BI Study Number: 1237.51

SATisfaction and adherence to COPD treatment

STATISTICAL ANALYSIS PLAN

Version 1.5, 22/09/2017

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Boehringer Ingelheim

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LIST OF ABBREVIATIONS

ACOS	Asthma COPD Overlap Syndrome
ADR	Adverse Drug Reaction
AE	Adverse Event
BI	Boheringer Ingelheim Italy S.p.A
B-IPQ	Brief-Illness Perception Questionnaire
BMI	Body Mass Index
BS	Biostatistician
CAT	COPD Assessment Test
CDM	Clinical Data Manager
COPD	Chronic Obstructive Pulmonary Disease
DLCO	Diffusion Lung Capacity for carbon monoxide
eCRF	electronic Case Report Form
ER	Emergency Room
FAS	Full Analysis Set
FEV1	Forced Expiratory Volume in the 1st second
FVC	Forced Vital Capacity
ICS	Inhaled corticosteroids
ICU	Intensive Care Unit
LABA	Long-acting β2-agonists
LAMA	Long-acting muscarinic agonists
Max	Maximum
Min	Minimum
MMAS-4	Morisky medication Adherence Scale, 4 items
mMRC	modified Medical Research Council dyspnea scale
N	Number of observations
NA	Not Available
NK	Not Known
PDE4-I	Phosphodiesterase type 4 inhibitors
PRO	Patient-Reported Outcome
R-DMS	Responsible Data Management and Statistics Unit
SABA	Short-acting β-agonists
SAE	Serious Adverse Event
SAMA	Short-acting muscarinic agonists
SAP	Statistical Analysis Plan
SD	Standard Deviation
TLC	Total Lung Capacity
TSQM-9	Treatment Satisfaction Questionnaire for Medication, 9 items
VC	Vital Capacity

1 STATISTICAL AANALYSIS PLAN OBJECTIVES

The *SATisfaction and adherence to COPD treatment* study (i.e. SAT study) is a multi-center, non-interventional (observational) cohort study based mainly on newly collected data. About 400 consecutive COPD patients will be enrolled in approximately 8 months (from first patient enrolled). Patients will be followed up for 1 year, with an intermediate evaluation after 6 (+/-1) months from baseline (which is compatible with current clinical practice in Italy for COPD patients management).
The present Statistical Analysis Plan has beed designed considering the following input documents:

- the Study Protocol v.1.0 31/07/2015,
- the electronic case report form v. 1.2 27/04/2016;
- the minutes of the Customer's Meeting held on the 26/06/2017.

This SAP is aimed at evaluating the following SAT study objectives:

Primary objective:

To describe the patients' satisfaction to COPD medical treatments (by means of the TSQM9) during a 12-month observation period (namely, at enrolment, and after 6 and 12 months) in real- world setting.

Secondary objectives:

1. To describe patient disease perception (by means of illness perception questionnaire B-IPQ), adherence to COPD treatment (by means of MMAS4), health status (by means of CAT questionnaire) and dyspnea (by means of mMRC) during a 12-month observation period.
2. To analyze the relation between treatment satisfaction and demographic (such as age, gender), clinical (such as number of exacerbations, spirometric parameters) parameters and PROs during a 12-month observation period.
3. To describe the health care resources utilization and related cost according to the Italian National Health Service (INHS) during a 12-month observation period.
4. To assess the correlation between patients' satisfaction and resource utilization.

In this document the eCRF fields are indicated as follows: "label of the field" [***name of the eCRF form.name of the variable in the dataset***].

2 DEFINITION OF EVALUABLE PATIENTS

2.1 Patients evaluable at enrolment (FULL ANALYSIS SET)

All enrolled patients meeting the following inclusion / exclusion / other criteria listed in the present paragraph will be considered evaluable at enrollment (Full analysis set) (i.e. COPD patients aged ≥40 years, with stable pharmacological treatment for COPD and no exacerbations for at least 3 months, who signed informed consent and privacy form, with at least one Treatment Satisfaction Questionnaire for Medication (TSQM-9) domain score calculated at enrollment visit):

Inclusion criteria

Criterion 1: Patients aged ≥40 years

- *Question "1. Is the patient aged ≥40 years?" = "Yes" **[F01_INC_EXC_CRITERIA.CI_1]** AND*
- *Inclusion criterion "1. Patients aged ≥40 years?" not checked in the PROTOCOL DEVIATION FORM **[F24_PROTOCOL_DEVIATION_FORM. PD_CI_1]** AND*
- *Age at enrollment visit (years) ≥ 40 **[_PatientInfo.Age]***

Criterion 2: Patients must have a documented diagnosis of chronic obstructive pulmonary disease (COPD)

- *Question "2. Has the patient a documented diagnosis of chronic obstructive pulmonary disease (COPD)?" = "Yes" **[F01_INC_EXC_CRITERIA.CI_2]***
  AND
- *Inclusion criterion "2. Patients must have a documented diagnosis of chronic obstructive pulmonary disease (COPD)" not checked in the PROTOCOL DEVIATION FORM **[F24_PROTOCOL_DEVIATION_FORM. PD_CI_2]** AND*
- *Date of COPD diagnosis (mm/yyyy) not missing **[F04_COPD_MEDICAL_HISTORY.MH_Date_diagnosis]***

Criterion 3: Patients with no exacerbations in the last 3 months

- *Question "3. Patient without any exacerbation in the last 3 months" = "Yes" **[F01_INC_EXC_CRITERIA.QUESTION 3. CI_3]** AND*
- *Inclusion criterion "3. Patients with no exacerbations in the last 3 months" not checked in the PROTOCOL DEVIATION FORM **[F24_PROTOCOL_DEVIATION_FORM. PD_CI_3]** AND*
- *Onset dates at each follow-up visit (Row 1 to 10) **[F08_EXACERBATIONS.Ex_exacer_1-10_onset_date]** > Date of enrolment visit (dd/mm/yyyy) **[_PatientInfo.Date_enrollment]***

Criterion 4: Patients requiring regular treatment according to GOLD guidelines, i.e.: undergoing stable pharmacological treatment for COPD since at least 3 months

- *Question "4. Does the patient require a regular treatment according to GOLD guidelines, i.e.: undergoing stable pharmacological treatment for COPD since at least 3 months?" = "Yes" **[F01_INC_EXC_CRITERIA.CI_4]** AND*
- *Inclusion criterion "4. Patients requiring regular treatment according to GOLD guidelines, i.e.: undergoing stable pharmacological treatment for COPD since at least 3 months" not checked in the PROTOCOL DEVIATION FORM **[F24_PROTOCOL_DEVIATION_FORM. PD_CI_4]** AND*
- *COPD Pharmacological therapy form: Start date of therapy (dd/mmm/yyyy) not missing AND (Start date of therapy (dd/mmm/yyyy) [**F20_COPD PHARMACOLOGICAL THERAPY.START_DATE_THER]** < Date of enrolment visit (dd/mm/yyyy) – 3*30.4375 **[_PatientInfo.Date_enrollment]** OR Start date of therapy (dd/mmm/yyyy) > Date of enrolment visit (dd/mm/yyyy)) AND*
- *COPD Pharmacological therapy form: End date of therapy (dd/mmm/yyyy) **[F20_COPD PHARMACOLOGICAL THERAPY.END_DATE_THER]** = missing OR End date of therapy (dd/mmm/yyyy) > Date of enrolment visit (dd/mm/yyyy) **[_PatientInfo.Date_enrollment]***

