, Preferred Term and Relationship to IMP
Summary Statistics: Safety Analysis Set
Part 1

System Organ Class Preferred Term	[14C]-GDC-9545 Cap (N=XX) Yes n(%)	 No n(%)
AEs	xx (xx.x)	xx (xx.x)
SYSTEM ORGAN CLASS 1	xx (xx.x)	xx (xx.x)
PREFERRED TERM 1	xx (xx.x)	xx (xx.x)
PREFERRED TERM 2	xx (xx.x)	xx (xx.x)
etc	…	…
SYSTEM ORGAN CLASS 2	xx (xx.x)	xx (xx.x)
PREFERRED TERM 1	xx (xx.x)	xx (xx.x)
PREFERRED TERM 2	xx (xx.x)	xx (xx.x)
etc	…	…
…	…	…

Note: The data in this table are presented in listing x.x
All subjects were planned to receive a single oral dose of [14C]-GDC-9545 capsule, 30mg (NMT 4.6 MBq [124 µCi]) in Part 1
AEs are coded using MedDRA vXX.X and are presented in descending order of frequency
"Yes"= there is a plausible temporal relationship between the onset of the AE ad the administration of the study drug
"No"= the AE has no plausible temporal relationship to the administration of the study drug
Counts are given for total number of subjects, not for events
Counts are given by closest relationship, i.e. subjects experiencing more than 1 AE are counted only once within each SOC and PT using the most closely related event

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(Programming note: This table will be continued for all SOC and PT)

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TABLE 14.3.2.1
Overall Summary of Adverse Events
Summary Statistics: Safety Analysis Set
Part 2

	GDC-9545 IV (N=X)		GDC-9545/F12 Cap (N=X)		GDC-9545/F18 Cap (N=X)		Overall (N=X)	
Event	n(%)	Total Number of Events	n(%)	Total Number of Events	n(%)	Total Number of Events	n(%)	Total Number of Events
AEs	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
Grade 3 AEs (1)	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
Grade 4 AEs (2)	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
IMP related AEs	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
AE of Special Interest	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
Serious AEs	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
AEs leading to IMP withdrawal	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
Grade 5 AEs (3)	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx

Note: The data in this table are presented in listing x.x
All subjects were to receive GDC-9545 IV administration 30 mg as a solution for infusion, 3 mg/mL (10 mL)[B] in Period 1 and GDC-9545/F12 capsule 30 mg [C] and GDC-9545/F18 capsule 30 mg [D] in a randomized manner in Period 2 and 3 in Part 2
AEs are coded using MedDRA vXX.X
(1) NCI CTCAE Grade 3: Severe or medically significant but not immediately life threatening, (2) NCI CTCAE Grade 4: Life-Threatening consequences or urgent intervention indicated, (3) NCCI CTCAE Grade 5: Death related to AE
Serious AEs are those AEs which are graded as NCI CTCAE Grade 4 or 5

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TABLE 14.3.2.2
Adverse Events
By MedDRA System Organ Class and Preferred Term
Summary Statistics: Safety Analysis Set
Part 2

	GDC-9545 IV (N=X)		GDC-9545/F12 Cap (N=X)		GDC-9545/F18 Cap (N=X)	
	n(%)	Total Number of Events	n(%)	Total Number of Events	n(%)	Total Number of Events
AEs	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
SYSTEM ORGAN CLASS 1	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
PREFERRED TERM 1	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
PREFERRED TERM 2	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
etc	…	…	…	…	…	…
SYSTEM ORGAN CLASS 2	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
PREFERRED TERM 1	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
PREFERRED TERM 2	xx (xx.x)	xx	xx (xx.x)	xx	xx (xx.x)	xx
etc	…	…	…	…	…	…

Note: The data in this table are presented in listing x.x
All subjects were to receive GDC-9545 IV administration 30 mg as a solution for infusion, 3 mg/mL (10 mL)[B] in Period 1 and GDC-9545/F12 capsule 30 mg [C] and GDC-9545/F18 capsule 30 mg [D] in a randomized manner in Period 2 and 3 in Part 2
AEs are coded using MedDRA vXX.X and are presented in descending order of frequency
Subjects experiencing more than 1 episode of a AE within a treatment are counted only once within each SOC and PT
Counts of number of subjects are by maximum severity, i.e. subjects experiencing more than 1 episode of a AE are counted only once within each SOC and PT using the most severe episode

PROGRAM PATH: X:\~\QSCXXXXXX\~\TFLS\PRODUCTION\TAB-XX DDMMMYYYY HH:MM

(Programming note: This table will be continued for all SOC and PT)
(Programming note: Similar tables will be produced for AEs of Special Interest, i.e. Table 14.3.2.5 and SAEs, i.e. Table 14.3.2.6.)

