Division	:	Worldwide Development
Information Type	:	Reporting and Analysis Plan (RAP)

Title	:	Reporting and Analysis Plan for Study 204981: A low interventional clinical study comparing error rates (critical and overall); between the ELLIPTA dry powder inhaler (DPI) and other DPIs, prior to any retraining in correct use, and as prescribed to treat COPD patients.
Compound Number	:	GSK573719+GW642444+GW685698 (GSK2834425)
Effective Date	:	26-APR-2018

Description:

- The purpose of this RAP is to describe the planned analyses and output to be produced in the Clinical Study Report for Protocol 204981 (2016N301286_00).
- This RAP will be provided to the study team members to convey the content of the Statistical Analysis Complete (SAC) deliverables.

RAP Author(s):

Authors	Date	Approval Method
PPD Associate Statistician ([Respiratory]) QSI.	N/A	N/A
PPD Senior Programmer ([Respiratory]) QSI.	N/A	N/A

RAP Team Approvals:

Approver	Date	Approval Method
PPD Statistics Leader, [Respiratory] (RD PCPS SPDS Clinical Statistics)	26-APR-2018	Pharma TMF
PPD Clinical Development Scientist, [Respiratory] ([RD Respiratory HUP Clin Dev])	25-APR-2018	Pharma TMF
PPD Principal Clinical Data Manager, [Respiratory] ([RD PCPS Therapy Area Delivery)	25-APR-2018	Pharma TMF
PPD Clinical Development Manager, [Respiratory] RD PCPS Therapy Area Delivery Resp 3	25-APR-2018	Pharma TMF
PPD SERM Manager, [Respiratory] RD CMO GCSP SERM UK 3	25-APR-2018	E-mail
PPD Principal Statistician [Respiratory] (RD PCPS SPDS Clinical Statistics)	25-APR-2018	Pharma TMF

Clinical Statistics and Clinical Programming Line Approvals:

Approver	Date	Approval Method
PPD General Manager, Biostatistics and Programming ([Respiratory] QSI)	25-APR-2018	E-mail
PPD Senior Manager, Biostatistics and Programming (Respiratory QSI)	25-APR-2018	E-mail

TABLE OF CONTENTS

PAGE

1. INTRODUCTION

The purpose of this reporting and analysis plan (RAP) is to describe the analyses to be included in the Clinical Study Report for Protocol:

Revision Chronology:		
2016N301286_00	24-JAN-2017	Original

2. SUMMARY OF KEY PROTOCOL INFORMATION

2.1. Changes to the Protocol Defined Statistical Analysis Plan

There were no changes or deviations to the originally planned statistical analysis specified in the protocol.

2.2. Study Objective(s) and Endpoint(s)

Objectives	Endpoints
Primary Objectives	**Primary Endpoints**
To compare the number of COPD patients making critical errors, when using their current prescribed inhaled medication, at V1 and prior to any re-training in correct use.	The percentage of participants making at least one critical error at V1 for each DPI tested.
Secondary Objectives	**Secondary Endpoints**
To compare the number of COPD patients making overall errors, when using their current prescribed inhaled medication at V1 and prior to any re-training in correct use.	The percentage of participants making at least one overall error at V1 for each DPI tested.
To compare the number of COPD patients making critical and overall errors, when using their current prescribed inhaled medication at V2 (week 6).	• The percentage of participants making at least one critical error at V2 for each DPI tested. • The percentage of participants making at least one overall error at V2 for each DPI tested.
Exploratory Objectives	**Exploratory Endpoints**
To explore, across all DPIs tested, if any association between critical errors, and key patient characteristics including: • Age. • Educational Status. • Co-Morbidities (Arthritis (upper limbs), Neurological Disorders & Visual impairment). • Time on current DPI(s). • Time since last trained on DPI(s). • Level of control (COPD Assessment Test (CAT) and Exacerbation History).	Exploration of these characteristics will be investigated using a logistic regression model on the primary endpoint of the percentage of participants making at least one critical error at V1 for each inhaler tested, including each of these factors as terms in the model. • Age obtained from Demography. • Educational status from time in full time education. • Co-morbidities will be documented as relevant to DPI use. • Time on current DPI(s) and time since last trained will be documented categorically; however time on current DPI(s) will be included in the primary analysis model.

Objectives	Endpoints
	Level of control will be assessed by: ○ COPD Assessment Test. ○ Exacerbation History (Previous 1 year and required treatment with antibiotics and/or steroids).

2.3. Study Design

Overview of Study Design and Key Features	
	
	• This is an open-label, low interventional study which does not involve administration of active study treatment nor placebo. • COPD diagnosed participants will attend the clinic for the screening visit and subsequent assessment visit and will be included in the study if they are prescribed any of the following DPIs for maintenance treatment of their COPD: ELLIPTA (RELVAR ELLIPTA™, ANORO ELLIPTA™ or INCRUSE ELLIPTA™), Turbuhaler (Symbicort Turbuhaler), DISKUS (Seretide DISKUS™), HandiHaler (Spiriva HandiHaler), and Breezhaler (Ultibro or Seebri Breezhaler). • Participants will be allocated to one of nine different treatment groups depending on the maintenance inhalers they use. • Participants will be assessed for critical and overall errors on the maintenance inhalers they use. Following error assessment, participants will be instructed in correct use of their DPI(s) if required. Participants will return after 6 weeks and will be reassessed for critical and overall errors.
Dosing	• Not applicable as no active treatment will be provided in this study
Time & Events	• Refer to Appendix 2: Schedule of Activities
Treatment Assignment	• All participants will be assigned to their relative treatment groups based on their current prescribed treatment. Refer to study Protocol Section 7.2
Interim Analysis	• No interim Analysis planned

2.4. Statistical Hypotheses

The primary purpose of this study is to assess the number of critical errors made by COPD patients for each DPI tested. The primary endpoint of the study is the percentage of participants making at least one critical error (critical error rate) for each DPI at V1. This will be analysed using logistic regression and will be adjusted for the covariate of time on current DPI.

For each DPI comparison:

- The null hypotheses are no difference between DPIs: H0: p1=p2
- The alternative hypothesis is that there is a difference between DPIs: HA: p1≠p2

Primary Endpoint

The primary endpoint of the study is the percentage of participants making at least one critical error (critical error rate) for each DPI at V1

Table 1 Treatment groups

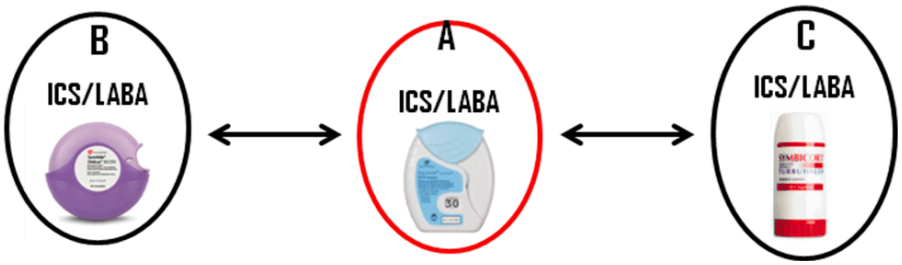
Treatments		**Combination DPI Treatment Groups**		
Single DPI Treatment Groups		ICS-LABA With Spiriva HandiHaler (LAMA)	OR	ICS-LABA With Incruse ELLIPTA™ (LAMA)
Relvar ELLIPTA™ (ICS/LABA)	A	G		
Symbicort Turbuhaler (ICS/LABA)	B	H		
Seretide DISKUS™ (ICS/LABA)	C	I		
Spiriva HandiHaler (LAMA)	D			
Incruse ELLIPTA™ (LAMA)	E			
Anoro ELLIPTA ™(LAMA/LABA)				
Ultibro Breezhaler (LAMA/LABA)	F			
Seebri Breezhaler (LAMA)				

For this table the groups are referred to as treatment groups. For all other references in this RAP they will be referred to as ***cohorts***.

Primary comparisons:

1. RELVAR ELLIPTA DPI vs. any other ICS/LABA (Seretide DISKUS™ or Symbicort Turbuhaler) DPI.

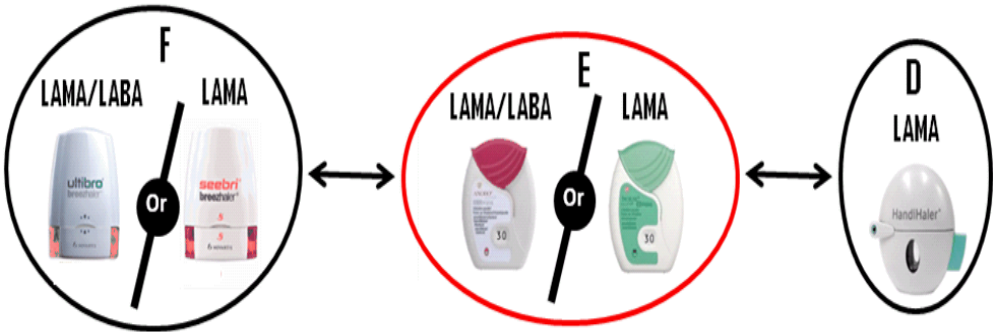
    - *This comparison aims to compare critical error rates in the primary ICS/LABA DPIs.*



- **Group A versus group B**
- **Group A versus group C**

2. INCRUSE ELLIPTA™ or ANORO ELLIPTA™ DPI vs. any other LAMA (Spiriva HandiHaler or Seebri Breezhaler), or LAMA/LABA (Ultibro Breezhaler) DPIs.