Criterion 5: Written informed consent to both participation in the study and privacy form

- *Question "5. Is a written informed consent to both participation in the study and privacy form available?" = "Yes"* ***[F01_INC_EXC_CRITERIA.CI_5]*** *AND*
- *Inclusion criterion "5. Written informed consent to both participation in the study and privacy form" not checked in the PROTOCOL DEVIATION FORM* ***[F24_PROTOCOL_DEVIATION_FORM. PD_CI_5]*** *AND*
- *Date of informed consent signature (dd/mm/yyyy) not missing* ***[_PatientInfo.Date_CI]*** *AND*
- *Date of privacy form signature (dd/mm/yyyy) not missing* ***[_PatientInfo.Date_privacy]*** *AND*
- *Date of informed consent signature (dd/mm/yyyy) = Date of privacy form signature (dd/mm/yyyy) AND*
- *Date of informed consent signature (dd/mm/yyyy) ≤ Date of enrolment visit (dd/mm/yyyy)*

Criterion 6: Patients capable of discernment and able to read or write in Italian language

- *Question "6. Is the patient capable of discernment and able to read or write in Italian language? " = "Yes"* ***[F01_INC_EXC_CRITERIA.CI_6]*** *AND*
- *Inclusion criterion "6. Patients capable of discernment and able to read or write in Italian language" not checked in the PROTOCOL DEVIATION FORM* ***[F24_PROTOCOL_DEVIATION_FORM. PD_IC_6]***

Exclusion criteria

Criterion 7: Patients who are currently participating in a clinical trial on experimental drugs

- *Question "7. Does the patient currently participate in a clinical trial on experimental drugs? " = "No"* ***[F01_INC_EXC_CRITERIA.EC_1]*** *AND*
- *Exclusion criterion "1. Patients who are currently participating in a clinical trial on experimental drugs" not checked in the PROTOCOL DEVIATION FORM* ***[F24_PROTOCOL_DEVIATION_FORM. PD_EC_1]***

Criterion 8: Patients naïve to pharmacological treatment for COPD

- *Question "8. Is the patient naïve to pharmacological treatment for COPD? " = "No"* ***[F01_INC_EXC_CRITERIA.EC_2]*** *AND*
- *COPD Pharmacological therapy form: Start date of therapy (dd/mmm/yyyy) (earliest record) not missing AND*
- *Exclusion criterion "2. Patients naïve to pharmacological treatment for COPD" not checked in the PROTOCOL DEVIATION FORM* ***[F24_PROTOCOL_DEVIATION_FORM. PD_EC_2]***

Criterion 9: Diagnosis of Asthma COPD Overlap Syndrome (ACOS)

- *Question " 9. Does the patient have a diagnosis of Asthma COPD Overlap Syndrome (ACOS)? " = "No"* ***[F01_INC_EXC_CRITERIA.EC_3]*** *AND*
- *Exclusion criterion "3. Diagnosis of Asthma COPD Overlap Syndrome (ACOS)" not checked in the PROTOCOL DEVIATION FORM* ***[F24_PROTOCOL_DEVIATION_FORM. PD_EC_3]***

Other criteria

Criterion 10: patients with at least one Treatment Satisfaction Questionnaire for Medication (TSQM-9) domain score calculated at enrollment visit

- *TSQM-9 items #1,2,3 [**TSQM9_1-3**] not missing & ≠ "Non risponde" at enrollment visit, OR*
- *TSQM-9 items #4,5,6 [**TSQM9_4-6**] not missing & ≠ "Non risponde" at enrollment visit, OR*
- *TSQM-9 items #7,8,9 [**TSQM9_7-9**] not missing & ≠ "Non risponde" at enrollment visit*

2.2 Patients evaluable at 6-month follow-up

All enrolled patients meeting the following criteria will be considered evaluable at enrollment and at 6 month follow-up visit:

Patients considered evaluable at enrollment (i.e., responding to criteria of par 2.1 Full Analysis Set) who fulfill also the following criteria (i.e. all FAS patients who performed the 6-month follow-up visit and with at least one Treatment Satisfaction Questionnaire for Medication (TSQM-9) domain score calculated at the 6-month follow-up visit).

Criterion 11: Data collected at 6-month follow-up

- *"Data collected at 6 (±1) month follow up?" = "Yes"* **[F19_PATIENT_DISPOSITION, 6 month f-up.PD_1]**

Criterion 12: Follow-up performed 6+/- 1 month from enrollment

- *(Date of follow up visit (dd/mmm/yyyy)* **[F19_PATIENT_DISPOSITION, 6 month f-up.PD_2]***– Date of enrolment visit (dd/mm/yyyy)* **[_PatientInfo. Date_enrollment]***/30.4375 ≥ 5) AND*
- *(Date of follow up visit (dd/mmm/yyyy)* **[F19_PATIENT_DISPOSITION, 6 month f-up.PD_2]** *– Date of enrolment visit (dd/mm/yyyy)* **[_PatientInfo. Date_enrollment]** */30.4375 ≤ 7)*

The Biostatistician will evaluate the opportunity to apply a tolerance window during the analysis of data; the Sponsor will be informed of any possible changes in this range.

Criterion 13: patients with at least one Treatment Satisfaction Questionnaire for Medication (TSQM-9) domain score calculated at 6-month follow-up visit

- *TSQM-9 items #1,2,3 [**TSQM9_1-3**] not missing & ≠ "Non risponde" at 6-month follow-up, OR*
- *TSQM-9 items #4,5,6 [**TSQM9_4-6**] not missing & ≠ "Non risponde" at 6-month follow-up, OR*
- *TSQM-9 items #7,8,9 [**TSQM9_7-9**] not missing & ≠ "Non risponde" at 6-month follow-up*

2.3 Patients evaluable at 12-month follow-up

All enrolled patients meeting the following criteria will be considered evaluable at enrollment and at 12 month follow-up visit:

Patients considered evaluable at enrollment (i.e., responding to criteria of par 2.1 Full Analysis Set) who fulfill also the following criteria (i.e. all FAS patients who performed the 12-month follow-up visit and with at least one Treatment Satisfaction Questionnaire for Medication (TSQM-9) domain score calculated at the 12-month follow-up visit).

Criterion 14: Data collected at 12-month follow-up

- *"Data collected at 12 (±1) month follow up?" = "Yes"* **[F19_PATIENT_DISPOSITION, 12 month f-up.PD_1]**

Criterion 15: Follow-up performed 12+/- 1 month from enrollment

- *(Date of follow up visit (dd/mmm/yyyy)* **[F19_PATIENT_DISPOSITION, 12 month f-up.PD_2]***– Date of enrolment visit (dd/mm/yyyy)* **[_PatientInfo. Date_enrollment]***/30.4375 ≥ 11) AND*
- *(Date of follow up visit (dd/mmm/yyyy)* **[F19_PATIENT_DISPOSITION, 12 month f-up.PD_2]** *– Date of enrolment visit (dd/mm/yyyy)* **[_PatientInfo. Date_enrollment]** */30.4375 ≤ 13)*

The Biostatistician will evaluate the opportunity to apply a tolerance window during the analysis of data; the Sponsor will be informed of any possible changes in this range.