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TABLE 14.3.2.3
Adverse Events
By MedDRA System Organ Class, Preferred Term and Severity
Summary Statistics: Safety Analysis Set
Part 2

GDC-9545 IV (N=X)

System Organ Class Preferred Term	Mild n(%)	Moderate n(%)	Severe n(%)	Life-threatening n(%)	Death n(%)
AEs	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
SYSTEM ORGAN CLASS 1	xx (xx.x)	xx (xx.x)	xx (xx.x	xx (xx.x)	xx (xx.x)
PREFERRED TERM 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
PREFERRED TERM 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc	…	…	…		
SYSTEM ORGAN CLASS 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
PREFERRED TERM 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
PREFERRED TERM 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc	…	…	…		
…	…	…	…		

Note: The data in this table are presented in listing x.x
All subjects were to receive GDC-9545 IV administration 30 mg as a solution for infusion, 3 mg/mL (10 mL)[B] in Period 1 and GDC-9545/F12 capsule 30 mg [C] and GDC-9545/F18 capsule 30 mg [D] in a randomized manner in Period 2 and 3 in Part 2
AEs are coded using MedDRA vXX.X and are presented in descending order of frequency
Counts are given for total number of subjects, not for events
Counts of number of subjects are by maximum severity, i.e. subjects experiencing more than 1 episode of a AE within a treatment are
counted only once within each SOC and PT using the most severe episode

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(Programming note: This table will be continued for all SOC and PT)
(Programming note: This table will be continued for each treatment with a separate page for each)

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TABLE 14.3.2.4
Adverse Events
By MedDRA System Organ Class, Preferred Term and Relationship to IMP
Summary Statistics: Safety Analysis Set
Part 2

	GDC-9545 IV (N=X)		GDC-9545/F12 Cap (N=X)		GDC-9545/F18 Cap (N=X)	
	Yes n(%)	No n(%)	Yes n(%)	No n(%)	Yes n(%)	No n(%)
AEs	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
SYSTEM ORGAN CLASS 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
PREFERRED TERM 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
PREFERRED TERM 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc	…	…	…	…	…	…
SYSTEM ORGAN CLASS 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
PREFERRED TERM 1	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
PREFERRED TERM 2	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc	…	…	…	…	…	…

Note: The data in this table are presented in listing x.x
All subjects were to receive GDC-9545 IV administration 30 mg as a solution for infusion, 3 mg/mL (10 mL)[B] in Period 1 and GDC-9545/F12 capsule 30 mg [C] and GDC-9545/F18 capsule 30 mg [D] in a randomized manner in Period 2 and 3 in Part 2
AEs are coded using MedDRA vXX.X and are presented in descending order of frequency
"Yes"= there is a plausible temporal relationship between the onset of the AE and the administration of the study drug
"No"= the AE has no plausible temporal relationship to the administration of the study drug
Counts are given for total number of subjects, not for events
Counts are given by closest relationship, i.e. subjects experiencing more than 1 AE within a treatment are counted only once within each SOC and PT using the most closely related event

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(Programming note: This table will be continued for all SOC and PT)

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TABLE 14.4.1.1
Hematology and Coagulation
Summary Statistics: Safety Analysis Set
Part 1

[14C]-GDC-9545 Cap (N=XX)
<Parameter> (<units>) [ref range xxx - xxx]

	Result						Change from Baseline					
Time Point	n	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
BASELINE	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x						
480 H	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x

Note: The data in this table are presented in listing x.x
All subjects were planned to receive a single oral dose of [14C]-GDC-9545 capsule, 30mg (NMT 4.6 MBq [124 µCi]) in Part 1
BASELINE is defined as Day -1, Admission

PROGRAM PATH: X:\~\QSCXXXXXX\~\TFLS\PRODUCTION\TAB-XX DDMMMYYYY HH:MM

(Programming note: This table will be continued for all hematology and coagulation parameters and all time points
A similar table will be produced for
• Clinical Chemistry, i.e. Table [14.4.1.3]
Parameter may be added as the first column in this table)

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TABLE 14.4.1.2
Hematology and Coagulation
Shift Analysis: Safety Analysis Set
Part 1

[14C]-GDC-9545 Cap (N=XX)
<Parameter> (<units>) [ref range xxx - xxx]

		Baseline		
Time Point Assessment	N#	Below n(%)	Within n(%)	Above n(%)
480 H	xx			
Below		xx (xx.x)	xx (xx.x)	xx (xx.x)
Within		xx (xx.x)	xx (xx.x)	xx (xx.x)
Above		xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: The data in this table are presented in listing x.x
All subjects were planned to receive a single oral dose of [14C]-GDC-9545 capsule, 30mg (NMT 4.6 MBq [124 µCi]) in Part 1
BASELINE is defined as Day -1, Admission
N# is the total number of subjects that have a value at baseline and each given time-point and is used in the denominator for calculating the percentages of subjects, n indicates the number of subjects with a baseline and a post baseline assessment at the time point indicated. Below/within/above indicate the number (%) of subjects with assessments below/within/above the normal reference range