    - *This comparison aims to compare critical error rates in the primary LAMA and LAMA/LABA DPIs.*

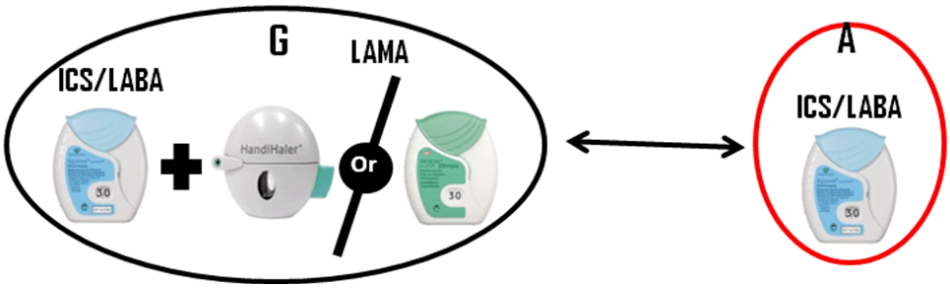


- **Group E versus Group D**
- **Group E versus Group F**

Other comparisons:

3. RELVAR ELLIPTA™ DPI vs. RELVAR ELLIPTA™ with any other LAMA (Spiriva HandiHaler or INCRUSE ELLIPTA™) DPI.

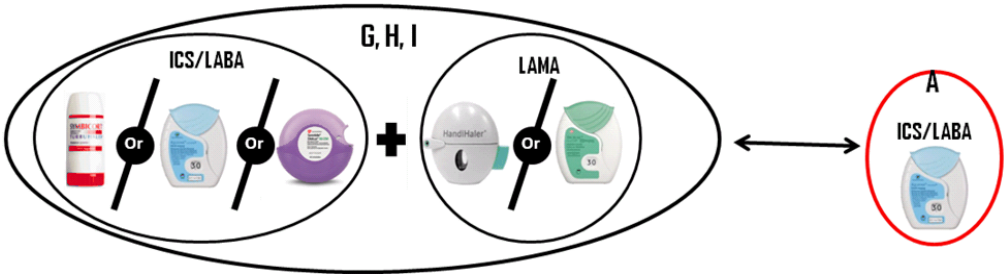
    - *This aims to compare critical error rates in the primary DPI, simulating a triple therapy from one DPI (ELLIPTA) against triple therapy from two ELLIPTA DPIs, or from ELLIPTA DPI with any other LAMA DPI.*



- **Group A versus Group G**

4. RELVAR ELLIPTA™ DPI vs. all ICS/LABA (Seretide DISKUS™, RELVARELLIPTA™ or Symbicort Turbuhaler) DPIs with a LAMA (Spiriva HandiHaler, Seebri Breezhaler or INCRUSE ELLIPTA™) second DPI.

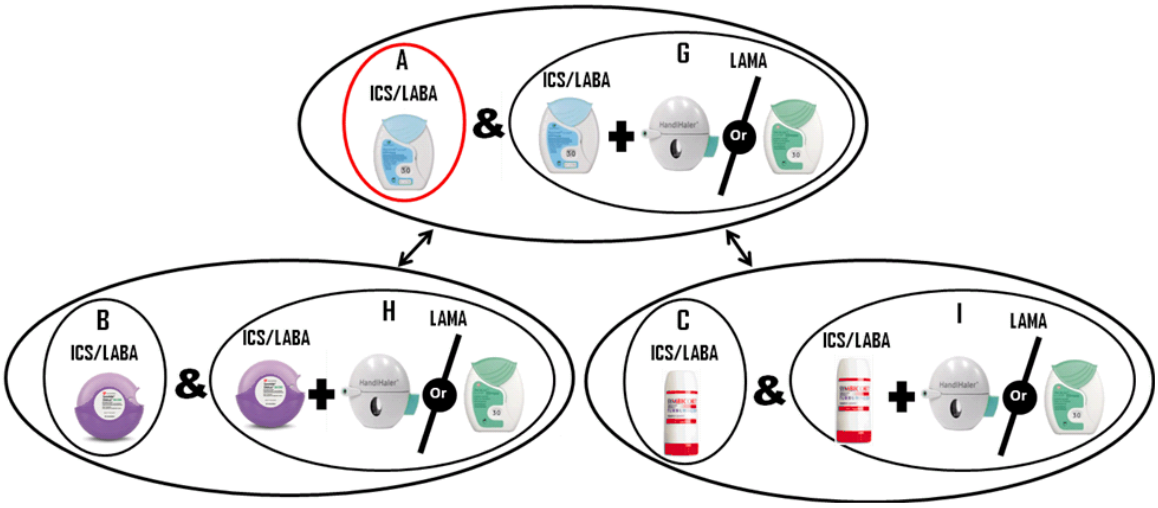
    - *This aims to compare critical error rates in the primary DPI, simulating a triple therapy delivered in one ELLIPTA DPI against a triple therapy from any two other DPIs used in the study.*



- **Group A versus Group G+H+I**

5. RELVAR ELLIPTA™ DPI with or without a LAMA DPI (Spiriva HandiHaler, Seebri Breezhaler or INCRUSE ELLIPTA™) vs. any other ICS/LABA (Seretide DISKUS™ or Symbicort Turbuhaler) DPI with or without a LAMA (Spiriva HandiHaler or Seebri Breezhaler) DPI.

    - *This aims to compare critical error rates in the primary DPI, simulating a triple therapy delivered in one ELLIPTA DPI or combination of DPIs against a triple therapy using any other ICS/LABA delivering primary DPI.*



- **Group A+G versus B+H**
- **Group A+G versus C+I**

Additionally, where there are 2 DPIs within a cohort, a further comparison will be made to compare the single DPI arm with the multiple DPI arm where errors from both devices are taken into consideration. See Table 2, Section 2.4.

These treatment comparisons above can be summarised in the following Table 2:

Table 2 Treatment comparisons

Cohort:	A	B	C	D	E	F	G	H	I
Primary device	Relvar Ellipta	Symb Turb	SFC Diskus	Spiriva HH	Inc. or Anoro Ellipta	Ultibro or Seebri BH	(1) Relvar Ellipta	(1) Symb Turb	(1) SFC Diskus
Secondary Device							(2) Spiriva HH OR Inc. Ellipta		
Primary Comparisons									
A vs B	A	B							
A vs C	A		C						
E vs D				D	E				
E vs F					E	F			
Other Comparisons									
A vs G (primary device)	A						G1		
A v G (both devices)	A						G1/G2		
A vs G+H+I (primary device)	A						G1	H1	I1
A vs G+H+I (both devices)	A						G1/G2	H1/H2	I1/I2
A+G vs B+H (primary device)	A	B					G1	H1	
A+G vs B+H (both devices)	A	B					G1/G2	H1/H2	
A+G vs C+I (primary device)	A		C				G1		I1
A+G vs C+I (both devices)	A		C				G1/G2		I1/I2

Symb Turb: Symbicort Turbuhaler; SFC: Seretide; Inc.: Incruse; BH: Breezhaler;
HH: Handihaler
G1/G2 refers to errors in either primary device G1 or secondary device G2
H1/H2 refers to errors in either primary device H1 or secondary device H2
I1/I2 refers to errors in either primary device I1 or secondary device I2

Secondary Endpoints

The following secondary endpoints will be analysed in the same way as for the primary endpoint and using the same treatment comparisons:

- The percentage of participants making at least one overall error at V1 for each DPI tested.
- The percentage of participants making at least one critical error at V2 for each DPI tested.
- The percentage of participants making at least one overall error at V2 for each DPI tested.

For all formal statistical analyses where more than one DPI has been used, the comparison will be between the critical errors recorded on the primary DPI. Error rates will not be combined when dual DPIs are being used.

Exploratory Analysis

The association between participants making at least one critical error (irrespective of the cohorts) and the key patient characteristics including age, educational Status, co-Morbidities (Arthritis (upper limbs), Neurological Disorders & Visual impairment), time on current DPI(s), time since last trained on DPI(s) and Level of control (CAT and Exacerbation History) will be examined at visit 1 for all the available subjects, irrespective of cohorts they belongs to.

3. PLANNED ANALYSES

3.1. Interim Analyses

No interim Analysis planned

3.2. Final Analyses

All final planned analyses will be performed after the completion of the following sequential steps:

1. All subjects have completed the study as defined in the protocol.
2. All required database cleaning activities have been completed and final database release has been declared by Data Management.
3. All criteria for unblinding the randomisation codes have been met.
4. Source database is locked and Data Management declare Source Data Lock.
5. Randomization codes have been distributed according to RandAllNG procedures.
   Note that this procedure will still be followed although the study is not formally randomized.
6. Database freeze has been declared by Data Management.

4. ANALYSIS POPULATIONS

This study did not require formal randomisation to study treatment as subjects continued to use the maintenance medication they were already taking for COPD. However, in order to ensure that enrolment to treatment cohorts did not exceed the required number of subjects the study has implemented the use of RAMOS NG in order to monitor this. This also required that a randomisation was generated via RandallNG. The randomisation generated has a single treatment group (Own Treatment) and 9 strata levels (cohorts) for each of the treatment options detailed in Section 5.1 and Table 1 of the protocol.

Population	Definition / Criteria	Analyses Evaluated
All Subjects Enrolled (ASE)	Comprises of all participants who sign the ICF and for whom a record exists in the study database, including screen failures and any participant who was not screened but experienced an SAE between the date of informed consent and the planned date of the screening visit.	For subjects who do not enrol into a treatment group: • Summary of study populations. • Reason for screen failures • Listing of SAEs
Randomised	All participants who were randomised.	No formal analysis will be performed on this population
Intent-To-Treat (ITT)	All enrolled participants who have demonstrated use of their primary DPI. The population will be based on the treatment cohort to which the subject enrolled. Any subject who receives a treatment randomisation number will be considered to have been enrolled.	• Study Population • Efficacy • Safety
Safety	This population will be the same as the ITT population.	

NOTES :

- Please refer to Appendix 8: List of Data Displays which details the population to be used for each displays being generated.

4.1. Protocol Deviations

- Important protocol deviations (including deviations related to study inclusion/exclusion criteria, conduct of the trial, patient management or patient assessment) will be summarised and listed.
- Protocol deviations will be tracked by the study team throughout the conduct of the study in accordance with the Protocol Deviation Management Plan (PDMP).
    - Data will be reviewed prior to unblinding and freezing the database to ensure all important deviations are captured and categorised on the protocol deviations dataset.
    - This dataset will be the basis for the summaries and listings of protocol deviations.
- A separate summary and listing of all inclusion/exclusion criteria deviations will also be provided. This summary will be based on data as recorded on the inclusion/exclusion page of the eCRF.

5. CONSIDERATIONS FOR DATA ANALYSES AND DATA HANDLING CONVENTIONS

5.1. Study Treatment & Sub-group Display Descriptors

		Combinations DPI Treatment Groups	
RandAll NG		Data Displays for Reporting	
Code	Description	Description	Order in TFL
A	Own Medication	Relvar Ellipta	1
B	Own Medication	Symbicort Turbuhaler	2
C	Own Medication	Seretide Diskus	3
D	Own Medication	Spiriva Handihaler	4
E	Own Medication	Incruse/Anoro Ellipta	5
F	Own Medication	Ultibro/Seebri Breezhaler	6
G	Own Medication	Relvar Ellipta + LAMA	7
H	Own Medication	Symbicort Turbuhaler + LAMA	8
I	Own Medication	Seretide Diskus + LAMA	9

NOTES:
1. Order represents treatments being presented in TFL, as appropriate.
2. Add a footnote to displays: LAMA = Spiriva Handihaler or Incruse Ellipta.

5.2. Baseline Definitions

There are no baseline definitions to be defined.

5.3. Multicentre Studies

Data from all participating centres will be pooled prior to analysis.

