Statistical Analysis Plan

BI Trial No.:	0352-2119
Title:	Digital Auscultation Test - Development of an Innovative Approach - using modern technologies - to improve the diagnosis of rare lung diseases – expanded data collection Idiopathic Pulmonary Fibrosis.
Investigational product(s):	Not applicable
Responsible trial statistician:	Tel: Fax:
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LIST OF TABLES

Not applicable.

1. LIST OF ABBREVIATIONS

AE	Adverse Event
BI	Boehringer Ingelheim
BMI	Body Mass Index
CRF	Case Report Form
CTCAE	Common Terminology Criteria for Adverse Events
CTP	Clinical Trial Protocol
ECG	Electrocardiography
EMA	European Medicines Agency
ENMST	All Subjects Entered Main-Study Set
ENR	All Subjects Enrolled Set
ENSST	All Subjects Entered Sub-Study Set
ENT	All Subject Entered Set
IPF	Idiopathic Pulmonary Fibrosis
IRB	Institutional Review Board
MedDRA	Medical Dictionary for Regulatory Activities
SAE	Serious Adverse Event
SOC	System Organ Class
SOP	Standard Operating Procedure
TCM	Trial Clinical Manager
TSAP	Trial Statistical Analysis Plan

2. INTRODUCTION

This TSAP assumes familiarity with the Clinical Trial Protocol (CTP), including Protocol Amendments.

There is no investigational drug being used in this study. Focus will be on two complimentary groups, the one group includes only patients diagnosed with IPF (IPF group) and the other group only includes patients not diagnosed with IPF (non-IPF group).

In addition a sub-study is planned to collect sound recordings using two different electronic stethoscope sequentially from approximately 50 additional patients (approximately 20 patients diagnosed with IPF and approximately 30 diagnosed with a non-IPF lung disease).

SAS® Version xx will be used for all analyses.

3. CHANGES IN THE PLANNED ANALYSIS OF THE STUDY

Not applicable

4. OUTCOMES

4.1 PRIMARY OUTCOMES

For each patient the auscultation sound files will be collected at 12 points of the body. The primary outcome will be the percentage collected auscultation point.

4.2 SECONDARY OUTCOMES

The secondary outcomes are:

- Patient reported symptoms (8 questions)
- Smoking status
- BMI
- Gender

4.3 OTHER OUTCOMES

The other outcomes are:

- Age
- Height
- Weight
- Blood pressure
- Pulse rate
- Weight loss

5. GENERAL ANALYSIS DEFINITIONS

5.1 EXPOSURE

Not applicable.

5.2 IMPORTANT PROTOCOL VIOLATIONS

For this trial no important protocol violations are defined. However all protocol violations will be listed and tabulated.

5.3 PATIENT SETS ANALYSED

As this is a one visit trial without any trial medication only one patient set will be defined.

5.3.1 All subject enrolled Set (ENR)

The all subject enrolled set will contain all subjects that signed informed consent.

5.3.2 All Subjects Entered Set (ENT)

The all subjects entered set will contain all subjects for which visit data is available.

5.3.3 All Subjects Entered Main-Study Set (ENMST)

The all subjects entered main study set will contain all subjects for which visit data is available and are not part of the Sub-Study.

5.3.4 All Subjects Entered Sub-Study Set (ENSST)

The all subjects entered sub-study set will contain all subjects for which visit data is available and are part of the Sub-Study.

5.5 POOLING OF CENTRES

Not applicable.

5.6 HANDLING OF MISSING DATA AND OUTLIERS

No imputation for missing data nor for outliers is planned in this trial. Missing or incomplete AE dates will be handled as described in “Handling of missing and incomplete AE dates [1].

5.7 BASELINE, TIME WINDOWS AND CALCULATED VISITS

Not applicable.

6. PLANNED ANALYSIS

All tables will be presented by diagnose group (IPF group and non-IPF group) and overall. At least the following descriptive statistics will be calculated for all continuous endpoints: N, arithmetic mean, standard deviation, minimum, median, maximum.

6.1 DISPOSITION

Only descriptive statistics are planned for this section of the report and will be presented for the ENT set.

6.2 DEMOGRAPHIC AND OTHER BASELINE CHARACTERISTICS

Only descriptive statistics are planned for this section of the report and will be presented for the ENT, ENMST and ENSST set.