Criterion 16: patients with at least one Treatment Satisfaction Questionnaire for Medication (TSQM-9) domain score calculated at 12-month follow-up visit

- *TSQM-9 items #1,2,3 [**TSQM9_1-3**] not missing & ≠ "Non risponde" at 12-month follow-up, OR*
- *TSQM-9 items #4,5,6 [**TSQM9_4-6**] not missing & ≠ "Non risponde" at 12-month follow-up, OR*
- *TSQM-9 items #7,8,9 [**TSQM9_7-9**] not missing & ≠ "Non risponde" at 12-month follow-up*

Three sets of patients have been identified for the evaluation of SAT study objectives.
Chart 1 displays the analysis sets considered for the statistical analyses foreseen in the Study Protocol.

Chart 1: Sets of patients considered for each statistical analysis

	Patients evaluable at enrollment (FAS)	**Patients evaluable at enrollment and at 6 month follow-up**	**Patients evaluable at enrollment and at 12 month follow-up**
Enrolled and evaluable patients	X	X	X
Main socio-demographics and life habits (age, gender, race, education, employment status) at enrollment	X		
Medical history for COPD (number of exacerbations in the 12 months prior to enrollment)	X		
Patients' satisfaction to COPD medical treatments (by means of the TSQM9) at each study visit	X*	X*	X*
Patient disease perception (by means of illness perception questionnaire B-IPQ) at each study visit	X*	X*	X*
Patient adherence to COPD treatment (by means of MMAS4) at each study visit	X*	X*	X*
Patient health status (by means of CAT questionnaire) at each study visit	X*	X*	X*
Measurement of dyspnea (by means of mMRC) at each study visit	X*	X*	X*
Patient's COPD awareness (COPD awareness questionnaire) at each study visit	X*	X*	X*
Relation between treatment satisfaction and demographic (such as age, gender), clinical (such as number of exacerbations, spirometric parameters) parameters and PROs during a 12-month observation period			X
Description of health care resources utilization and related cost according to the Italian National Health Service (INHS) during a 12-month observation period.	X		
To assess the correlation between patients' satisfaction and resource utilization during a 12-month observation period			X
Ongoing pharmacological and non-pharmacological treatments for COPD	X		
Exacerbations occurred during observation period	X		

*Patients having PRO score computable at the visit will be considered for this analysis (i.e. PRO filled in at the visit and having a sufficient number of items recorded to allow score computation (PROs computation details are reported in Section 3. "Computed Variables")).

2.4 Safety set

All enrolled patients meeting the inclusion criteria #4 and #5 and not meeting the exclusion criteria #7, #8 and #9 (i.e. all enrolled subjects who provided informed consent to both participation in the study and privacy form, requiring regular treatment according to GOLD guidelines) will be included in the safety analysis.

3 COMPUTED VARIABLES

The following variables will be computed as described below.

BMI Classes
Underweight: BMI **[F05_PHYSICAL_EXAMINATION.PE_BMI]** < 18.5, normal weight: BMI 18.5-24.9, overweight: BMI 25-29.9, obese: BMI >= 30.

Age at COPD diagnosis
Is calculated as the difference between age at enrollment visit (years) **[_PatientInfo.Age]**and the difference between the date of enrollment **[_PatientInfo.Date_enrollment]** and the date of COPD diagnosis**[F04_COPD_MEDICAL_HISTORY.MH_Date_diagnosis]**/365.25 .

Smoking duration at enrolment (years)

- For patient who are current smokers by the time of enrolment ([**F03_LIFE_HABITS.RF_smoking**] = "Current smoker"):
  Smoking duration at enrolment = YEAR(Date of enrolment visit [**_PatientInfo.Date_enrollment**]) – Start year [***F03_LIFE_HABITS.RF_start_year_Num***], if Start year and Date of enrolment visit are not missing.
- For patient who are former smokers by the time of enrolment ([**F03_LIFE_HABITS.RF_smoking**] = "Former smoker"):
  Smoking duration at enrolment = Stop year [**F03_LIFE_HABITS.RF_stop_year_Num**] – Start year [**F03_LIFE_HABITS.RF_Start_year_Num**], if Stop year and Start year are not missing.

COPD duration (years)
Is calculated as the difference between the date of enrollment **[_PatientInfo.Date_enrollment]** and the date of COPD diagnosis**[F04_COPD_MEDICAL_HISTORY.MH_Date_diagnosis]**/365.25 .

COPD severity
In patients with FEV1/FVC at a certain visit [***F07_FUNCTIONAL_ASSESSMENT. FA_FEV1_FVC***] < 70%, the patient's COPD severity will be assessed according to the FEV1 of the predicted (%) value reported at each visit [***F07_FUNCTIONAL_ASSESSMENT. FA_FEV1_predicted***].
In particular, patients will be classified in the following ordinal groups:

- GOLD 1 (Mild): FEV1 of the predicted (%) ≥ 80%;
- GOLD 2 (Moderate): 50% ≤ FEV1 of the predicted (%) < 80%;
- GOLD 3 (Severe): 30% ≤ FEV1 of the predicted (%) < 50%;
- GOLD 4 (Very Severe): FEV1 of the predicted (%) < 30%.

Source: GLOBAL STRATEGY FOR THE DIAGNOSIS, MANAGEMENT, AND PREVENTION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE - UPDATED 2015.

COPD awareness questionnaire composite scores (from the COPD awareness structured interview)

The questionnaire is designed to measure patient's COPD awareness assessing the patient's knowledge of the disease, acceptance of the disease, perception of the disease and symptoms, and awareness of the patient's need to be treated.

Each COPD awareness questionnaire's item can be answered by means of a 4-point categorical scale (ranging from "I definitely do not agree" to "I totally agree"). However, the answer options are ordinal and, since they represent different grades of agreement, these answer options can be converted in a 4-point scale ranging from 0 to 3, as described in Appendix 8.1.

The COPD awareness questionnaire composite scores will be computed (according to the algorithm validated in the SAT substudy) starting from the scores given to non-missing items [**F12_AWARENESS. AWARENESS_01 – AWARENESS_27**], after having assigned the appropriate weight to each item, as described in Appendix 8.1. In particular, the following composite scores can be computed:

- 'Acknowledgement of disease' domain score (ranging from 0 to 15) is computed as the sum of the items #7, #15, #22, #24, and #25, when all of them are not missing;
- 'Awareness of treatment needs' domain score (ranging form 0 to 18) is computed as the sum of the items #4, #9, #12, #14, #18, and #23, when all of them are not missing;
- 'Knowledge of disease' domain score (ranging form 0 to 12) is computed as the sum of the items #1, #2, #19, and #26, when all of them are not missing;
- 'Disease perception' domain score (ranging form 0 to 15) is computed as the sum of the items #5, #8, #10, #20, and #21, when all of them are not missing;
- COPD awareness questionnaire total score (ranging form 0 to 60) is computed as the sum of all above-listed items, when all of them are not missing

Higher score reflect a patient's higher grade of awareness regarding his/her COPD in the respective investigated domain, and vice versa.