PROGRAM PATH: X:\~\QSCXXXXXX\~\TFLS\PRODUCTION\TAB-XX DDMMMYYYY HH:MM

(Programming note: This table will be continued for all hematology and coagulation parameters and all time points
A similar table will be produced for
• Clinical Chemistry, i.e. Table [14.4.1.4]
Parameter may be added as the first column in this table)

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TABLE 14.4.2.1
Hematology and Coagulation
Summary Statistics: Safety Analysis Set
Part 2

<Parameter> (<units>) [ref range xxx-xxx]

		Result						Change from Baseline					
Treatment	Time Point	n	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
	BASELINE	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x						
GDC-9545 IV (N=X)	TIME POINT X	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x
GDC-9545/F12 Cap (N=X)	TIME POINT X	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x
GDC-9545/F18 Cap (N=XX)	TIME POINT X	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x

Note: The data in this table are presented in listing x.x
All subjects were to receive GDC-9545 IV administration 30 mg as a solution for infusion, 3 mg/mL (10 mL)[B] in Period 1 and GDC-9545/F12 capsule 30 mg [C] and GDC-9545/F18 capsule 30 mg [D] in a randomized manner in Period 2 and 3 in Part 2
BASELINE is defined as Day -1, Period 1

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(Programming note: This table will be continued for all hematology and coagulation parameters and all time points
A similar table will be produced for Clinical Chemistry i.e. Table [14.4.2.3])
(Programming note: Parameter may be added as the first column in this table)
(Programming note: The post-baseline timepoint for Period 1 is the Day -1 of Period 2 etc. and for Period 3 is 168h post-dose)

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TABLE 14.4.2.2
Hematology and Coagulation
Shift Analysis: Safety Analysis Set
Part 2

<Parameter> (<units>) [ref range, xxx-xxx (female)]

	GDC-9545 IV (N=X) Baseline			GDC-9545/F12 Cap (N=X) Baseline			GDC-9545/F18 Cap (N=X) Baseline		
Time Point Assessment	Below n(%)	Within n(%)	Above n(%)	Below n(%)	Within n(%)	Above n(%)	n(%)	n(%)	n(%)
TIMEPOINT X N#	xx			xx			xx		
Below	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Within	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Above	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: The data in this table are presented in listing x.x
All subjects were to receive GDC-9545 IV administration 30 mg as a solution for infusion, 3 mg/mL (10 mL)[B] in Period 1 and GDC-9545/F12 capsule 30 mg [C] and GDC-9545/F18 capsule 30 mg [D] in a randomized manner in Period 2 and 3 in Part 2
BASELINE is defined as Day -1, Period 1
N# indicates the number of subjects with a baseline and a post baseline assessment at the time point indicated
Below/within/above indicate the n(%)=number(%) of subjects with assessments below/within/above the normal reference range at baseline

PROGRAM PATH: X:\~\QSCXXXXXX\~\TFLS\PRODUCTION\TAB-XX DDMMMYYYY HH:MM

(Programming note: This table will be continued for all hematology and coagulation parameters and all time points
A similar table will be produced for Clinical Chemistry i.e. Table [14.4.2.4])
(Programming note: Parameter may be added as the first column in this table)

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TABLE 14.5.1.1
Vital Signs
Summary Statistics: Safety Analysis Set
Part 1

[14C]-GDC-9545 Cap (N=XX)
<Parameter> (<units>) [ref range xxx - xxx (age xx - xx), xxx - xxx (age > xx)]

	Result						Change from Baseline						Substantial Change		
Time Point	n	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max	DEC	NONE	INC
BASELINE	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x									
TIME POINT 1	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx	xx
TIME POINT 2	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx	xx
TIME POINT 3	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx	xx
…	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…
<All other time points>	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx	xx

Note: The data in this table are presented in listing x.x
All subjects were planned to receive a single oral dose of [14C]-GDC-9545 capsule, 30mg (NMT 4.6 MBq [124 µCi]) in Part 1
BASELINE is defined as Day 1, Pre-dose
Substantial change is defined as: > ± 20 mmHg Systolic BP, > ± 10 mmHg Diastolic BP and > ± 15 bpm pulse rate
DEC: number of subjects with substantial decrease from baseline, NONE: number of subjects with no substantial change from baseline,
INC: number of subjects with substantial increase from baseline

PROGRAM PATH: X:\~\QSCXXXXXX\~\TFLS\PRODUCTION\TAB-XX DDMMMYYYY HH:MM

(Programming note: This table will be continued for all vital signs parameters
Parameter may be added as the first column in this table)