5.4. Examination of Covariates, Other Strata and Subgroups

5.4.1. Covariates and Other Strata

- The following is a list of covariates that will be used to explore, across all cohorts combined, if there is any association between critical errors and the key patient characteristic listed

Category	Covariates and / or Subgroups
Age	40-49; 50-59; 60-69; 70-79; 80+ years
Educational Status	0-5; 6-10; 11-15; 16-20; 21+ years
Co-morbidities	• Arthritis ○ Upper Limbs:(Shoulders, Elbows, Hands/wrists/Fingers, Jaw and neck)

Category	Covariates and / or Subgroups
	vs Not upper limbs or No Arthritis (None, Back or lower body) *Note:If both upper limbs and another location has been identified then the subject will be identified as upper limbs* • Visual impairment o No visual impairment reported for either eye OR visual impairment in one eye only and marked as correctable OR visual impairment in both eyes and both eyes marked as correctable Vs Visual impairment in both eyes with neither or only 1 eye correctable OR Visual impairment in one eye which is not correctable. • Neurological Disorder o Functional Disorder (Only current medical conditions) vs No Functional Disorder o Dementia vs No Demintia o Psychological Disorder vs. No psychological disorder
Time since last trained on primary DPI	Categories are: • 3 months < x ≤ 6 months • 6 months < x ≤ 1 year • 1 year < x ≤ 2 years • 2 years < x ≤ 3 years • x > 3 years
Time on current primary DPI(s)	Categories are: • 3 months < x ≤ 6 months • 6 months < x ≤ 1 year • 1 year < x ≤ 2 years • 2 years < x ≤ 3 years • x > 3 years
Level of control	• CAT (<10; >=10) • Exacerbation history in the prior year. (0, 1, ≥2 moderate/severe exacerbations in the prior year.

Note: If any visual impairment present and data doesn't exist whether it is correctable, then it is considered to be not-correctable

5.5. Multiple Comparisons and Multiplicity

There will be no adjustment for multiple comparisons on multiple endpoints in the analysis.

Given the exploratory nature of the study, multiplicity adjustments are not planned. There are 2 primary treatment comparisons. All other treatment comparisons are secondary.

5.6. Other Considerations for Data Analyses and Data Handling Conventions

Other considerations for data analyses and data handling conventions are outlined in the appendices:

Section	Component
Section 10.1	Appendix 1: Protocol Deviation Management
Section 10.2	Appendix 2: Time & Events
Section 10.3	Appendix 3: Treatment States and Phases
Section 10.4	Appendix 4: Data Display Standards & Handling Conventions
Section 10.5	Appendix 5: Derived and Transformed Data
Section 10.6	Appendix 6: Premature Withdrawals & Handling of Missing Data

6. STUDY POPULATION ANALYSES

6.1. Overview of Planned Study Population Analyses

The study population analyses will be based on the ITT population, unless otherwise specified.

Study population displays including those of subject disposition, protocol deviations, demographic and baseline characteristics and prior and concomitant medications compliance will be based on GSK Core Data Standards. Details of the planned displays are presented in Appendix 8: List of Data Displays.

6.1.1. Subject Disposition

The study population summary will show the number of subjects overall who were enrolled, the number of screen failure and the number with each reason for screen failure, the number of subjects in each cohort and overall who were in the ITT population.

The end of study record summary shows the number of subjects who completed the study as well as the number who withdrew early from the study along with reasons for early withdrawal.

6.1.2. Medical Conditions

The number and percentage of subjects reporting each current medical condition will be presented. This table will include a category of 'Cardiovascular Risk Factors'. All medical conditions must be summarised on this table regardless of frequency.

This will be repeated for past medical conditions.

6.1.3. Concomitant medication

Non-COPD medications will be summarised by Anatomical-Therapeutic-Chemical (ATC) level 1 and ingredient. COPD medications will be summarised by Respiratory Medication Class (RMC) and will be derived for each COPD concomitant medication. Multi-ingredient medications will be presented according to their combination ATC classification rather than the classifications of the ingredients.

COPD and non-COPD medications will be listed separately.

A listing of the relationship between ATC Level 1, ingredient and verbatim text will be produced for non-COPD medications only.

7. EFFICACY ANALYSES

7.1. Primary Efficacy Analyses

7.1.1. Endpoint / Variables

The percentage of participants making at least one critical error at V1 for each DPI tested. See Table 2 (Section 2.4) for the cohort comparisons.

7.1.2. Summary Measure

Odds ratio at V1 for each of the comparisons detailed in Table 2 (Section 2.4).

7.1.3. Population of Interest

All subjects included in the ITT population.

7.1.4. Strategy for Intercurrent (Post-Randomization) Events

Subjects who have not performed the error assessment at V1 on their primary DPI will not form part of the ITT population (see Section 4).

There are no intercurrent events that impact treatment effect at V1. No missing data is anticipated at V1. There will be no imputation planned in the rare situation that subjects fail to complete an error assessment either in full or in part for one or both devices (where applicable).

7.1.5. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 9: List of Data Displays and will be based on GSK data standards and statistical principles.

The endpoint defined in Section 7.1.1 will be summarised using descriptive statistics, analysed as described in Section 7.1.5.1, graphically presented and listed.

7.1.5.1. Statistical Methodology Specification

Endpoint / Variables
• The proportion of non-responders (defined as making at least one critical error at V1). Non-response includes subjects where error assessment information is missing or incomplete at V1.
Model Specification
• This endpoint will be analysed using logistic regression with treatment cohort as fixed effect and adjusting for the covariate of time on current primary DPI. All available data for all cohorts will be included in the model and pairwise treatment cohort comparisons for primary DPI vs primary DPI comparisons will be obtained from this model. • In addition, a second model will be required in order to examine the pairwise treatment cohort comparisons for the dual device vs primary device comparisons.

Model Checking & Diagnostics
• Pearson residuals will be plotted for the model.
Model Results Presentation
• The odds ratio, 95% CI and p-value will be presented for the pairwise comparisons between DPIs/cohorts as detailed in Table 2 (Section 2.4). It will be based on a two-sided hypothesis testing approach of superiority.
Subgroup Analyses
• No subgroup analysis will be performed
Sensitivity and Supportive Analyses
• No sensitivity analysis is planned for Primary endpoint

7.2. Secondary Efficacy Analyses

7.2.1. Endpoint / Variables

- The percentage of participants making at least one overall error at V1 for each DPI tested.
- The percentage of participants making at least one critical error at V2 for each DPI tested.
- The percentage of participants making at least one overall error at V2 for each DPI tested.

7.2.2. Summary Measure

For each of the endpoints detailed in 7.2.1 the summary measure is the odds ratio at the visit stated for each of the comparisons detailed in Table 2 (Section 2.4).

7.2.3. Population of Interest

All subjects included in the ITT population.

7.2.4. Strategy for Intercurrent (Post-Randomization) Events

Intercurrent events for secondary endpoint on visit 1 follow same handling method described in 7.1.4

The following intercurrent event is considered for V2;

Subject switches medication between V1 and V2

- New maintenance medication uses the same devices as previous maintenance medication at V1 and error assessments are performed on these new devices.
- New maintenance medication uses different devices to V1, but devices that are assessed in the study and for which error assessments are performed.
- New maintenance medication uses devices which are not being assessed in this study and thus no error assessment is available at V2.

For the purposes of this secondary endpoint analyses any error assessments following these events will be treated as missing. (i.e. if there are partial error assessments, the response will be

set to missing, or if there are full error assessments on alternative devices (or the same devices, but different medication) then these responses will also be set to missing)

Additionally, subjects may not provide an assessment at V2 for a number of reasons:

- Subject prematurely withdraws from the study before completing V2 assessments.
- For the treatment comparisons which take both devices into consideration (where applicable) a subject may have missed performing the assessment on the secondary device at V2.
- A subject may miss a component of a device assessment and all other question responses indicate correct use

For the purposes of these secondary analyses no imputation will be made for these missing scenarios.

In the situation where a subject may miss a component of a device assessment and one or more of the other question responses (critical error or overall error as applicable) indicate an error was made, then the subject would be a non-responder since the existing data already indicates this and the missing value has no additional impact on the response outcome.

7.2.5. Statistical Analyses / Methods

Details of the planned displays are provided in Appendix 8: List of Data Displays and will be based on GSK data standards and statistical principles.

Endpoints defined in Section 7.2.1 will be summarised using descriptive statistics, analysed using appropriate statistical methods and graphically presented.

7.2.5.1. Statistical Methodology Specification

Endpoint / Variables
• The percentage of participants making at least one overall error at V1 for each DPI tested. • The percentage of participants making at least one critical error at V2 for each DPI tested. • The percentage of participants making at least one overall error at V2 for each DPI tested.
Model Specification
• These secondary endpoints will be analysed using logistic regression with treatment cohort as fixed effect and adjusting for the covariate of time on current primary DPI. All available data for all cohorts will be included in the model and pairwise treatment cohort comparisons for primary DPI vs primary DPI comparisons will be obtained from this model. • A second model will be required in order to examine the pairwise treatment cohort comparisons for the dual device vs primary device comparisons.
Model Checking & Diagnostics
• No model checking will be required for secondary endpoints.
Model Results Presentation
• The odds ratio, 95% CI and p-value will be presented for the pairwise comparisons between

DPIs/cohorts as detailed in Table 2 (Section 2.4). It will be based on a two-sided hypothesis testing approach of superiority.
Subgroup Analyses
• No subgroup analysis will be performed
Sensitivity and Supportive Analyses
• No sensitivity analysis is planned for these endpoints. • If sufficient missing data warrants, a sensitivity analysis will be performed where the above scenarios are deemed to be non-responders.

7.3. Exploratory Efficacy Analyses

To explore, across all DPIs tested, if there is any association between critical errors, and key patient characteristics (Covariate or subgroups) including:

- Age.
- Educational Status.
- Co-Morbidities
    - Arthritis
    - Neurological Disorders
    - Visual impairment.
- Time on current DPI(s).
- Time since last trained on DPI(s).
- Level of control using the CAT.
- Exacerbation History.

The categories of interest for each of the covariates are described in Section 5.4.1.

For this analysis, all cohort data will be combined.

A summary table of errors will be produced for each patient characteristics.

Relationship of these characteristics will be investigated using a separate logistic regression model on the primary endpoint of the percentage of participants making at least one critical error and overall error at Visit 1 for each DPI tested, including each of these factors as terms in the model.

The interaction term between treatment cohort and characteristic will be added to the above model to investigate the interaction effect.

These analysis will be performed for each characteristic at a time. P-value from the first model and the interaction p-value from the second model will be produced for each characteristic adjusted seperately.