Changes in the COPD awareness questionnaire composite scores at each follow-up visit from enrollment will be calculated, for each patient, as the following difference: (composite score at 6/12 months - composite score at enrollment), if both scores are available.

CAT score

The COPD Assessment Test (CAT) is an 8-item unidimensional measure of health status impairment in COPD (*P.W. Jones, G. Harding, P. Berry, I. Wiklund, W-H. Chen and N. Kline Leidy Development and first validation of the COPD Assessment Test. Eur Respir J 2009; 34: 648–654*). It is designed to measure the impact of COPD on a person's life, and how this changes over time. It contains eight short, simple, patient-completed questions. Patients can choose a score from 0 to 5 for the extent to which the described impairment is true for them, thereby providing a measure of the impact of COPD on their individual health.

The score ranges from 0 to 40; higher scores represent worse health.

The following categories can be identified on the basis of the CAT total score: < 10 ; 10 - 20 ; 21 - 30 ; > 30.

The CAT score will be calculated as the sum of the responded items [**F16_CAT.CAT_ITEM_1 - CAT_ITEM_8**].

If more than two responses are missing, the score cannot be calculated; when one or two items are missing, their scores can be estimated by calculating the average of the non-missing item scores.

Changes in the CAT score at each follow-up visit from enrollment will be calculated, for each patient, as the following difference: (score at 6/12 months - score at enrollment), if both scores are available.

B-IPQ total score

The Brief Illness Perception Questionnaire (B-IPQ) is a validated 9-item questionnaire designed to rapidly assess cognitive and emotional representations of illness (*Broadbent E et al. "The Brief Illness Perception Questionnaire". Journal of Psychosomatic Research. 2006; 60: 631– 637*). All of the questionnaire items (except the causal question, item 9) are rated using a 0-to-10 response scale. Five of the items assess cognitive illness representations: consequences (Item 1), timeline (Item 2), personal control (Item 3), treatment control (Item 4), and identity (Item 5).

Two of the items assess emotional representations: concern (Item 6) and emotions (Item 8). One item assesses illness comprehensibility (Item 7). Assessment of the causal representation is by an opened response item, which asks patients to list the three most important causal factors in their illness (Item 9).
The B-IPQ total score will be computed as follows: the reversed scores of items 3, 4, and 7 [**F14_BIPQ.BIPQ_3, BIPQ_4, BIPQ_7**] will be added to the scores of items 1, 2, 5, 6, and 8 [**F14_BIPQ.BIPQ_1, BIPQ_2, BIPQ_5, BIPQ_6, BIPQ_8**]. A higher score reflects a more threatening view of the illness). The B-IPQ total score can be computed only if items #1-8 are filled in: only item 9 can be missing. Missing values will not be replaced.
Changes in the B-IPQ total score at each follow-up visit from enrollment will be calculated, for each patient, as the following difference: (score at 6/12 months - score at enrollment), if both scores are available.

TSQM-9 subscales scores

The Treatment Satisfaction Questionnaire for Medication, 9 items (TSQM-9) was derived from the original version, and it has a total of 9 items with responses to nearly all items rated on a five-point or seven-point rating scale that provide scores on three scales: effectiveness (3 items), convenience (3 items) and global satisfaction (3 items). The TSQM-9 domain scores (effectiveness, convenience and global satisfaction) will be calculated as recommended by the instrument authors (*Atkinson MJ, Kumar R, Cappelleri JC, Hass SL: Hierarchical construct validity of the treatment satisfaction questionnaire for medication (TSQM version II) among outpatient pharmacy consumers. Value Health. 2005 Nov-Dec;8 Suppl 1:S9-S24*).
In particular, Here below is provided the algorithm to compute each domain score:

- Effectiveness = [(item1 + item2 + item3) – 3]/18*100 = [(**TSQM9_1**+**TSQM9_2**+**TSQM9_3**) – 3]/18*100
- Convenience = [(item4 + item5 + item6) – 3]/18*100 = [(**TSQM9_4**+**TSQM9_5**+**TSQM9_6**) - 3]/18*100
- Global satisfaction = [(item7 + item8 + item9) – 3]/14*100 = [(**TSQM9_7**+**TSQM9_8**+**TSQM9_9**) - 3]/14*100

Each domain score can be calculated only if all the three items considered in the calculation of that score are not missing. Missing values will not be replaced.
The TSQM-9 domain scores range from 0 to 100 with higher scores representing higher satisfaction on that domain.
Changes in the TSQM-9 subscale scores at each follow-up visit from enrollment will be calculated, for each patient, as the following difference: (subscales score at 6/12 months - subscale score at enrollment), if both scores are available.

MMAS-4 score

The Morisky medication Adherence Scale 4 items (MMAS-4) is a self-reported, medication-taking behavior scale and consists of four questions about the way patients might experience drug errors or omissions. Each item [**F13_MMAS_4.MMAS_4_1 – MMAS_4_4**] has a scoring scheme of "Yes" = 0 and "No" = 1. Items are summed to give a non-adherence score ranging from 0 to 4; a higher score means better adherence to therapy (Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. Med Care. 1986 Jan;24(1):67-74).
The score can be calculated if at least 3 out of 4 of the items are completed. If only one item is omitted, the value for the missing item is the group median of this item that has been completed by all eligible participants. This median value will be imputed for all eligible cases who did not answer this item.
Changes in the MMAS-4 score at each follow-up visit from enrollment will be calculated, for each patient, as the following difference: (score at 6/12 months - score at enrollment), if both scores are available.

COPD pharmacological treatments (classes) ongoing at enrollment

All COPD pharmacological treatments having "End date of therapy" **[F20_COPD_PHARMACOLOGICAL_THERAPY. END_DATE_THER]** > "Date of enrollment visit" **[_PatientInfo.Date_enrollment]**) OR ("End date of therapy" missing and "Ongoing at the end of observation?" **[F20_COPD_PHARMACOLOGICAL_THERAPY. ONGOING_THER]** = "Yes").
Drug names will be coded by CDM and grouped according to the following categories:

- LAMA alone
- LABA alone

- ICS alone
- LABA + LAMA (Fixed dose combination or not)
- LABA + ICS (Fixed dose combination or not)
- LABA + LAMA + ICS
- SABA or SAMA on demand
- Other: pharmacological therapies for COPD not included in the previous classes.

Categories above are not mutally exclusive: a patient could be classified in more than one cathegory (i.e if a patient is receveing LAMA and SABA on demand, [redacted] will be classified both in the "LAMA alone" and in the "SABA or SAMA on demand" classes).
Only therapies for COPD will be considered (i.e. those records with field Therapy for **[F20_COPD PHARMACOLOGICAL THERAPY. THERAPY_FOR]** = "COPD"), while therapies for COPD exacerbations or for COPD-related adverse events will not be considered nor classified.

COPD pharmacological treatments (classes) ongoing at 6- and 12-month follow-up visit

At each follow-up visit, all COPD treatments classes (see algorithm above) having

- ("Start date of therapy" **[F20_COPD PHARMACOLOGICAL THERAPY. START_DATE_THER]** not missing AND < "Date of follow up visit" **[F19_PATIENT_DISPOSITION. PD_2]**) AND
- "End date of therapy" **[F20_COPD PHARMACOLOGICAL THERAPY. END_DATE_THER]** not missing AND > "Date of follow up visit" **[F19_PATIENT_DISPOSITION. PD_2]**) OR ("End date of therapy" missing AND "Ongoing at the end of observation?" **[F20_COPD PHARMACOLOGICAL THERAPY.ONGOING_THER]** = "Yes").