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TABLE 14.5.1.2.1
ECGs
Summary Statistics: Safety Analysis Set
Part 1

[14C]-GDC-9545 Cap (N=XX)
<Parameter> (<units>) [<ref range xxx - xxx (age xx - xx), xxx - xxx (age > xx)> / <ref range xxx - xxx >]

	Result						Change from Baseline					
Time Point	n	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
BASELINE	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x						
TIME POINT 1	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x
TIME POINT 2	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x
TIME POINT 3	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x
…	…	…	…	…	…	…	…	…	…	…	…	…
<All other time points>	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x

Note: The data in this table are presented in listing x.x
All subjects were planned to receive a single oral dose of [14C]-GDC-9545 capsule, 30mg (NMT 4.6 MBq [124 µCi]) in Part 1
BASELINE is defined as Day 1, Pre-dose

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(Programming note: This table will be continued for all ECG parameters, which will follow the order given in the RAP text
Parameter may be added as the first column in this table)

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TABLE 14.5.1.2.2
ECGs
QTcF Categorical Data
Summary Statistics: Safety Analysis Set
Part 1

[14C]-GDC-9545 Cap (N=XX)

		QTcF Interval (msec)				QTcF Interval Increase (msec)		
Time Point	N#	<=450 n(%)	451-480 n(%)	481-500 n(%)	>500 n(%)	<30 n(%)	30-60 n(%)	>60 n(%)
BASELINE	xx	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)			
TIME POINT 1	xx	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
TIME POINT 2	xx	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
TIME POINT 3	xx	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
…	…	…	…	…	…	…	…	…
<All other time points>	xx	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: The data in this table are presented in listing x.x
All subjects were planned to receive a single oral dose of [14C]-GDC-9545 capsule, 30mg (NMT 4.6 MBq [124 µCi]) in Part 1
BASELINE is defined as Day 1, Pre-dose
Categories for QTcF interval and QTcF interval increases are based on ICH E14 guidelines
N# is the total number of subjects at the relevant time point and is used in the denominator for calculating the percentages of subjects, n indicates the number of subjects with observations at the given time point

PROGRAM PATH: X:\~\QSCXXXXXX\~\TFLS\PRODUCTION\TAB-XX

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TABLE 14.5.2.1
Vital Signs
Summary Statistics: Safety Analysis Set
Part 2

<Parameter> (<units>) [ref range xxx - xxx (age xx - xx), xxx - xxx (age > xx)]

		Result						Change from Baseline						Substantial Change (1)		
Treatment	Time Point	n	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max	DEC	NONE	INC
GDC-9545 IV	BASELINE	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x									
(N=X)	TIME POINT 1	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx	xx
	TIME POINT 2	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx	xx
	TIME POINT 3	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx	xx
	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…
	<All other time points>	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx	xx
GDC-9545/F12	BASELINE	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x									
Cap (N=X)	TIME POINT 1	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx	xx
	TIME POINT 2	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx	xx
	TIME POINT 3	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx	xx
	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…
	<All other time points>	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx	xx
…	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…	…

Note: The data in this table are presented in listing x.x
All subjects were to receive GDC-9545 IV administration 30 mg as a solution for infusion, 3 mg/mL (10 mL)[B] in Period 1 and GDC-9545/F12 capsule 30 mg [C] and GDC-9545/F18 capsule 30 mg [D] in a randomized manner in Period 2 and 3 in Part 2
BASELINE is defined as Day 1, Pre-dose of the corresponding study period
Substantial change is defined as: > ± 20 mmHg Systolic BP, > ± 10 mmHg Diastolic BP and > ± 15 bpm pulse rate
DEC: number of subjects with substantial decrease from baseline NONE: number of subjects with no substantial change from baseline, INC: number of subjects with substantial increase from baseline

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(Programming note: This table will be continued for all vital signs parameters)
(Programming note: Parameter may be added as the first column in this table)

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TABLE 14.5.2.2.1
ECGs
Summary Statistics: Safety Analysis Set
Part 2

<Parameter> (<units>) [<ref range xxx - xxx (age xx - xx), xxx - xxx (age > xx)> / <ref range xxx-xxx >]

		Result						Change from Baseline					
Treatment	Time Point	n	Mean	SD	Median	Min	Max	n	Mean	SD	Median	Min	Max
GDC-9545 IV	BASELINE	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x						
(N=X)	TIME POINT 1	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x
	TIME POINT 2	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x
	TIME POINT 3	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x
	…	…	…	…	…	…	…	…	…	…	…	…	…
	<All other time points>	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x
GDC-9545/	BASELINE	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x						
F12 Cap	TIME POINT 1	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x
(N=X)	TIME POINT 2	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x
	TIME POINT 3	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x
	…	…	…	…	…	…	…	…	…	…	…	…	…
	<All other time points>	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x	xx	xx.xx	xx.xx	xx.xx	xx.x	xx.x
…	…	…	…	…	…	…	…	…	…	…	…	…	…