If any interaction is evident at the 10% significance level then further examination of the data may be performed in order to describe the interaction. It should be noted that due to the smaller groups of data and the number of tests, this investigation may highlight something which is a chance finding.

Graphical presentations of critical errors and overall errors for each patient characterstic will be produced.

8. SAFETY ANALYSES

The safety analyses will be based on the ITT population, unless otherwise specified.

8.1. Adverse Events Analyses

Adverse event summaries including the summary of adverse events (AEs), Serious (SAEs) and other significant AEs will be based on GSK Core Data Standards. The details of the planned displays are provided in Appendix 8: List of Data Displays.

AE incidence will be summarised overall using the primary System Organ Class (SOC) and preferred term. All listings of AEs/SAEs will identify whether each adverse event occurred pre-study, during-study or post-study.

8.2. Adverse Events of Special Interest

A comprehensive list of MedDRA terms based on clinical review will be used to identify each type of event.

Note: Changes to the MedDRA dictionary may occur between the start of the study and the time of reporting and/or emerging data from on-going studies may highlight additional adverse events of special interest, therefore the list of terms to be used for each event of interest and the specific events of interest will be based on the safety review team agreements in place at the time of reporting.

A listing of subject numbers for individual adverse events of special interest will be produced along with a listing identifying all preferred terms which belong to each event of special interest.

The details of these planned displays are provided in Appendix 8: List of Data Displays.

9. REFERENCES

GlaxoSmithKline Document Number 2016N301286_00, Protocol: An open-label, low interventional clinical study investigating error rates (critical and overall) prior to any retraining in correct use of the ELLIPTA dry powder inhaler (DPI) compared to other DPIs including; DISKUS, Turbuhaler, HandiHaler and Breezhaler as a monotherapy or in combination, in adult patients with Chronic Obstructive Pulmonary Disease (COPD), 24-January-2017.

10. APPENDICES

Section	Appendix
RAP Section 4 : Analysis Populations	
Section 10.1	Appendix 1: Protocol Deviation Management
RAP Section 5 : General Considerations for Data Analyses & Data Handling Conventions	
Section 10.2	Appendix 2: Schedule of Activities
Section 10.3	Appendix 3: Treatment States & Phases
Section 10.4	Appendix 4: Data Display Standards & Handling Conventions • Study Treatment & Sub-group Display Descriptors • Baseline Definitions & Derivations • Reporting Process & Standards
Section 10.5	Appendix 5: Derived and Transformed Data • General, Study Population & Safety • Efficacy
Section 10.6	Appendix 6: Premature Withdrawals & Handling of Missing Data • Premature Withdrawals • Handling of Missing Data
Other RAP Appendices	
Section 10.7	Appendix 7: Abbreviations & Trade Marks
Section 10.8	Appendix 8: List of Data Displays
Section 10.9	Appendix 9: Example Mock Shells for Data Displays

10.1. Appendix 1: Protocol Deviation Management and Definitions for Per Protocol Population

A per protocol population is not defined for this study therefore there are no criteria leading to exclusion from a per protocol population. All deviations will be managed during the study according to the PDMP.

10.2. Appendix 2: Schedule of Activities

10.2.1. Protocol Defined Schedule of Events

	Visit 0 Screening	Visit 1 Baseline	Visit 2	Notes
	Day 1 (Can occur on same day as V1)	Day 1 (Can occur on same day as V0)	Week 6 ± 7 days	
Procedure				
Screening (V0)	X			Completed prior to V1 assessments.
Written informed consent	X			V0 can take place on the same day as V1. V1 should be completed no later than 30 days after consent.
Participant demography	X			Age, height, weight, year of birth, sex, ethnicity and geographic ancestry will be recorded.
Medical/disease history including COPD, smoking And Arthritis/Ophthalmic /Neurological history	X			Participant will have a medical history of COPD, smoking history, time on current DPI(s), time since last trained on DPI(s) and any comorbidities that may affect correct use of DPI recorded.
Exacerbation History	X			Exacerbation history for previous year recorded.
COPD diagnosis	X			Documented confirmation of COPD diagnosis from Physician.
Concomitant medication history including COPD	X			All current concomitant medication of relevance (Arthritic, Ophthalmic, Neurological medications) or related to an

	Visit 0 Screening	Visit 1 Baseline	Visit 2	Notes
therapy history				AE will be recorded. A minimum COPD therapy history for the preceding 2 years will be recorded.
Inclusion/exclusion criteria	X			All criteria must be met prior to inclusion at V1.
Register the patient	X			To ensure the correct number of patients are included on each arm.
CAT Score	X			Take this for reference (exploratory).
Educational status	X			No. of years spent in full time education.
Study Assessments (V1 +V2)		X	X	
Assess participant's ability to correctly use their DPI(s) and MDI(s) with Checklists		X	X	No instruction provided by HCP before or during this assessment.
Correct use of DPI training		X	X	Train participants should they make errors during demonstration
Adverse event/Serious adverse event assessment		X	X	Collected until completion of study.
Prescriptions and health review		X	X	Review changes in prescription and health between beginning and end of study.

10.3. Appendix 3: Study Phases and Treatment Emergent Adverse Events

10.3.1. Study Phases

All data, where applicable, will be categorised according to the following treatment phases; pre-study, during- study and post- study. These definitions will be defined based on the date of Visit 1 and visit 2 given in the below table.

10.3.2. Treatment Phase Definitions

Definition	Treatment Phase		
	Pre-study	During-study	Post-study
Before Visit 1	Y		
Between V 1 and V 2 inclusive		Y	
After Visit 2			Y

10.4. Appendix 4: Data Display Standards & Handling Conventions

10.4.1. Reporting Process

Software	
• The currently supported versions of SAS software and S-plus will be used.	
Reporting Area	
HARP Server	: uk1salx00175
HARP Area	: gsk2834425\mid204981\final_01
Analysis Datasets	
• Analysis datasets will be created according to Legacy GSK A&R dataset standards.	
Generation of RTF Files	
• RTF files will be generated for the final_01 reporting effort.	

10.4.2. Reporting Standards

General

• The current GSK Integrated Data Standards Library (IDSL) will be applied for reporting, unless otherwise stated: (IDSL Standards Location: https://spope.gsk.com/sites/IDSLLibrary/SitePages/Home.aspx):
  • 4.03 to 4.23: General Principles
  • 5.01 to 5.08: Principles Related to Data Listings
  • 6.01 to 6.11: Principles Related to Summary Tables
  • 7.01 to 7.13: Principles Related to Graphics

Formats
• All data will be reported according to the actual treatment (cohort) the subject belongs to. • GSK IDSL Statistical Principles (5.03 & 6.06.3) for decimal places (DP's) will be adopted for reporting of data based on the raw data collected. • Numeric data will be reported at the precision collected on the eCRF.
Planned and Actual Time

• Reporting for tables, figures and formal statistical analysis:
  • Inhaler device errors nominal visit will be used in figures, summaries, statistical analyses and calculation of any derived parameters, unless otherwise stated.
• Reporting for Data Listings:
  • Planned and actual time relative to study drug dosing will be shown in listings if applicable (Refer to IDSL Statistical Principle 5.5.1).

Descriptive Summary Statistics	
Continuous Data	Refer to IDSL Statistical Principle 6.06.1
Categorical Data	N, n, frequency, %
Graphical Displays	
• Refer to IDSL Statistical Principles 7.01 to 7.13.	

10.5. Appendix 5: Derived and Transformed Data

10.5.1. General

Study Day
• Calculated as the number of days from V1 Date • Ref Date = Missing → Study Day = Missing • Ref Date < First Dose Date → Study Day = Ref Date – First Dose Date • Ref Data ≥ First Dose Date → Study Day = Ref Date – (First Dose Date) + 1 Note: Visit 1 date = Day 1
Study and Treatment Completion Definitions
• A participant is considered to have completed the study if he/she has completed all phases of the study including the last scheduled procedure shown in the Schedule of Activities.

10.5.2. Study Population

Demography
Age
• Age will be calculated based on the Screening visit date (V0) • Only year of birth is collected on the eCRF therefore day and month of birth are imputed as '30JUN' in order to derive age. • Birth date will be presented in listings as 'YYYY'.
Body Mass Index
• Calculated as weight (kg) / [height (m)]2

Subject disposition
Treatment Compliance
• Treatment compliance will not be calculated since no study treatment is dispensed in this study. Subjects are using their usual prescribed medication.

COPD Exacerbation History
• COPD exacerbation history is collected at visit 0/1. The eCRF collects the number of exacerbations in the unique categories of moderate or severe where a moderate COPD exacerbation is defined as an exacerbations that required treatment with systemic/oral corticosteroids and/or antibiotics (not involving hospitalization) and a severe COPD exacerbation is defined as an exacerbation that required in-patient hospitalization. • Total number of moderate/severe COPD exacerbations for COPD exacerbation history are defined as the sum of moderate and severe COPD exacerbations for each subject.

10.6. Appendix 6: Reporting Standards for Missing Data

10.6.1. Premature Withdrawals

Element	Reporting Detail
General	• Subject study completion (i.e. as specified in the protocol) was defined as completion of all phases of the study, including the last scheduled procedure shown in the schedule of activities. • Withdrawn subjects were not replaced in the study. • All available data from subjects who were withdrawn from the study will be listed and all available planned data will be included in summary tables and figures, unless otherwise specified.

10.6.2. Handling of Missing Data

Element	Reporting Detail
General	• Missing data occurs when any requested data is not provided, leading to blank fields on the collection instrument: o These data will be indicated by the use of a "blank" in subject listing displays. Unless all data for a specific visit are missing in which case the data is excluded from the table. o Answers such as "Not applicable", "Not evaluable" and "never trained on their DPI" are not considered to be missing data and should be displayed accordingly.
Outliers	• Any subjects excluded from the summaries and/or statistical analyses will be documented along with the reason for exclusion in the clinical study report.

10.6.2.1. Handling of Missing and Partial Dates

Element	Reporting Detail
General	Partial dates will be displayed as captured in subject listing displays.
Adverse Events	• The eCRF allows for the possibility of partial dates (i.e., only month and year) to be recorded for AE start and end dates; that is, the day of the month may be missing. In such a case, the following conventions will be applied for calculating the time to onset and the duration of the event: o Missing Start Day: First of the month will be used unless this is before the start date of study treatment; in this case the study treatment start date will be used and hence the event is considered On-treatment as per Appendix 3: Study Phases and Treatment Emergent Adverse Events. o Missing Stop Day: Last day of the month will be used, unless this is after the stop date of study treatment; in this case the study treatment stop date will be used. • Completely missing start or end dates will remain missing, with no imputation applied. Consequently, time to onset and duration of such events will be missing.