Drug names will be coded by CDM and grouped according to the categories specified above.
Only therapies for COPD will be considered (i.e. those records with field Therapy for **[F20_COPD PHARMACOLOGICAL THERAPY. THERAPY_FOR]** = "COPD"), while therapies for COPD exacerbations or for COPD-related adverse events will not be considered.

COPD pharmacological treatments: fixed and non-fixed therapy

Patients with fixed COPD pharmacological treatments are those having at least one record of the COPD PHARMACOLOGICAL THERAPY form with "Is it a fixed dose combination?" **[F20_COPD PHARMACOLOGICAL THERAPY.DOSE_2]** = "Yes" for therapies ongoing at enrollment (see above).
Patients with non-fixed COPD pharmacological treatments are those having at least one record of the COPD PHARMACOLOGICAL THERAPY form with "Is it a fixed dose combination?" **[F20_COPD PHARMACOLOGICAL THERAPY.DOSE_2]** = "No" for therapies ongoing at enrollment (see above).
Patients who satisfy both conditions will be defined as **patients receiving both COPD pharmacological fixed and non-fixed therapy** at enrollment.
Data manager will check the congruence between the field "Drug" **[F20_COPD PHARMACOLOGICAL THERAPY.DRUG]** and the question "Is it a fixed dose combination?": if any fixed dose drug will be entered in the field "Drug" and the question "Is it a fixed dose combination?" = "No" a query will be sent to the investigator. The vice-versa will be checked as well.
Only therapies for COPD will be considered, while therapies for COPD exacerbations or for COPD-related adverse events will not be considered.

COPD pharmacological treatments: patients switching and not switching treatments

Considering only COPD pharmacological treatments (i.e. those records with field "Therapy for" **[F20_COPD PHARMACOLOGICAL THERAPY. THERAPY_FOR]** = "COPD") ongoing at enrollment or started after enrollment (i.e. with "Ongoing at the end of observation?" **[F20_COPD PHARMACOLOGICAL THERAPY. ONGOING_THER]** = "Yes" OR with "Start date of therapy" **[F20_COPD PHARMACOLOGICAL THERAPY. START_DATE_THER]** > "Enrollment date"), patients who switched treatment during the observation period* will be those with more than one record with the above-mentioned characteristics in the COPD PHARMACOLOGICAL THERAPY log form, excluding therapies started the very same day according to Start date of therapy. In particular, patients switching treatment are those with at least one change in the drug/frequency/route/formulation/device of administration after enrollment (also adding / stopping a COPD treatment is a switch).

*switches occurred before enrollment will not be considered.

Number of therapies administered for COPD, COPD-related adverse events and COPD exacerbations

The **number of therapies administered for COPD per patient during observation period** will be calculated as the sum of records of the COPD PHARMACOLOGICAL THERAPY log form considering only pharmacological treatments for COPD (i.e. those records with field "Therapy for" **[F20_COPD PHARMACOLOGICAL THERAPY. THERAPY_FOR]** = "COPD") ongoing at enrollment or started after enrollment (i.e. with "Ongoing at the end of observation?" **[F20_COPD PHARMACOLOGICAL THERAPY. ONGOING_THER]** = "Yes" OR with "Start date of therapy" **[F20_COPD PHARMACOLOGICAL THERAPY. START_DATE_THER]** > "Enrollment date").

Similarly, the **number of therapies administered for COPD-related adverse events and COPD exacerbations per patient during observation period** will be calculated as the sum of records of the COPD PHARMACOLOGICAL THERAPY log form considering only pharmacological treatments for COPD-related adverse events and COPD exacerbations (i.e. those records with field "Therapy for" **[F20_COPD PHARMACOLOGICAL THERAPY. THERAPY_FOR]** = "COPD-related adverse event" OR "COPD exacerbation") ongoing at enrollment or started after enrollment (i.e. with "Ongoing at the end of observation?" **[F20_COPD PHARMACOLOGICAL THERAPY. ONGOING_THER]** = "Yes" OR with "Start date of therapy" **[F20_COPD PHARMACOLOGICAL THERAPY. START_DATE_THER]** > "Enrollment date").

Exacerbations during the observation period

Exacerbation is defined as "an increase or new onset of more than 1 symptom (cough, sputum, wheezing, dyspnoea or chest tightness) with at least 1 symptom lasting at least 3 days and leading to patient's attending physician to initiate treatment with systemic steroids and/or antibiotics (moderate exacerbation) or hospital admission (severe exacerbation)".

Patients with at least one exacerbation during observation period are those with "Did any exacerbation occur since the previous visit?" **[F08_EXACERBATIONS.EX_Exacerbation_YN]** = "Yes", considering the 6- and 12-month follow-up visits and the End of observation visit.

The **total number of exacerbations occurred during observation period per patient** will be computed as the sum of the number of the matrix rows filled in the following fields: **[F08_EXACERBATIONS.Ex_exacer_1-10_Ons_date]**, considering the 6- and 12-month follow-up visits and the End of observation visit.

Hospitalizations for COPD, COPD exacerbations or COPD related adverse events during observation period

The **total number of hospitalizations not in ICU for each patient** will be the number of records in the matrix with "Patient admitted to intensive care unit?" **[F10_RESOURCE_CONS. RES_Hosp_matrix_1__ICU_YN - RES_Hosp_matrix_10__ICU_YN]** = "No", considering the visit form HEALTHCARE RESOURCE CONSUMPTION at the 6- and 12-month follow-up visits and the End of observation visit.

The **total number of hospitalizations in ICU for each patient** will be the number of records in the matrix with "Patient admitted to intensive care unit?" **[F10_RESOURCE_CONS. RES_Hosp_matrix_1__ICU_YN - RES_Hosp_matrix_10__ICU_YN]** = "Yes", considering the visit form HEALTHCARE RESOURCE CONSUMPTION at the 6- and 12-month follow-up visits and the End of observation visit.

The **total number of days of hospitalization not in ICU for each patient** will be the sum of the fields "Overall duration of admission (days)" **[F10_RESOURCE_CONS. RES_Hosp_matrix_1__Adm - RES_Hosp_matrix_10__Adm]**, considering only the records referred to hospitalizations not in ICU (see above) at the 6- and 12-month follow-up visits and the End of observation visit.

The **total number of days of hospitalization in ICU for each patient** will be the sum of the fields "Overall duration of admission (days)" **[F10_RESOURCE_CONS. RES_Hosp_matrix_1__Adm - RES_Hosp_matrix_10__Adm]**, considering only the records referred to hospitalizations in ICU (see above) at the 6- and 12-month follow-up visits and the End of observation visit.

ER accesses for COPD, COPD exacerbations or COPD related adverse events during observation period

The **total number of ER accesses for each patient** will be the sum of the fields "N° ER accesses" **[F10_RESOURCE_CONS. RES_ER_matrix_1__n_acc - RES_ER_matrix_12__n_acc]** considering the 6- and 12-month follow-up visits and the End of observation visit.