Note: The data in this table are presented in listing x.x
All subjects were to receive GDC-9545 IV administration 30 mg as a solution for infusion, 3 mg/mL (10 mL)[B] in Period 1 and GDC-9545/F12 capsule 30 mg [C] and GDC-9545/F18 capsule 30 mg [D] in a randomized manner in Period 2 and 3 in Part 2
BASELINE is defined as Day 1, Pre-dose of the corresponding study period

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(Programming note: This table will be continued for all ECG parameters)
(Programming note: Parameter may be added as the first column in this table)

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TABLE 14.5.2.2.2
ECGs
QTcF Categorical Data
Summary Statistics: Safety Analysis Set
Part 2

			QTcF Interval (msec)				QTcF Interval Increase (msec)		
Treatment	Time Point	N#	<=450 n(%)	451-480 n(%)	481-500 n(%)	>500 n(%)	<30 n(%)	30-60 n(%)	>60 n(%)
GDC-9545 IV	BASELINE		xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)			
(N=X)	TIME POINT 1	xx	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	TIME POINT 2	xx	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	TIME POINT 3	xx	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	…	…	…	…	…	…	…	…	…
	<All other time points>	xx	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
GDC-9545/	BASELINE		xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)			
F12 Cap	TIME POINT 1	xx	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
(N=X)	TIME POINT 2	xx	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	TIME POINT 3	xx	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	…	…	…	…	…	…	…	…	…
	<All other time points>	xx	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
…	…	…	…	…	…	…	…	…	…

Note: The data in this table are presented in listing x.x
All subjects were to receive GDC-9545 IV administration 30 mg as a solution for infusion, 3 mg/mL (10 mL)[B] in Period 1 and GDC-9545/F12 capsule 30 mg [C] and GDC-9545/F18 capsule 30 mg [D] in a randomized manner in Period 2 and 3 in Part 2
BASELINE is defined as Day 1, Pre-dose of the corresponding study period
Categories for QTcF interval and QTcF interval increases are based on ICH E14 guidelines
N# is the number of subjects with a value at baseline and the relevant post-dose time point. It is the denominator for calculating the percentages of subjects, n indicates the number of subjects with observations at the given time point

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Appendix 1: Part 1 Schedule of Activities

Study Procedures	Screening	Residency in Clinical Unit																		
Days	–28 to –2	–1[a]	1												2	3	4	5	6	
Time after study drug dosing (hours) [b]			Pre-dose	0	1	1.5	2	2.5	3	4	5	6	8	12	24	48	72	96	120	
Informed consent	X[c]																			
Inclusion/exclusion criteria	X	X	X																	
Medical history	X	X[d]																		
Complete physical examination [e]	X																			
Limited physical examination [f]		X																		
Height, weight and BMI	X																			
Vein assessment	X																			
12-lead safety ECG	X		X		X					X					X					
Vital signs [g]	X		X		X					X					X					
Laboratory safety tests [h]	X	X																		
Urinalysis [i]	X	X																		
Urine drug screen [j]	X	X																		
Alcohol breath test	X	X																		
Carbon monoxide breath test	X	X																		
Virology screen [k]	X																			
Estradiol and FSH [l]	X																			
Pregnancy test [m]	X	X																		

Study Procedures	Screening	Residency in Clinical Unit																	
Days	–28 to –2	–1[a]	1											2	3	4	5	6	
Time after study drug dosing (hours) [b]			Pre-dose	0	1	1.5	2	2.5	3	4	5	6	8	12	24	48	72	96	120
Adverse event monitoring [n]	◄	►																	
Prior and concomitant medications [o]	◄	►																	
Study drug administration				X															
Plasma samples for GDC-9545 and total radioactivity PK [p]			X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Whole blood samples for total radioactivity PK [p]			X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Plasma samples for metabolite profiling and ID [p]			X		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Urine samples for total radioactivity and metabolite profiling and identification [q]			◄	►															
Feces samples for total radioactivity and metabolite profiling and identification [r]		◄	►																
Confinement in the clinic		◄	►																