Element	Reporting Detail
	• Start or end dates which are completely missing (i.e. no year specified) will remain missing, with no imputation applied. • Any partial dates for adverse events will be raised to data management. If the full date cannot be ascertained, the following assumptions will be made: o If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month. o However, if these result in a date prior to Week 1 Day 1 and the event could possibly have occurred during treatment from the partial information, then the Week 1 Day 1 date will be assumed to be the start date. o The AE will then be considered to start on-treatment (worst case). o If the partial date is a stop date, a '28/29/30/31' will be used for the day (dependent on the month and year) and 'Dec' will be used for the month. • The recorded partial date will be displayed in listings.
Concomitant Medications	• Partial dates for any concomitant medications recorded in the CRF will be imputed using the following convention: o If the partial date is a start date, a '01' will be used for the day and 'Jan' will be used for the month o If the partial date is a stop date, a '28/29/30/31' will be used for the day (dependent on the month and year) and 'Dec' will be used for the month. • The recorded partial date will be displayed in listings.

10.7. Appendix 7: Abbreviations & Trade Marks

10.7.1. Abbreviations

Abbreviation	Description
AE	Adverse Event
ASE	All Participants Enrolled
ATC	Anatomical Therapeutic Chemical Classification
CAT	COPD Assessment Test
COPD	Chronic Obstructive Pulmonary Disease
CRF	Case Report Form
DPI	Dry Powder Inhaler
GSK	GlaxoSmithKline
ICS	Inhaled Corticosteroid
IDSL	Integrated Data Standards Library
ITT	Intent-to-Treat
Kg	Kilogram
LABA	Long Acting β2-Agonist
LAMA	Long Acting Anticholinergic
m	Metre
MDI	Metered Dose Inhaler
MedDRA	Medical Dictionary for Regulatory Activities
PDMP	Protocol Deviation Management Plan
RAP	Reporting and Analysis Plan
RAMOS NG	Randomization & Medication Ordering System – Next Generation
RANDALLNG	GSK Randomization System – Next Generation
RMC	Respiratory Medication Class
RTF	Rich Text Format
SAC	Statistical Analysis Complete
SAE	Serious Adverse Event
SoA	Schedule of Activities
SOC	System Organ Class
TFL	Tables, Figures & Listings

10.7.2. Trademarks

Trademarks of the GlaxoSmithKline Group of Companies
ANORO ELLIPTA
INCRUSE ELLIPTA
RELVAR ELLIPTA
SERETIDE DISKUS

Trademarks not owned by the GlaxoSmithKline Group of Companies
HandiHaler
SAS
Seebri Breezhaler
Spiriva Handihaler
Symbicort Turbuhaler
Ultibro Breezhaler

10.8. Appendix 8: List of Data Displays

10.8.1. Data Display Numbering

The following numbering will be applied for RAP generated displays:

Section	Tables	Figures
Study Population	1.01 to 1.23	N.A
Efficacy	2.01 to 2.19	2.01 to 2.08
Safety	3.01 to 3.11	N.A
Section	**Listings**	
ICH Listings	1 to 16	
Other Listings	17 to 39	

10.8.2. Mock Example Shell Referencing

Non IDSL specifications will be referenced as indicated and if required example mock-up displays provided in Appendix 9: Example Mock Shells for Data Displays.

Section	Figure	Table	Listing
Study Population	POP_Fn	POP_Tn	POP_Ln
Efficacy	EFF_Fn	EFF_Tn	EFF_Ln
Safety	SAFE_Fn	SAFE_Tn	SAFE_Ln

NOTES:

- Non-Standard displays are indicated in the 'IDSL / Example Shell' or 'Programming Notes' column as '[Non-Standard] + Reference.'

10.8.3. Deliverables

Delivery	Description
SAC	Final Statistical Analysis Complete

10.8.4. Study Population Tables

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Population Analysed					
1.01	ASE	IDSL_SP01	Summary of Subject Populations		SAC
1.02	ITT	POP_T1	Summary of Attendance at Each Clinic Visit	Summarize for Screening, Visit1 and visit2 Summarize for Screening, Visit1 and visit2 Summarize for Screening, Visit1 and visit2Summarize for Screening, Visit 1 and Visit 2	SAC
Subject Disposition					
1.03	ASE	IDSL_ES6	Summary of Screening Status and Reasons for Screen Failures	Percentage for reason should be calculated based on number of screening failures refer Protocol Section 6.4	SAC
1.04	ITT	IDSL_ES1	Summary of Subject Disposition for the Subject Conclusion Record		SAC
1.05	ITT	IDSL_NS1	Summary of Number of Subjects by Country and Centre		SAC
1.06	ITT	IDSL_IE1	Summary of Inclusion and Exclusion Criteria Deviations		SAC
1.07	ITT	IDSL_DV1	Summary of Important Protocol Deviations		SAC

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Demographic and Baseline Characteristics					
1.08	ITT	IDSL_DM1	Summary of Demographic Characteristics	Age category not required	SAC
1.09	ITT	IDSL_DM1	Summary of Demographic Characteristics by Country	Age category not required: Page by country	SAC
1.10	ASE	IDSL_DM11	Summary of Age Ranges	Categorise 18-64;65-84; >=85; Disclosure requirement	SAC
1.11	ITT	IDSL_DM5	Summary of Race and Racial Combination		SAC
1.12	ITT	IDSL_DM6	Summary of Race and Racial Combinations details		SAC
1.13	ITT	POP_T2	Summary of COPD Duration at Screening		SAC
1.14	ITT	POP_T3	Summary of COPD Exacerbation History at Screening		SAC
1.15	ITT	IDSL_FH1	Summary of Family History of Cardiovascular Risk Factors		SAC
1.16	ITT	IDSL_SU1	Summary of Smoking History and Smoking Status at Screening	Include Years Smoked, Cigarettes/Day, Smoking Pack Years*, Smoking Status categories	SAC
1.17	ITT	POP_T4	Summary of Baseline COPD Assessment Test (CAT)	For category refer Section 5.4.1	SAC
1.18	ITT	IDSL_MH4	Summary of Current Medical Conditions		SAC
1.19	ITT	IDSL_MH4	Summary of Past Medical Conditions		SAC

Study Population Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
1.20	ITT	POP_T5	Summary of Current Arthritis Location Details		SAC
1.21	ITT	POP_T6	Summary of Current Visual Impairment Details		SAC
Prior and Concomitant Medications					
1.22	ITT	IDSL_CM1	Summary of COPD Concomitant Medications		SAC
1.23	ITT	IDSL_CM1	Summary of Non-COPD Concomitant Medications		SAC

10.8.5. Efficacy Tables

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Primary Endpoint					
2.01	ITT	EFF_T1	Summary of Critical and Overall Errors	See shell for notes	SAC
2.02	ITT	EFF_T1	Summary of Critical and Overall Errors by country		SAC
2.03	ITT	EFF_T2	Logistic Regression Analysis of percentage of Subjects making at least one critical error at Visit 1 – Primary Device Comparisons	For comparisons of Primary devices Refer Section 2 Table 2	SAC
2.04	ITT	EFF_T2	Logistic Regression Analysis of percentage of Subjects making at least one critical error at Visit 1 – Dual device vs Primary device Comparisons	For comparisons of Dual vs Primary devices Refer Section 2 Table 2	SAC
Secondary Endpoint					
2.05	ITT	EFF_T2	Logistic Regression Analysis of percentage of Subjects making at least one overall error at Visit 1 – Primary Device Comparisons	For comparisons of Primary devices Refer Section 2 Table 2	SAC
2.06	ITT	EFF_T2	Logistic Regression Analysis of percentage of Subjects making at least one overall error at Visit 1 – Dual device vs Primary device Comparisons	For comparisons of Dual vs Primary devices Refer Section 2 Table 2	SAC
2.07	ITT	EFF_T2	Logistic Regression Analysis of percentage of Subjects making at least one critical error at Visit 2 – Primary Device Comparisons	For comparisons of Primary devices Refer Section 2 Table 2	SAC
2.08	ITT	EFF_T2	Logistic Regression Analysis of percentage of Subjects making at least one critical error at Visit 2 – Dual device vs Primary device Comparisons	For comparisons of Dual vs Primary devices Refer Section 2 Table 2	SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.09	ITT	EFF_T2	Logistic Regression Analysis of percentage of Subjects making at least one overall error at Visit 2 – Primary Device Comparisons	For comparisons of Primary devices Refer Section 2 Table 2	SAC
2.10	ITT	EFF_T2	Logistic Regression Analysis of percentage of Subjects making at least one overall error at Visit 2 – Dual device vs Primary device Comparisons	For comparisons of Dual vs Primary devices Refer Section 2 Table 2	SAC
Exploratory Endpoint					
2.11	ITT	EFF_T3	Summary of Exploratory Subroups	Refer Section 5.4.1	SAC
2.12	ITT	EFF_T4	Summary of Subjects with at Least one Critical and Overall Error at Visit 1 by Age Group	Refer Section 5.4.1 for Age group	SAC
2.13	ITT	EFF_T4	Summary of Subjects with at Least one Critical and Overall Error at Visit 1 by Educational Status Group	Refer Section 5.4.1 for Education status	SAC
2.14	ITT	EFF_T4	Summary of Subjects with at Least one Critical and Overall Error at Visit 1 by Co-morbidities	Refer Section 5.4.1 for Comorbidities.	SAC
2.15	ITT	EFF_T4	Summary of Subjects with at Least one of Critical and Overall Error at Visit 1 by Time Since Last Trained on Primary DPI	Refer Section 5.4.1 for time since last trained on primary DPI	SAC
2.16	ITT	EFF_T4	Summary of Subjects with at Least one Critical and Overall Error at Visit 1 by Time on Current Primary DPI	Refer Section 5.4.1 for time on current primary DPI	SAC
2.17	ITT	EFF_T4	Summary of Subjects with at Least one Critical or Overall Error at Visit 1 by Level of Control	Refer Section 5.4.1 for time on current primary DPI for level of control – this includes both CAT and Exac history	SAC

Efficacy: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.18	ITT	EFF_T6	Exploratory Analysis of Patient Characteristics and Interaction with Cohort using Logistic Regression for Critical Error and Overall Errors at Visit 1		SAC
Additional Tables					
2.19	ITT	EFF_T1	Summary of Rescue MDI Critical and Overall Errors		SAC