Specialist outpatient visits for COPD, COPD exacerbations or COPD related adverse events during observation period

Patients with at least one specialist outpatient visit will be those with "Did the patient have any specialist outpatient visit for COPD, COPD exacerbations or COPD-related adverse events since the previous visit?" **[F10_RESOURCE_CONS. RES_OUTP_YN]** = "Yes" at 6-month follow-up visit OR at 12-month follow-up visits OR at End of observation visit.

The **total number of specialist outpatient visits per patient during observation period** will be computed as the sum of the field "Nr Visits" **[F10_RESOURCE_CONS. RES_Nr_Visits]**, considering the 6- and 12-month follow-up visits and the End of observation visit.

General practitioner visits for COPD, COPD exacerbations or COPD related adverse events during observation period

The **total number of general practitioner visits per patient during observation period** will be computed as the sum of the field "N° of office visits (…)" **[F10_RESOURCE_CONS. RES_GP_Visit_YN_Num]**, considering the 6- and 12-month follow-up visits and the End of observation visit.

Laboratory test for COPD, COPD exacerbations or COPD related adverse events during observation period

The **total number of laboratory test per patient during observation period** will be computed as the sum of the fields "N° of tests" [**F10_RESOURCE_CONS. RES_Lab_matrix_1_num - RES_Lab_matrix_20_num**] for each row of the matrix LABORATORY TESTS/EXAMINATIONS, considering the 6- and 12-month follow-up visits and the End of observation visit.

Patients with oxygen therapy during the observational period

They will be defined as patients with at least one record in the OXYGEN THERAPY log form with ("Start date of therapy" [**F21_OXYGEN_THERAPY. SART_DATE_NF**] >= "Date of enrollment visit" **[_PatientInfo.Date_enrollment]** OR "Ongoing at the end of observation?" [**F21_OXYGEN_THERAPY ONGOING_NF_THER**] = "Yes").

Patients with adverse events, serious adverse events, and adverse drug reactions

Patients with at least one adverse event (AE) will be those with at least one record in the AEs and ADRs log form with "AE brief description (in English)" [**F22_AES_AND_ADRS. AE_DSCRPT**] not missing.

Patients with at least one serious adverse event (SAE) will be those with at least one record in the AEs and ADRs log form with "AE brief description (in English)" not missing AND "Is it a serious AE?" [**F22_AES_AND_ADRS. AE_1**] = "Yes".

Patients with at least one adverse drug reaction (ADR) to one of the products marketed by Boheringer Ingelheim (namely: Spiriva Handihaler, Spiriva Respimat, Striverdi Respimat, Spiolto Respimat, Oxivent, Dosberotec, Duovent) will be those with at least one record in the AEs and ADRs log form with "AE brief description (in English)" not missing AND "Is there a reasonable causal relationship with one of the products marketed by Boheringer Ingelheim*?" [**F22_AES_AND_ADRS. AE_2**] ="Yes".

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The analyses will be performed on the Analysis set specified for each table.
Missing data will not be imputed and so patients with missing data will be excluded from the analyses of that variable(s).
If the investigator is unable to collect the requested information the data will be "NK" (Not Known) or "NA" (Not Available), if the investigator did not record the information the data will be "Not Recorded".

4.1 Patient disposition

Table 1. Enrolled and evaluable patients
The table will provide absolute and relative frequencies of:

- patients enrolled in the SAT study
- patients evaluable for safety analysis (Safety set) (as described in par. 2.4)
- patients evaluable at enrollment (Full analysis set) (as described in par. 2.1)
- patients evaluable at enrollment and at 6 month follow-up visit (as described in par. 2.2)
- patients evaluable at enrollment and at 12 month follow-up visit (as described in par. 2.3)

The percentages will be computed over the total number of enrolled patients.

Table 2. Reasons for non-eligibility to analyses
The table will describe the reasons for patient non-eligibility.
Absolute and relative frequency distribution will be performed; the percentages will be computed out of the total number of enrolled patients.

Table 3. Premature study termination
The table will describe the distribution of patients withdrawn from the study ("Did the patient complete the study?" **[F18_STUDY_COMPLETION.SC_1]** = "No"); moreover, absolute and relative frequency of reasons for premature study termination ("Cause of drop out" **[F18_STUDY_COMPLETION.SC_2]**) will be provided.
Percentages will be computed out of the total number of enrolled patients.
The distribution of patients withdrawn for other reasons will be also reported in a separate table ("If other cause, specify:" ≠ missing **[F18_STUDY_COMPLETION.SC_3]**), if other reason frequency is >20%.

4.2 Demographics and baseline characteristics

Table 4. Socio-demographic characteristics at enrollment
The table will provide:

- Main descriptive statistics (mean, median, standard deviation, quartiles, min, max) of patients' Age at enrollment (**[_PatientInfo.Age]**)
- Patient distribution by Gender (**[_PatientInfo.Gender]**)
- Patient distribution by Race (**[F02_SOCIO_DEMOGRAPHICS.SD_Race]**)
- Patient distribution by Highest education level at baseline (**[F02_SOCIO_DEMOGRAPHICS. SD_Education]**)
- Patient distribution by Employment status at baseline (**[F02_SOCIO_DEMOGRAPHICS. SD_Employment]**)
- Patient distribution by Housing situation at baseline (**[F02_SOCIO_DEMOGRAPHICS.SD_Housing]**)
- Patient distribution by Marital status at baseline (**[F02_SOCIO_DEMOGRAPHICS. SD_Marital_status]**)

Statistics will be computed out of the total number of FAS patients.

Table 5. Smoke habilts at enrollment
The table will provide:

- Patient distribution by Smoking status (**[F03_LIFE_HABITS.RF_Smoking]**)
- Patient distribution by Kind of tobacco (**[F03_LIFE_HABITS.RF_Kind_Tobacco]**)
- Main descriptive statistics (mean, median, standard deviation, quartiles, min, max) of the Estimated amount of tobacco consumed on average (pack/year) (**[F03_LIFE_HABITS.RF_Estimated_amount_Num]**)
- Main descriptive statistics (mean, median, standard deviation, quartiles, min, max) of Smoking duration in years (see 'Computed variables' chapter).

Percentages of smoking status will be computed out of the total number of FAS patients; for Kind of tobacco, Estimated amount of tobacco consumed on average, and Smoking duration, statistics will be computed over the total number of current / former smokers in the FAS.

Table 6. COPD medical history at enrollment
The table will provide:

- Main descriptive statistics (mean, median, standard deviation, quartiles, min, max) of COPD duration at enrollment in years (see 'Computed variables' chapter)
- Main descriptive statistics (mean, median, standard deviation, quartiles, min, max) of age at COPD diagnosis (see 'Computed variables' chapter)
- Frequency distribution of Number of exacerbations in the last year at enrollment (in classes) (**[F04_COPD_MEDICAL_HISTORY.MH_nr_exacerbations_num]**)
- Main descriptive statistics (mean, median, standard deviation, quartiles, min, max) of Number of exacerbations in the last year at enrollment (**[F04_COPD_MEDICAL_HISTORY.MH_nr_exacerbations_num]**)

Descriptives will be computed out of the total number of FAS patients.