6.3 CONCOMITANT DISEASES AND SURGIRICAL PROCEDURES

Only descriptive statistics are planned for this section of the report and will be presented for the ENT, ENMST and ENSST set.

6.4 TREATMENT ADHERENCE

Not applicable.

6.5 METHODS ADDRESSING BIAS

Not applicable.

6.6 METHODS ADDRESSING CONFOUNDING / EFFECT MEASURE MODIFICATION

Not applicable

6.7 PRIMARY ANALYSES

Only descriptive statistics are planned for this section of the report and will be presented for the ENT, ENMST and ENSST set.

6.8 SECONDARY ANALYSES

Only descriptive statistics are planned for this section of the report and will be presented for the ENT, ENMST and ENSST set.

6.9 OTHER ANALYSES

Only descriptive statistics are planned for this section of the report and will be presented for the ENT, ENMST and ENSST set.

6.10 EXPOSURE TIME

Not applicable.

6.11 SAFETY ANALYSIS

All safety analyses will be performed on the ENR set.

6.11.1 Adverse events

Unless otherwise specified, the analyses of adverse events will be descriptive in nature. All analyses of AEs will be based on the number of subjects with AEs and NOT on the number of AEs.

Adverse Events (AEs) will be coded using MedDRA central coding dictionary, Version 21.0 or higher. The system organ classes will be sorted by internationally agreed EMA SOC order (refer to Section 8); preferred terms will be sorted by decreasing frequencies (within system organ class).

For analysis multiple AE occurrence data on the CRF will be collapsed into an AE provided that all of the following applies:

- All AE attributes are identical.

- The occurrences were time-overlapping or time-adjacent (time-adjacency of 2 occurrences is given if the second occurrence started on the same day or on the day after the end of the first occurrence.

For further details on summarization of AE data, please refer to (1, 2).
An overall summary of adverse events will be presented.

The frequency of subjects with adverse events will be summarised by treatment, primary system organ class and preferred term (mention MedDRA levels to be displayed in the tables). Separate tables will be provided for subjects with serious adverse events.

In addition the system organ classes will be sorted alphabetically, preferred terms will be sorted by frequency (within system organ class).

6.11.2 Laboratory data

Not applicable.

6.11.3 Vital signs

Only descriptive statistics are planned for this section of the report.

6.11.4 ECG

Not applicable.

6.11.5 Others

Only descriptive statistics are planned for this section of the report.

6.12 INTERIM ANALYSES

Not applicable.

7. REFERENCES

1.	*001-MCG-156_RD-01:* "Handling of missing and incomplete AE dates", current version; IDEA for CON.
2.	*001-MCG-156*: "Handling and summarization of adverse event data for clinical trial reports and integrated summaries", current version; IDEA for CON.

8. EMA SOC ORDER FOR PRESENTATION OF THE AE IN THE TABLES

Order System Organ Class

0 Uncoded

1 Infections and infestations

2 Neoplasms benign, malignant and unspecified (incl cysts and polyps)

3 Blood and lymphatic system disorders

4 Immune system disorders

5 Endocrine disorders

6 Metabolism and nutrition disorders

7 Psychiatric disorders

8 Nervous system disorders

9 Eye disorders

10 Ear and labyrinth disorders

11 Cardiac disorders

12 Vascular disorders

13 Respiratory, thoracic and mediastinal disorders

14 Gastrointestinal disorders

15 Hepatobiliary disorders

16 Skin and subcutaneous tissue disorders

17 Musculoskeletal and connective tissue disorders

18 Renal and urinary disorders

19 Pregnancy, puerperium and perinatal conditions

20 Reproductive system and breast disorders

21 Congenital, familial and genetic disorders

22 General disorders and administration site conditions

23 Investigations

24 Injury, poisoning and procedural complications

25 Surgical and medical procedures

26 Social circumstances

27 Product issues

9. HISTORY TABLE

Shared; dependent on section changed

APPROVAL / SIGNATURE PAGE

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Signatures (obtained electronically)

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Approval-Trial Clinical Monitor		26 Jul 2018 15:22 CEST
Approval-Biostatistics		27 Jul 2018 01:19 CEST

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