10.8.6. Efficacy Figures

Efficacy: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.01	ITT	EFF_F1	Percentage of Subjects with at Least One critical Error	Present both visit 1 and visit 2 on the same panel	SAC
2.02	ITT	EFF_F1	Percentage of Subjects with at Least One Overall Error	Present both visit 1 and visit 2 on the same panel	SAC
2.03	ITT	EFF_F2	Percentage of Subjects with at Least One Critical Error and Overall Error at Visit 1 – by Age group	Present critical and overall in side by side plots on the same page	SAC
2.04	ITT	EFF_F2	Percentage of Subjects with at Least One Critical Error and Overall Error at Visit 1 – by Educational Status Group	Present critical and overall in side by side plots on the same page	SAC
2.05	ITT	EFF_F2	Percentage of Subjects with at Least One Critical Error and Overall Error at Visit 1 – by Comorbidity group	Present critical and overall in side by side plots on the same page, page by each comorbidity (Arthritis, Visual Impairment, Neurological)	SAC
2.06	ITT	EFF_F2	Percentage of Subjects with at Least Critical Error and Overall Error at Visit 1 – by Time Since Last Trained on Primary DPI	Present critical and overall in side by side plots on the same page	SAC
2.07	ITT	EFF_F2	Percentage of Subjects with at Least One Critical Error and Overall Error at Visit 1 – by Time on Current Primary DPI	Present critical and overall in side by side plots on the same page	SAC

Efficacy: Figures					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
2.08	ITT	EFF_F2	Percentage of Subjects with at Least One Critical Error and Overall Error at Visit 1 – by Level of Control	Present critical and overall in side by side plots on the same page.	SAC

10.8.7. Safety Tables

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Adverse Events (AEs)					
3.01	ITT	IDSL_AE13	Overview of Adverse Events		SAC
3.02	ITT	IDSL_AE1	Summary of During-Study Adverse Events by System Organ Class and Preferred Term		SAC
3.03	ITT	IDSL_AE1	Summary of Post-Study Adverse Events by System Organ Class and Preferred Term		SAC
3.04	ITT	IDSL_AE16	Summary of Serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)	Include Serious, Drug-Related Serious, Fatal and Drug-Related Serious	SAC
3.05	ITT	IDSL_AE1	Summary of During-Study Serious Adverse Events by System Organ Class and Preferred Term		SAC

Safety: Tables					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
3.06	ITT	IDSL_AE1	Summary of During-Study Fatal Serious Adverse Events by System Organ Class and Preferred Term		SAC
3.07	ITT	IDSL_AE1	Summary of During-Study Drug-Related Adverse Events by System Organ Class and Preferred Term		SAC
3.08	ITT	IDSL_AE1	Summary of During-Study Drug-related Fatal Serious Adverse Events by System Organ Class and Preferred Term		SAC
3.09	ITT	IDSL_AE15	Summary of During-study Common (>=3% in Either Cohort) Non-serious Adverse Events by System Organ Class and Preferred Term (Number of Subjects and Occurrences)		SAC
Serious and Other Significant Adverse Events					
3.10	ITT	IDSL_AE1	Summary of During-Study Non-Fatal Serious Adverse Events by System Organ Class and Preferred Term		SAC
3.11	ITT	IDSL_AE1	Summary of During-Study Adverse Events Leading to Permanent Discontinuation of Study Treatment or Withdrawal from Study by System Organ Class and Preferred Term		SAC

10.8.8. ICH Listings

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Disposition					
01	ASE	IDSL_ES7	Listing of Reasons for Screen Failure		SAC
02	ITT	IDSL_ES2	Listing of Reasons for Study Withdrawal	Followup columns are not needed	SAC
Protocol Deviations					
03	ITT	IDSL_DV2	Listing of Important Protocol Deviations		SAC
04	ITT	IDSL_IE3	Listing of Subjects with Inclusion/Exclusion Criteria Deviations		SAC
Demographic and Baseline Characteristics					
05	ITT	IDSL_DM2	Listing of Demographic Characteristics	Include BMI in the listing	SAC
06	ITT	IDSL_DM9	Listing of Race		SAC
Adverse Events					
07	ASE	IDSL_AE8	Listing of All Adverse Events		SAC
08	ITT	IDSL_AE7	Listing of Subject Numbers for Individual Adverse Events		SAC
09	ITT	IDSL_AE8	Listing of Non-Fatal Adverse Events		SAC
10	ITT	IDSL_AE8	Listing of Fatal Adverse Events		SAC

ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
11	ITT	IDSL_AE2	Listing of Relationship Between Adverse Event System Organ Class, Preferred Term and Verbatim Text		SAC
Serious and Other Significant Adverse Events					
12	ITT	IDSL_AE8	Listing of Fatal Serious Adverse Events		SAC
13	ITT	IDSL_AE8	Listing of Non-Fatal Serious Adverse Events		SAC
14	ITT	IDSL_AE8	Listing of Adverse Events Leading to Withdrawal from Study / Permanent Discontinuation of Study Treatment		SAC
Inhaler errors					
15	ITT	EFF_L1	Listing of Inhaler Used at Visit 1 and Visit 2		SAC
16	ITT	EFF_L2	Listing of Subject Errors		SAC

10.8.9. Non-ICH Listings

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Subject Population					
17	ITT	POP_L1	Listing of Subjects by Country and Centre		SAC
18	ITT	POP_L2	Listing of Family History of Cardiovascular Risk Factors at Screening		SAC
19	ITT	POP_L3	Listing of COPD Duration at Screening		SAC
20	ITT	POP_L4	Listing of Smoking History and Smoking Status at Screening		SAC
21	ITT	POP_L5	Listing of COPD Assessment Test (CAT) at Screening		SAC
22	ITT	POP_L6	Listing of Current Arthritis Location details		SAC
23	ITT	POP_L7	Listing of Visual Impairment details		SAC
Medical Conditions					
24	ITT	IDSL_MH2	Listing of Medical Conditions		SAC

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Concomitant Medications					
25	ITT	IDSL_CM3	Listing of COPD Concomitant Medications		SAC
26	ITT	IDSL_CM3	Listing of Non-COPD Concomitant Medications		SAC
27	ITT	IDSL_CM6	Relationship between ATC Level 1, Ingredient and Verbatim Text for non-COPD medications		SAC
Adverse Events of Special Interest					
28	ITT	SAFE_L1	Listing of Subject Numbers for Individual Adverse Events of Special Interest		SAC
29	ITT	SAFE_L2	Listing of Adverse Event of Special Interest Group, Subgroup, Sub-SMQ and Preferred Term		SAC

Non-ICH: Listings					
No.	**Population**	**IDSL / Example Shell**	**Title**	**Programming Notes**	**Deliverable [Priority]**
Cardiovascular Events (Patient profiles)					
30	ASE	IDSL_ CVEND1	Lisiting of Arrhythmias		SAC
31	ASE	IDSL_ CVEND2	Lisiting of Congestive Heart Failure		SAC
32	ASE	IDSL_ CVEND3	Lisiting of Cerebrovascular Events Stroke (CVA) and Transient Ischemic Attack (TIA)		SAC
33	ASE	IDSL_ CVEND4	Lisiting of Deep Vein Thrombosis (DVT)/Pulmonary Embolism (PE)		SAC
34	ASE	IDSL_ CVEND5	Lisiting of Myocardial Infarction/Unstable Angina		SAC
35	ASE	IDSL_ CVEND6	Lisiting of Peripheral Arterial Thromboembolism		SAC
36	ASE	IDSL_ CVEND7	Lisitng of Pulmonary Hypertension		SAC
37	ASE	IDSL_ CVEND8	Lisiting of Revascularisation		SAC
38	ASE	IDSL_ CVEND9	Listing of Valvulopathy		SAC
39	ASE	IDSL_DEATH	Listing of All cause deaths		SAC

10.9. Appendix 9: Example Mock Shells for Data Displays

POP_T1

Protocol: 204981 Page 1 of x
Population: Intent-to-Treat

Table 1.x

Summary of Attendance at Each Clinic Visit

Visit	Cohort A (N=XXX)	Cohort B (N=XXX)	Cohort C (N=XXX)	Cohort D (N=XXX)	……	Cohort I (N=XXX)	Total (N=XXX)
Screening	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Visit1	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)
Visit2	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)	XX (XX%)

Note: Display Cohort name given in the section 5

Split onto 2 pages if space insufficient

POP_T2

Protocol: 204981
Population: Intent-to-Treat

Table 1.x
Summary of COPD Duration at Screening

	Cohort A (N=XXX)	Cohort B (N=XXX)	Cohort C (N=XXX)	……	Cohort I (N=XXX)	Total (N=XXX)
Duration of COPD						
n	xx	xx	xx	xx	xx	xx
< 6 months	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
>= 6 months to < 1 year	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
>= 5 years to < 10 years	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
>= 10 years to < 15 years	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
>= 15 years to < 20 years	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
>= 20 years to < 25 years	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
>= 25 years	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
COPD Type						
n	xx	xx	xx	xx	xx	xx
Chronic bronchitis	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
Emphysema	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)

Note: Display Cohort name given in the section 5

Split onto 2 pages if space insufficient

POP_T3
Protocol: 204981
Population: Intent-to-Treat

Table 1.x
Summary of COPD Exacerbation History at Screening

	Cohort A (N=XXX)	Cohort B (N=XXX)	Cohort C (N=XXX)	……	Cohort I (N=XXX)	Total (N=XXX)
Moderate COPD exacerbations						
n	xxx	xxx	xxx	xxx	xxx	xxx
0	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
1	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
>=2	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
Severe COPD exacerbations						
n	xxx	xxx	xxx	xxx	xxx	xxx
0	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
1	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
>=2	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
Total number of moderate/severe COPD exacerbations						
n	xxx	xxx	xxx	xxx	xxx	xxx
0	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
1	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
>=2	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)

Note: Display Cohort name given in the section 5

Split onto 2 pages if space insufficient

POP_T4
Protocol: 204981
Population: Intent-to-Treat

Table 1.x
Summary of Baseline COPD Assessment Test (CAT)

	Cohort A (N=XXX)	Cohort B (N=XXX)	Cohort C (N=XXX)	……	Cohort I (N=XXX)	Total (N=XXX)
CAT Score						
n	xxx	xxx	xxx	xxx	xxx	xxx
Mean	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
SD	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
Min.	Xxx	Xxx	Xxx	Xxx	Xxx	Xxx
Q1	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Median	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Q3	xx.x	xx.x	xx.x	xx.x	xx.x	xx.x
Max.	Xxx	Xxx	Xxx	Xxx	Xxx	Xxx
CAT Category						
n	xxx	Xxx	xxx	xxx	xxx	xxx
< 10	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
>=10	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)

Note: Display Cohort name given in the section 5

Split onto 2 pages if space insufficient

POP_T5

Protocol: 204981
Population: Intent-to-Treat

Table 1.x
Summary of Current Arthritis Location Details

	Cohort A (N=XXX)	Cohort B (N=XXX)	Cohort C (N=XXX)	……	Cohort I (N=XXX)	Total (N=XXX)
Current Arthritis	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
Arthritis Location						
Back	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
Neck	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
Shoulders	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
Elbows	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
Hands, Wrists and fingers	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
Lower body	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
Jaw	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)

Footnote:

Subjects may have more than one Arthritis location, so percentages may sum to more than 100%.