Table 7. Comorbidities at enrollment
The table will provide the patient distribution by ongoing Comorbidity(ies) at enrollment (
(**[F06_COMORBIDITIES.COM_Comorbidities]**). A patient could have more than one comorbidity.
Moreover, the patient distribution by Other comorbidities* will be provided.
Percentages will be computed out of the total number of FAS patients .

Table 8. Vital signs at enrollment
The table will provide:

- Main descriptive statistics (mean, median,standard deviation, quartiles, min, max) of patients' Weight at enrollment **[F05_PHYSICAL_EXAMINATION.PE_Weight_Num]**
- Main descriptive statistics (mean, median,standard deviation, quartiles, min, max) of patients' Height at enrollment **[F05_PHYSICAL_EXAMINATION.PE_Height_Num]**
- Patient distribution by BMI classes (see 'Computed variables' chapter)
- Main descriptive statistics (mean, median, standard deviation, quartiles, min, max) of BMI at enrollment **[F05_PHYSICAL_EXAMINATION. PE_BMI]**

Descriptives will be computed out of the total number of FAS patients.

Table 9. Respiratory Functions at enrollment

The table will provide:

- Main descriptive statistics (mean, median,standard deviation, quartiles, min, max) of patients' values of FEV1 (L) at enrollment **[F07_FUNCTIONAL_ASSESSMENT.FA_FEV1]**
- Main descriptive statistics (mean, median,standard deviation, quartiles, min, max) of patients' values of FEV1 of the predicted (%) at enrollment **[F07_FUNCTIONAL_ASSESSMENT.FA_FEV1_predicted]**
- Main descriptive statistics (mean, median,standard deviation, quartiles, min, max) of patients' values of FVC (L) at enrollment **[F07_FUNCTIONAL_ASSESSMENT. FA_FVC]**
- Main descriptive statistics (mean, median,standard deviation, quartiles, min, max) of patients' values of FEV1/FVC (%) at enrollment **[F07_FUNCTIONAL_ASSESSMENT.FA_FEV1_FVC]**
- Main descriptive statistics (mean, median,standard deviation, quartiles, min, max) of patients' values of Residual Volume (L) at enrollment (**F07_FUNCTIONAL_ASSESSMENT.FA_RV_Num**)
- Main descriptive statistics (mean, median,standard deviation, quartiles, min, max) of patients' values of Inspiratory capacity (L) at enrollment **[F07_FUNCTIONAL_ASSESSMENT.FA_VCIN_Num]**
- Main descriptive statistics (mean, median,standard deviation, quartiles, min, max) of patients' values of Total lung capacity (L) at enrollment **[F07_FUNCTIONAL_ASSESSMENT.FA_TLC_Num]**
- Main descriptive statistics (mean, median,standard deviation, quartiles, min, max) of patients' values of DLCO at enrollment **[F07_FUNCTIONAL_ASSESSMENT.FA_DLCO_Num]**, along with the respective DLCO unit **[F07_FUNCTIONAL_ASSESSMENT.FA_DLCO_unit]**.

Descriptives will be computed out of the total number of FAS patients.

During data analysis, the Biostatistician will evaluate to perform the analyses described above also considering the evaluable patients at 6 months and/or at 12 months, depending on the number of patients of these analysis sets (in case the number of patients for these two analysis sets is relevantly different from the number of FAS patients), in order to understand if a selection bias is present.

4.3 Patients' satisfaction for medical treatment (TSQM-9) (primary objective)

Table 10. Patients' satisfaction for medical treatment (TSQM-9 items) at each study visit
The table will provide absolute and relative frequency of patients' answers to TSQM-9 items (see Appendix 8.3) at each study visit.
Percentages will be calculated over the number of patients respectively evaluable at the time point considered, namely at enrollment (i.e. FAS patients), at 6 months (i.e. evaluable patients at 6 months) and at 12 months (i.e. evaluable patients at 12 months) .

Table 11. Patients' satisfaction for medical treatment (TSQM-9 subscales) at each study visit
The table will provide the descriptive statistics (mean, median, standard deviation, quartiles, min, max) of the TSQM-9 subscales scores (as defined in "Computed variables" chapter) at each study visit.
Changes from enrollment in TSQM-9 subscales scores (see 'Computed variables' chapter) will be also summarized by visit.
95% confidence intervals limits of the mean will be provided for each estimate (i.e. TSQM-9 subscales scores and changes).
Descriptives will be calculated over the number of patients respectively evaluable at the time point considered, namely at enrollment (i.e. FAS patients), at 6 months (i.e. evaluable patients at 6 months) and at 12 months (i.e. evaluable patients at 12 months)

4.4 Patients' disease perception (B-IPQ) (secondary objective #1)

Table 12. Patients' disease perception (B-IPQ) at each study visit
The table will provide the descriptive statistics (mean, median, standard deviation, quartiles, min, max) of B-IPQ questionnaire total score (as defined in "Computed variables" chapter) at each study visit.
Changes from enrollment in B-IPQ total score (see 'Computed variables' chapter) will be also summarized by visit.
95% confidence intervals limits of the mean will be provided for each estimate.
Descriptives will be calculated over the number of patients respectively evaluable at the time point considered, namely at enrollment (i.e. FAS patients), at 6 months (i.e. evaluable patients at 6 months) and at 12 months (i.e. evaluable patients at 12 months).

4.5 Patients' adherence to COPD treatment (MMAS-4) (secondary objective #1)

Table 13. Patients' adherence to COPD treatment (MMAS-4) at each study visit
The table will provide patient distribution by MMAS-4 answers to items #1-4 (Yes/No) at each study visit.
95% confidence intervals limits will be provided for each proportion.Moreover descriptive statistics (mean, median, standard deviation, quartiles, min, max) of MMAS-4 questionnaire total score (as defined in "Computed variables" chapter) at each study visit.
Changes from enrollment in MMAS-4 total score (see 'Computed variables' chapter) will be also summarized by visit.
Descriptives will be calculated over the number of patients respectively evaluable at the time point considered, namely at enrollment (i.e. FAS patients), at 6 months (i.e. evaluable patients at 6 months) and at 12 months (i.e. evaluable patients at 12 months).
(Missing values will be replaced according scoring algorithm as defined in "Computed variables" chapter, maximum one missing value is accepted).

4.6 Patients' health status (CAT) (secondary objective #1)

Table 14. Patients' health status (CAT) at each study visit
The table will provide patient distribution by CAT questionnaire total score (as defined in "Computed variables" chapter, considering the following categories: < 10 / 10 - 20 / 21 - 30 / > 30) at each study visit.

The table will also provide the descriptive statistics (mean, median, standard deviation, quartiles, min, max) of CAT questionnaire total score (as defined in "Computed variables" chapter) at each study visit. Changes from enrollment in CAT total score (see 'Computed variables' chapter) will be also summarized by visit. 95% confidence intervals limits of the mean will be provided for each estimate.
Descriptives will be calculated over the number of patients respectively evaluable at the time point considered, namely at enrollment (i.e. FAS patients), at 6 months (i.e. evaluable patients at 6 months) and at 12 months (i.e. evaluable patients at 12 months).
(Missing values will be replaced according scoring algorithm as defined in "Computed variables" chapter, maximum two missing values are accepted).