Study Procedures	Residency in Clinical Unit															Return Visits		
Days	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21[s]	28[s]	35[s]	42[s]
Time after study drug dosing (hours) [b]	144	168	192	216	240	264	288	312	336	360	384	408	432	456	480	648	816	984
Limited physical examination [f]															X			
12-lead safety ECG															X			
Vital signs [g]															X			
Laboratory safety tests [h]															X			
Urinalysis [i]															X			
Adverse event monitoring [n]	←	—	—	—	—	—	—	—	—	—	—	—	—	—	→			
Prior and concomitant medications [o]	←	—	—	—	—	—	—	—	—	—	—	—	—	—	→			
Plasma samples for GDC-9545 and total radioactivity PK [p]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Whole blood samples for total radioactivity PK [p]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Plasma samples for metabolite profiling and ID [p]	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Urine samples for total radioactivity and metabolite profiling and identification [q]	←	—	—	—	—	—	—	—	—	—	—	—	—	—	→	X	X	X
Feces samples for total radioactivity and metabolite profiling and identification [r]	←	—	—	—	—	—	—	—	—	—	—	—	—	—	→	X	X	X
Confinement in the clinic	←	—	—	—	—	—	—	—	—	—	—	—	—	—	→	X	X	X

[a] Admission to the clinical unit. Eligibility will be reassessed at admission/pre-dose.

[b] All assessments will be timed and performed relative to the start of dosing

[c] Informed consent must be documented before any study-specific screening procedure is performed, and may be obtained more than 28 days before initiation of study treatment.

[d] Update only

[e] Includes evaluation of the head, eyes, ears, nose, and throat, and the cardiovascular, dermatologic, musculoskeletal, respiratory, GI, genitourinary, and neurologic systems.

[f] Perform a limited, symptom-directed examination at specified timepoints or as clinically indicated.

[g] Includes pulse rate, and systolic and diastolic blood pressure while the subject is in a supine position, and oral temperature at all time points.

[h] Hematology includes white blood cell (WBC) count, red blood cell (RBC) count, hemoglobin, hematocrit (packed cell volume), mean cell hemoglobin, mean cell hemoglobin concentration, mean cell volume, platelet count, and differential count (neutrophils, eosinophils, basophils, monocytes, lymphocytes). Chemistry panel (serum) includes magnesium, sodium, potassium, chloride, glucose, fasting glucose, urea, creatinine, creatine kinase, total protein, albumin, phosphate (inorganic), calcium, total bilirubin, direct bilirubin (only if total is elevated), alkaline phosphatase, alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma glutamyl transferase (GGT), and bicarbonate. Creatinine clearance will be estimated at screening from serum creatinine using the Cockcroft-Gault equation for eligibility purposes. Coagulation panel includes international normalized ratio (INR), activated partial thromboplastin time (APTT), thrombin time and prothrombin time (PT).

[i] Includes pH, specific gravity, glucose, protein, ketones, blood, bilirubin, leukocytes, nitrites, urobilinogen. Microbiology and/or microscopic urinalysis examination, at the discretion of the Investigator based on urinalysis results (sediment, RBCs, WBCs, casts, crystals, epithelial cells, bacteria).

[j] Amphetamines, barbiturates, benzodiazepines, cocaine, marijuana/cannabis, methadone, methamphetamine/ecstasy, morphine/opiates, phencyclidine, and tricyclic anti-depressants.

[k] HBsAg, HCV Antibody, HIV Antibody for all subjects.

[l] Estradiol and FSH for post-menopausal female subjects only.

[m] All subjects must have a negative highly sensitive serum pregnancy test result at screening and a negative highly sensitive urine pregnancy test at admission.

[n] After informed consent has been obtained but prior to initiation of study drug, only serious adverse events caused by a protocol-mandated intervention should be reported. After initiation of study drug, all adverse events will be reported until 28 days after the final dose of study drug. All deaths that occur during the protocol-specified adverse event reporting period (see protocol Section 5.3.1), regardless of relationship to study drug, must be recorded on the Adverse Event eCRF and immediately reported to the Sponsor (see protocol Section 5.4.2). Deaths that occur after the adverse event reporting period should be reported as described in protocol Section 5.6. In addition, the Sponsor should be notified if the Investigator becomes aware of any serious adverse event that is believed to be related to prior study drug treatment (see protocol Section 5.6).

[o] Medication (e.g., prescription drugs, over-the-counter drugs, HRT, vaccines, topical medications, herbal or homeopathic remedies, nutritional supplements) used by a subject in addition to protocol-mandated treatment from 14 days prior to initiation of study drug until discharge from the study.

[p] See Appendix 3 for detailed schedule. Blood sample collection will be at pre-dose, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 8, 12, 24 hours post-dose, and at 24-hour intervals thereafter until study completion/early termination. Permissible time windows for PK sampling are: pre-dose, ≤1 hour before dosing; 1 hour post-dose, ±5 minutes; 1.5 to 8 hours, ±15 minutes; 12 to 24 hours, ±30 minutes; 48 to 480 hours, ±4 hours; 648 to 984 hours, ±1 day

[q] A single urine sample will be collected at pre-dose (the first void of the day) and then at the following collection periods: 0 to 12 hours, 12 to 24 hours, and then daily (24 hour intervals) until the mass balance discharge criteria have been met or until Day 21, and then on a weekly basis starting on Day 28 (until criteria met or Day 42 reached).