Percentage for Current Arthritis are calculated based on number of subjects in each Cohort.

Percentage for Arthritis Location are calculated based on number of subjects having Current Athritis

Note: Display Cohort name given in the section 5

POP_T6

Protocol: 204981
Population: Intent-to-Treat

Table 1.x
Summary of Current Visual Impairment Details

	Cohort A (N=XXX)	Cohort B (N=XXX)	Cohort C (N=XXX)	……	Cohort I (N=XXX)	Total (N=XXX)
n	xxx	xxx	xxx	xxx	xxx	xxx
Left eye						
Correctable	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
Not- Correctable	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
Right eye						
Correctable	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
Not- Correctable	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
Both eyes						
Correctable	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
Not- Correctable	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)
Correctable in only one eye	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)	xxx (xx%)

Footnote:

[1] Percentage is calculated based on number of subjects having visual Impairment (n)

Note: Display Cohort name given in the section 5

EFF_T1

Protocol: 204981
Population: Intent-to-Treat

Table 2.01
Summary of Critical and Overall Errors

Cohort : A (N=XXX)
Device: Ellipta

Inhaler errors test	Visit 1	Visit 2
N	XX	XX
Number of Subjects with at least one Error	XX (XX%)	XX (XX%)
Number of Subjects with at least one Critical Error	XX (XX%)	XX (XX%)
Total Number of Errors	XX	XX
Total Number of Critical Errors	XX	XX
Failed to open cover [1]	XX (XX%)	XX (XX%)
Inhalation manoeuvre: long, steady, deep	XX (XX%)	XX (XX%)
Blocked air inlet during inhalation manoeuvre	XX (XX%)	XX (XX%)
Shook the device after dose preparation [1]	XX (XX%)	XX (XX%)
No exhalation before an inhalation	XX (XX%)	XX (XX%)
Exhaled directly into mouthpiece [1]	XX (XX%)	XX (XX%)
No seal by the lips round the mouthpiece during the inhalation [1]	XX (XX%)	XX (XX%)
Did not hold breath	XX (XX%)	XX (XX%)
Did not close the device (Note: this is an error but one which does not affect the medication that is inhaled)	XX (XX%)	XX (XX%)

[1] Indicates a Critical Error.
Note: Percentages for number of subjects with at least one error are calculated from the total number of subjects who used the device(s)
Note: Percentages for type of errors are calculated from the number of subjects with overall errors.

Repeat for each cohort. Within those cohorts with 2 devices, produce 3 pages, 1st page with the first 4 lines above, 2nd page with the primary device errors (in the same way as above) and 3rd page with the second device errors (as above). (i.e. see the error table in '215 for the treatment arms with multiple devices)
Also note that the device page heading should be the device alone and not the drug, the drug will be evident from the cohort label.

EFF_T2

Protocol: 204981
Population: Intent-to-Treat

Table 2.xx
Logistic Regression Analysis of percentage of Subjects making at least one critical error at Visit 1 – Primary Device Comparisons

Cohort	N	n	Critical Error	Zero Critical Error	O.R.	95% C.I.	p-value
A	xx	xx	xx (xx%)	xx (xx%)	x.xxx	(x.xxx,x.xxx)	x.xxx
B	xx	xx	xx (xx%)	xx (xx%)			
A	xx	xx	xx (xx%)	xx (xx%)	x.xxx	(x.xxx,x.xxx)	x.xxx
C	xx	xx	xx (xx%)	xx (xx%)			
E	xx	xx	xx (xx%)	xx (xx%)	x.xxx	(x.xxx,x.xxx)	x.xxx
D	xx	xx	xx (xx%)	xx (xx%)			
E	xx	xx	xx (xx%)	xx (xx%)	x.xxx	(x.xxx,x.xxx)	x.xxx
F	xx	xx	xx (xx%)	xx (xx%)			
A	xx	xx	xx (xx%)	xx (xx%)	x.xxx	(x.xxx,x.xxx)	x.xxx
G1	xx	xx	xx (xx%)	xx (xx%)			
A	xx	xx	xx (xx%)	xx (xx%)	x.xxx	(x.xxx,x.xxx)	x.xxx
G1+H1+I1	xx	xx	xx (xx%)	xx (xx%)			`
A+G1	xx	xx	xx (xx%)	xx (xx%)	x.xxx	(x.xxx,x.xxx)	x.xxx
B+H1	xx	xx	xx (xx%)	xx (xx%)			
A+G1	xx	xx	xx (xx%)	xx (xx%)	x.xxx	(x.xxx,x.xxx)	x.xxx
C+I1	xx	xx	xx (xx%)	xx (xx%)			

Note: Display Cohort name instead of Cohort codes

EFF_T3
Protocol: 204981
Population: Intent-to-Treat

Table 1.x
Summary of Exploratory Subgroups

Covariates and / or Subgroups	Cohort A (N=XX)	Cohort B (N=XX)	-----	Cohort I (N=XXX)	Total (N=XXX)
Age					
40-49 Years	XXX	XXX		XXX	XXX
50-59 years	XXX	XXX		XXX	XXX
60-69 years	XXX	XXX		XXX	XXX
70-79 years	XXX	XXX		XXX	XXX
>=80 years	XXX	XXX		XXX	XXX
Educational status					
0-5 years	XXX	XXX		XXX	XXX
6-10 years	XXX	XXX		XXX	XXX
11-15 years	XXX	XXX		XXX	XXX
16-20 years	XXX	XXX		XXX	XXX
>=21 years	XXX	XXX		XXX	XXX
Arthritis					
Upper Limbs	XXX	XXX		XXX	XXX
Not upper limbs or No Arthritis	XXX	XXX		XXX	XXX
Visual Impairment					
Visual Impairment not correctable	XXX	XXX		XXX	XXX
Visual Impairment correctable / No Visual Impairment	XXX	XXX		XXX	XXX
Neurological disorder					
Functional disorder	XXX	XXX		XXX	XXX
No functional disorder	XXX	XXX		XXX	XXX
Dementia	XXX	XXX		XXX	XXX
No dementia	XXX	XXX		XXX	XXX
Psychological disorder	XXX	XXX		XXX	XXX

No psychological disorder	XXX	XXX	XXX	XXX
Time since last trained on primary DPI				
>3 to ≤ 6 Months	XXX	XXX	XXX	XXX
>6 Months to ≤ 1 Year	XXX	XXX	XXX	XXX
>1 year to ≤ 2 Years	XXX	XXX	XXX	XXX
>2 Years to ≤ 3 Years	XXX	XXX	XXX	XXX
> 3 Years	XXX	XXX	XXX	XXX
Time on current primary DPI(s)				
>3 to ≤ 6 Months	XXX	XXX	XXX	XXX
>6 Months to ≤ 1 Year	XXX	XXX	XXX	XXX
>1 year to ≤ 2 Years	XXX	XXX	XXX	XXX
>2 Years to ≤ 3 Years	XXX	XXX	XXX	XXX
> 3 Years	XXX	XXX	XXX	XXX
COPD Assessment test (CAT)				
<10	XXX	XXX	XXX	XXX
>=10	XXX	XXX	XXX	XXX
Exacerbation history in Prior year				
0	XXX	XXX	XXX	XXX
1	XXX	XXX	XXX	XXX
>=2	XXX	XXX	XXX	XXX

EFF_T4

Protocol: 204981
Population: Intent-to-Treat

Table 2.XX
Summary of Critical and Overall Errors at Visit 1 by Age Group

Age Group	N	n	Critical Error	Overall Error
40-49 Years	XX	xx	XX (XX%)	XX (XX%)
50-59 years	XX	xx	XX (XX%)	XX (XX%)
60-69 years	Xx	xx	XX (XX%)	XX (XX%)
70-79 years	Xx	xx	XX (XX%)	XX (XX%)
>=80 years	Xx	xx	XX (XX%)	XX (XX%)

EFF_T5

Protocol: 204981
Population: Intent-to-Treat

Table 2.xx
Exploratory Analysis of Patient Characteristics and Interaction with Cohort using Logistic Regression for Critical Error and Overall Errors at Visit 1

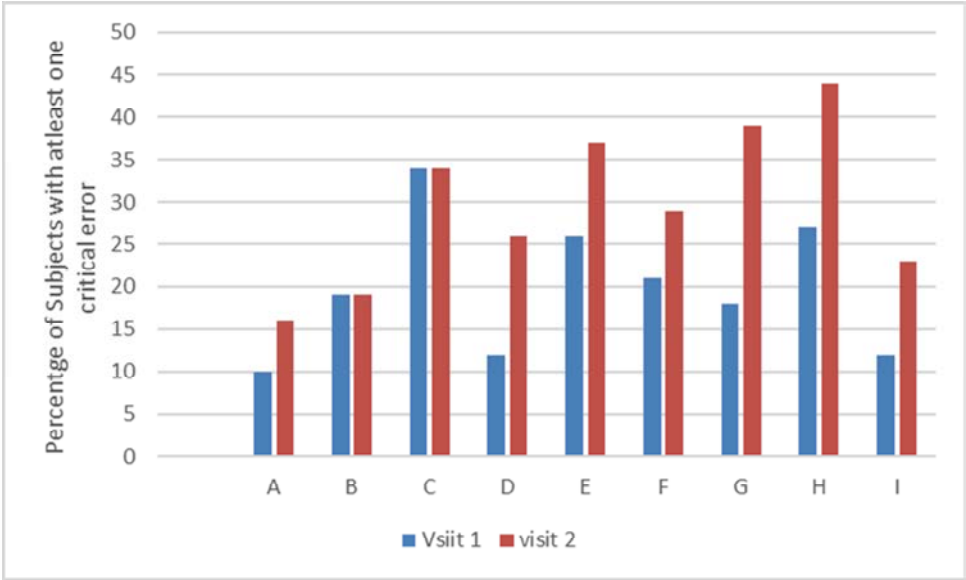
				Interaction with Cohort	
Covariates and / or Subgroups	Category	Critical Error p-value	Overall Error p-value	Critical Error p-value	Overall Error p-value
Age:	40-49 years 50-59 years 60-69 years 70-79 years >=80 years	X.XXX	X.XXX	X.XXX	X.XXX
Educational status	0-5 years 6-10 years 11-15 years 16-20 years >=21 years	X.XXX	X.XXX	X.XXX	X.XXX
Arthritis	Yes/ No	X.XXX	X.XXX	X.XXX	X.XXX
Visual Impairment	Yes/ No	X.XXX	X.XXX	X.XXX	X.XXX
Functional disorder	Yes/ No	X.XXX	X.XXX	X.XXX	X.XXX
Dementia	Yes/ No	X.XXX	X.XXX	X.XXX	X.XXX
Psychological disorder	Yes/ No	X.XXX	X.XXX	X.XXX	X.XXX
Time since last trained on primary DPI	>3 to ≤ 6 Months >6 Months to ≤ 1 Year >1 to ≤ 2 Yearrs; >2 to ≤ 3 Years; > 3 Years	X.XXX	X.XXX	X.XXX	X.XXX
Time on current primary DPI(s)	-"-	X.XXX	X.XXX	X.XXX	X.XXX