[r] The pre-dose feces sample will be taken in the 24 hours period before dosing (between admission and pre-dose). Post-dose feces will be collected at 24 hour intervals until the mass balance discharge criteria have been met or until Day 21, and then on a weekly basis starting on Day 28 (until criteria met or Day 42 reached).

[s] It is planned that subjects will remain resident in the clinical unit until 480 hours post-dose (Day 21) when they will be discharged from the clinical unit. The same procedures are to be performed at early termination/withdrawal as at discharge. Subjects may be discharged as a group earlier if the mass balance discharge criteria have been achieved. If the criteria have not been met by Day 21, subjects will be discharged from the clinical unit and those who have not met the discharge criteria will return for outpatient visits every 7 days for a 24-hour sample collection interval until the mass balance discharge criteria are met (the maximum number of 24hour return visits will not exceed 3). If additional residency is not considered appropriate or necessary, then home collections of urine and/or feces- may be requested at the discretion of the Investigator for individual subjects. Safety discharge assessments will be performed at the time of actual discharge or early termination/withdrawal from the clinical unit. PK, TR and metabolite profiling and identification blood samples to be collected at 480 hours post-dose or at time of actual discharge/early termination, if earlier. Any subject who discontinues or is withdrawal from the study after being discharge from the clinical unit will be asked to return to clinical unit to undergo early termination/withdrawal procedures.

Appendix 2: Part 2 Schedule of Activities

Study Procedures	Screening	Study days in each period																	
	–28 to –2	-1[a]	1																2
Time after study drug dosing (hours) – (relative to start of IV infusion for Treatment B) [b]			Pre-dose	0	0.25	0.5	0.58	0.67	1	1.5	2	2.5	3	4	5	6	8	12	24
Informed consent	X[c]																		
Inclusion/exclusion criteria	X	X[d]	X																
Medical history	X	X[e]																	
Complete physical examination [f]	X																		
Limited physical examination [g]		X[h]																	
Height, weight and BMI	X																		
Vein assessment	X																		
12-lead safety ECG	X		X			X			X					X					X
Vital signs [i]	X		X			X			X					X					X
Laboratory safety tests [j]	X	X[h]																	
Urinalysis [k]	X	X[h]																	
Urine drug screen [l]	X	X[d]																	
Alcohol breath test	X	X[d]																	
Carbon monoxide breath test	X	X[d]																	
Randomization			X[d]																
Virology screen [m]	X																		
Estradiol and FSH [n]	X																		
Pregnancy test [o]	X	X[d]																	

Study Procedures	Screening	Study days in each period																	
	–28 to –2	-1[a]	1																2
Time after study drug dosing (hours) – (relative to start of IV infusion for Treatment B) [b]			Pre-dose	0	0.25	0.5	0.58	0.67	1	1.5	2	2.5	3	4	5	6	8	12	24
Adverse event monitoring [p]	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	→
Prior and concomitant medications [q]	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	→
Study drug administration [r]				X															
Plasma samples for GDC-9545 PK [s]			X		X[t]	X[t]	X[t]	X[t]	X	X	X	X[u]	X	X	X[u]	X	X	X	X
Confinement in the clinic		←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	←	→

Study Procedures	Study days in each period						Follow-Up Phone Call
	3	4	5	6	7	8[v]	14 to 16[w]
Time after study drug dosing (hours) – (relative to start of IV infusion for Treatment B) [b]	48	72	96	120	144	168	
Limited physical examination [g]						X[x]	
12-lead safety ECG						X[x]	
Vital signs [i]						X[x]	
Laboratory safety tests [j]						X[x]	
Urinalysis [k]						X[x]	
Adverse event monitoring [p]	←	—	—	—	—	→	
Prior and concomitant medications [q]	←	—	—	—	—	→	
Plasma samples for GDC-9545 PK [s]	X	X	X	X	X	X[y]	
Confinement in the clinic	←	—	—	—	—	→	

0.25 hours = 15 minutes, 0.5 hours = 30 minutes, 0.58 hours = 35 minutes; 0.67 hours = 40 minutes

[a] Admission to the clinical unit (Period 1 only). Subjects will be resident in the clinical unit for 28 to 29 consecutive nights that will cover all 3 treatment periods. Eligibility will be reassessed at admission/pre-dose.

[b] All assessments will be timed and performed relative to the start of dosing

[c] Informed consent must be documented before any study-specific screening procedure is performed, and may be obtained more than 28 days before initiation of study treatment.

[d] Period 1 only

[e] Update only (Period 1 only).