COPD Assessment test (CAT).	<10/>=10	X.XXX	X.XXX	X.XXX	X.XXX
Exacerbation history	0,1, ≥2	X.XXX	X.XXX	X.XXX	X.XXX

EFF_F1

Protocol : 204981
Population : Intent to Treat

Figure X.X
Percentage of Subjects with at Least One Critical Error



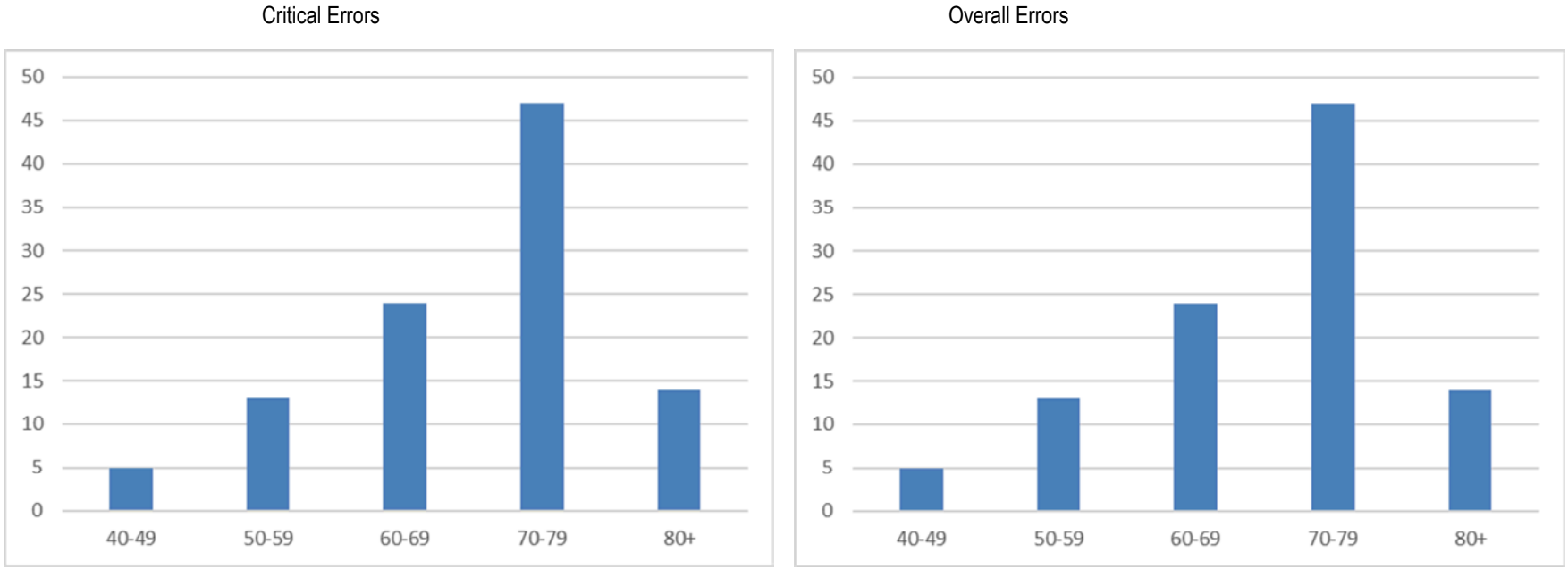
Programming note: Please present Cohort names instead of Cohort Codes. Please use different pattern for diifernt visit.

Footnote: For the cohort with two devices (G,H and I) , the critical error is counted only for primary devices.

EFF_F2

Protocol : 204981
Population : Intent to Treat

Figure X.X
Percentage of Subjects with at Least One Critical and Overall Error
By Age Group



.***Repeat for other exploratory covariates groups of interest***

POP_L1

Protocol: 204981
Population: Intent-to-Treat

Listing xx
Listing of Subjects by Country and Centers

Country	Inv. at Centre	Investigator Name	Subject	Cohort
Netherlands	PPD			DISKUS + HandiHaler
				ELLIPTA/DISKUS + HandiHaler
				DISKUS + HandiHaler/ELLIPTA
United Kingdom				DISKUS + HandiHaler
				ELLIPTA/DISKUS + HandiHaler

POP_L2

Protocol: 204981 Page 1 of x
Population: Intent-to-Treat

Listing xx
Listing of Family History of Cardiovascular Risk Factors at Screening

Inv. at Centre	Subject	Cohort	Family History [1]
PPD		DISKUS + HandiHaler/ELLIPTA/Q1	Yes
		ELLIPTA/DISKUS + HandiHaler/Q1	Unknown
		DISKUS + HandiHaler/ELLIPTA/Q2	Unknown
		ELLIPTA/DISKUS + HandiHaler/Q2	Yes
		DISKUS + HandiHaler/ELLIPTA/Q2	Unknown

Footnote: [1] Family history of premature coronary artery disease in women < 65 years or men < 55 years in first degree relatives only (e.g., biological mother or father, biological brother or sister, biological son or daughter).

POP_L3

Protocol: 204981
Population: Intent-to-Treat

Listing xx
Listing of COPD Duration at Screening

Inv. at Centre	Subject	Cohort	Duration
PPD		DISKUS + HandiHaler/ELLIPTA/Q1	>=1 year to <5 years
		ELLIPTA/DISKUS + HandiHaler/Q1	>=10 years to <15
		Years	
		DISKUS + HandiHaler/ELLIPTA/Q2	>=1 year to <5 years
		ELLIPTA/DISKUS + HandiHaler/Q2	>=5 years to <10
		Years	
		DISKUS + HandiHaler/ELLIPTA/Q2	>=1 year to <5 years

POP_L4

Protocol: 204981
Population: Intent-to-Treat

Listing xx
Listing of Smoking History and Smoking Status at Screening

Inv. at centre	Subject	Cohort	Years Smoked	Cigarettes per day	Smoking Pack Years [1]	Smoking status
PPD		DISKUS + HandiHaler/ELLIPTA/Q1	25	20	25	Former Smoker
		ELLIPTA/DISKUS + HandiHaler/Q1	50	30	75	Current Smoker
		DISKUS + HandiHaler/ELLIPTA/Q2	50	15	38	Former Smoker
		ELLIPTA/DISKUS + HandiHaler/Q2	26	20	26	Never Smoked

POP_L5

Protocol: 204981
Population: Intent-to-Treat

Listing xx
Listing of COPD Assessment Test (CAT) at Screening

Inv. at Centre	Subject	Cohort	CAT Total Score
PPD	[redacted]	DISKUS + HandiHaler/ELLIPTA/Q1	15
		ELLIPTA/DISKUS + HandiHaler/Q1	10
		DISKUS + HandiHaler/ELLIPTA/Q2	10
		ELLIPTA/DISKUS + HandiHaler/Q2	16

POP_L6

Protocol: 204981
Population: Intent-to-Treat

Listing xx
Listing of Current Arthritis Location Details

Inv. at Centre	Subject	Cohort	Arthritis Location
PPD		DISKUS + HandiHaler/ELLIPTA	Jaw
		ELLIPTA/DISKUS + HandiHaler/Q1	Back
		DISKUS + HandiHaler/ELLIPTA/Q2	shoulder
		ELLIPTA/DISKUS + HandiHaler/Q2	Elbow
		DISKUS + HandiHaler/ELLIPTA/Q2	shoulder

POP_L7

Protocol: 204981
Population: Intent-to-Treat

Listing xx
Listing of Visual Impairment Details

Inv. at Centre	Subject	Cohort	Eyes affected	Eyes corrected
PPD	[redacted]	DISKUS + HandiHaler/ELLIPTA/Q1	Left	Left
		ELLIPTA/DISKUS + HandiHaler/Q1	Right	Right
		DISKUS + HandiHaler/ELLIPTA/Q2	Left	Left
		ELLIPTA/DISKUS + HandiHaler/Q2	Both	Right
		DISKUS + HandiHaler/ELLIPTA/Q2	Both	Both

EFF_L1

Protocol: 204981
Population: Intent-to-Treat

Listing xx

Listing of Inhaler Use at Visit 1 and Visit 2

Inv. at centre	Subject	Visit 1	Visit 2	Switched the device/ medication
PPD		Relvar Ellipta + Spirivia HandiHaler	Relvar Ellipta	Y
		Relvar Ellipta	Relvar Ellipta	
		Relvar Ellipta	Relvar Ellipta+Other	Y

EFF_L2

Protocol: 204981
Population: Intent-to-Treat

Listing xx
Listing of Critical and Overall Inhaler Errors

Inv. at centre	Subject	Cohort	Actual Cohort	Visit	Total	Device	Type of Error
PPD		DISKUS + HandiHaler	DISKUS + HandiHaler	Visit 1	3	HandiHaler	Capsule did not rattle [1]
							Inhalation manoeuvre: was slow, deep
						DISKUS	No exhalation before an Inhalation

Footnote: [1] Indicates a Critical Error.

Programming note: The number in total column displays number of errors the subject had made irrespective of devices. Cohort and Actual Cohort are trtgrp and atrtgrp.

List only the error assessment not completed correctly under "Type of error" column.

SAFE_L1

Protocol: 204981 Page 1 of x
Population: Intent-to-Treat

Listing xx
Listing of Subject Numbers for Individual Adverse Events of Special Interest

AESI Group: CV effects/Hypertension (SMQ)

System Organ Class Preferred Term	Treatment	No. with Event	Subject
Investigations			
Blood pressure increased	DISKUS + HandiHaler	1	PPD
Vascular disorders	DISKUS + HandiHaler	2	
Hypertension		1	

SAFE_L2

Protocol: 204981 Page 1 of x
Population: Intent-to-Treat

Listing xx
Listing of Adverse Event of Special Interest Group, Subgroup, Sub-SMQ and Preferred Term

AESI Group	AESI Subgroup	Sub-SMQ	Preferred Term
Adrenal suppression			ACTH stimulation test abnormal
			Addison's disease
			Adrenal androgen deficiency
			Adrenal atrophy
			Adrenal insufficiency