[f] Includes evaluation of the head, eyes, ears, nose, and throat, and the cardiovascular, dermatologic, musculoskeletal, respiratory, GI, genitourinary, and neurologic systems.

[g] Perform a limited, symptom-directed examination at specified timepoints or as clinically indicated.

[h] Periods 1, 2 and 3

[i] Includes pulse rate, and systolic and diastolic blood pressure while the subject is in a supine position, and oral temperature at all time points.

[j] Hematology includes white blood cell (WBC) count, red blood cell (RBC) count, hemoglobin, hematocrit (packed cell volume), mean cell hemoglobin, mean cell hemoglobin concentration, mean cell volume, platelet count, and differential count (neutrophils, eosinophils, basophils, monocytes, lymphocytes). Chemistry panel (serum) includes magnesium, sodium, potassium, chloride, glucose, fasting glucose, urea, creatinine, creatine kinase, total protein, albumin, phosphate (inorganic), calcium, total bilirubin, direct bilirubin (only if total is elevated), alkaline phosphatase, alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma glutamyl transferase (GGT), and bicarbonate. Creatinine clearance will be estimated at screening from serum creatinine using the Cockcroft-Gault equation for eligibility purposes. Coagulation panel includes international normalized ratio (INR), activated partial thromboplastin time (APTT), thrombin time and prothrombin time (PT).

[k] Includes pH, specific gravity, glucose, protein, ketones, blood, bilirubin, leukocytes, nitrites, urobilinogen. Microbiology and/or microscopic urinalysis examination, at the discretion of the Investigator based on urinalysis results (sediment, RBCs, WBCs, casts, crystals, epithelial cells, bacteria).

[l] Amphetamines, barbiturates, benzodiazepines, cocaine, marijuana/cannabis, methadone, methamphetamine/ecstasy, morphine/opiates, phencyclidine, and tricyclic anti-depressants.

[m] HBsAg, HCV Antibody, HIV Antibody for all subjects.

[n] Estradiol and FSH for post-menopausal female subjects only.

[o] All subjects must have a negative highly sensitive serum pregnancy test result at screening and a negative highly sensitive urine pregnancy test at admission.

[p] After informed consent has been obtained but prior to initiation of study drug, only serious adverse events caused by a protocol-mandated intervention should be reported. After initiation of study drug, all adverse events will be reported until 28 days after the final dose of study drug. All deaths that occur during the protocol-specified adverse event reporting period (see protocol Section 5.3.1), regardless of relationship to study drug, must be recorded on the Adverse Event eCRF and immediately reported to the Sponsor (see protocol Section 5.4.2). Deaths that occur after the adverse event reporting period should be reported as described in protocol Section 5.6. In addition, the Sponsor should be notified if the Investigator becomes aware of any serious adverse event that is believed to be related to prior study drug treatment (see protocol Section 5.6).

[q] Medication (e.g., prescription drugs, over-the-counter drugs, HRT, vaccines, topical medications, herbal or homeopathic remedies, nutritional supplements) used by a subject in addition to protocol-mandated treatment from 14 days prior to initiation of study drug until discharge from the study.

[r] Treatment B will be administered intravenously over 30 minutes (as an infusion). For Treatment B only, to assess tolerability of the IV administration, the first subject will be dosed as a sentinel; then, at least 4 hours later, the second subject will be dosed only if there are no acute safety findings for the first subject. If the first two subjects tolerated the IV dose, in the opinion of the Principal Investigator and Medical Monitor, the remaining subjects will be dosed. The third subject will be dosed at least 20 hours after the second subject (i.e., at least 24 hours after the first subject). All subsequent dosing of the IV formulation will be staggered by at least 15 minutes. For Treatments C and D, all subjects will be dosed as a single cohort.

[s] See Appendix 4 for detailed schedule. Permissible time windows for PK sampling and other assessments are: pre-dose, ≤1 hour before dosing; 0.25 to 0.5 hours post-dose, ±2 minutes; 0.58 to 1 hour, ±5 minutes; 1.5 to 8 hours, ±15 minutes; 12 to 24 hours, ±30 minutes; 48 to 168 hours, ±4 hours.

[t] Treatment B (IV dose only). 0.5 hours sample to be taken immediately after IV administration (i.e., 30 minutes after the start of the IV administration)

[u] Treatments C and D (oral doses) only.

[v] Discharge from clinical unit in Period 3 only. The same procedures are to be performed at early termination/withdrawal as at discharge.

[w] Follow-up telephone call at 13 to 15 days post-final dose.

[x] Period 3 only; safety discharge assessments will be performed at the time of actual discharge/early termination from the clinical unit

[y] Periods 1, 2 and 3. In Period 3, PK blood samples to be collected at 168 hours post-dose or at time of actual discharge/early termination if earlier.