4.7 Patients' dyspnea (mMRC) (secondary objective #1)

Table 15. Patients' dyspnea (mMRC) at each study visit
Absolute and relative frequency of the mMRC grade at each study visit **[F15_MMRC.MMRC]** (see Appendix 8.2); percentages will be calculated over the number of patients respectively evaluable at the time point considered, namely at enrollment (i.e. FAS patients), at 6 months (i.e. evaluable patients at 6 months) and at 12 months (i.e. evaluable patients at 12 months).
95% confidence intervals limits will be provided for each proportion.

4.8 Patients' COPD awareness

Table 16. Patients' COPD awareness (Awareness structured interview) each study visit
The table will provide:

- absolute and relative frequencies of patients' answers to each the COPD awareness questionnaire item **[*F12_AWARENESS. AWARENESS_01 – AWARENESS_27*]** at each study visit;
- the descriptive statistics (mean, median, standard deviation, quartiles, min, max) of the COPD awareness questionnaire composite scores (see 'Computed variables' chapter) at each study visit.

Changes from enrollment in the COPD awareness composite scores (see 'Computed variables' chapter) will be also summarized by visit.
95% confidence intervals limits of the mean will be provided for each estimate.
Descriptives will be calculated over the number of patients respectively evaluable at the time point considered, namely at enrollment (i.e. FAS patients), at 6 months (i.e. evaluable patients at 6 months) and at 12 months (i.e. evaluable patients at 12 months).

4.9 Relation between treatment satisfaction and demographic/clinical parameters and PROs during 12 month observation period (secondary objective #2)

The purpose of this secondary analysis is not to obtain a predictive model, but to investigate the relationship among pre-defined variables and outcomes that are of clinical interest. In fact, the intent of this analysis is mainly exploratory and not confirmatory of any a priori hypotheses (consistently with the Study Protocol indications).

Among independent variables in the model, the PROs used in the study are symptomatic tools routinely used in clinical practice to evaluated disease activity and severity (i.e. mMRC and CAT) as per the patient's perspective. Patients' treatment satisfaction could also depend on their clinical status (that would be measured through the mMRC or the CAT) and on their adherence to treatment (MMAS-4 score). This is the reason why the PROs measures are taken into account in exploring the relationship between patient's treatment satisfaction and clinical status.
Contrary to what is stated in paragraph 9.7 of the Study Protocol, the Sponsor on the 12/09/2017 decided not to include the covariates post-baseline in this analysis: therefore, only data collected at enrollment visit will be considered in the mixed models for repeated measures described below, with the exception of the dependent variables (i.e.TSQM-9 scores, that will be considered at each timepoint).

Table 17. Relation between treatment satisfaction and demographic/clinical parameters and PROs during 12 month observation period (Repeated measures regression models) – Effectiveness domain
A regression model will be estimated; the dependent variable will be the effectiveness domain score of TSQM-9 and the independent ones will be the following:

- age and gender at enrollment;
- number of exacerbations at enrollment;
- relevant spirometry parameters at enrollment (a selection of the following parameter will be done, based on data availability: FEV1, FVC, FEV1 % of the predicted, RV, TLC, DLCO);
- patient's disease severity in terms of level of dyspnea (mMRC score) or CAT total score (depending on data availability) at enrollment (since they are expected to be intercorrelated measures, as reported by 2017 GOLD guidelines, only one of such measures will be considered in the model);
- MMAS-4 score at enrollment.

Center will be included as random effect and study visit (visit1/enrollment, visit2/6months, and visit3/12months) as timepoint.
During data elaboration, the Biostatistician will assess the intercorrelation between the proposed variables, in order to evaluate the opportunity to exclude some of the listed independent variables that are highly associated to each other; in case of important lack of data for certain parameters, such parameters may be excluded as well from the final model.
Because measures referred to the dependent variable will be collected at each study visit, a mixed model for repeated measures will be estimated; moreover, interaction terms between independent variables will be evaluated and, if not significant, they will not be included in the final model. The optimal covariance structure will be evaluated during analysis (preferably "first-order autoregressive correlation" or "unstructured" options). A stepwise selection method will be evaluated during the analysis in order to identify the variables to be included in the final model.
The patients switching treatment during observation period will not be excluded from analysis. The patients stopping treatment during study will be censored at last available visit.
The analysis will be performed considering only evaluable patients at 12 months.

Table 18. Relation between treatment satisfaction and demographic/clinical parameters and PROs during 12 month observation period (Repeated measures regression models) – Convenience domain
See previous model characteristics: in this analysis, the dependent variable will be the convenience domain score of TSQM-9.

Table 19. Relation between treatment satisfaction and demographic/clinical parameters and PROs during 12 month observation period (Repeated measures regression models) – Global satisfaction domain
See previous model characteristics: in this analysis, the dependent variable will be the global satisfaction domain score of TSQM-9.

4.10 Healthcare resource utilization (secondary objective #3)

Table 20. Hospitalizations not in ICU during observation period: patients' distribution
The table will provide:

- distribution of patients by number of hospitalization not in ICU per patient during observation period (see 'Computed variables' chapter);
- descriptive statistics (mean, median, standard deviation, quartiles, min, max) of number of hospitalization not in ICU during observation period per patient (see 'Computed variables' chapter);
- distribution of patients by "Type of admission" (**[F10_RESOURCE_CONS. RES_Hosp_matrix_1__Inw - RES_Hosp_matrix_10__Inw]**), considering only hospitalization not in ICU according to the field **[RES_Hosp_matrix_x__ICU_YN]**;
- descriptive statistics (mean, median, standard deviation, quartiles, min, max) of total number of days of hospitalization not in ICU per patient (see 'Computed variables' chapter);
- distribution of patients by reasons for hospitalization not in ICU (i.e. "Hospitalization for" **[F10_RESOURCE_CONS. RES_Hosp_matrix_1__hos_for - RES_Hosp_matrix_10__hos_for]**).

Descriptives and percentages will be computed out of the total number of FAS patients.

Table 21. Hospitalizations not in ICU during observation period: details
The table will provide:

- distribution of hospitalizations not in ICU by "Type of admission" (**[F10_RESOURCE_CONS. RES_Hosp_matrix_1__Inw - RES_Hosp_matrix_10__Inw]**), considering only hospitalization not in ICU according to the field **[RES_Hosp_matrix_x__ICU_YN]**;
- distribution of hospitalizations not in ICU by reasons for hospitalization (i.e. "Hospitalization for" **[F10_RESOURCE_CONS. RES_Hosp_matrix_1__hos_for - RES_Hosp_matrix_10__hos_for]**).

Statistics will be computed out of the total number of hospitalizations not in ICU during observation period in FAS patients.

Table 22. Hospitalizations in ICU during observation period: patients' distribution
The table will provide:

- distribution of patients by number of hospitalization in ICU during observation period (see 'Computed variables' chapter);
- descriptive statistics (mean, median, standard deviation, quartiles, min, max) of number of hospitalization in ICU during observation period per patient (see 'Computed variables' chapter);
- distribution of patients by "Type of admission" (**[F10_RESOURCE_CONS. RES_Hosp_matrix_1__Inw - RES_Hosp_matrix_10__Inw]**), considering only hospitalization in ICU according to the field **[RES_Hosp_matrix_x__ICU_YN]**;
- descriptive statistics (mean, median, standard deviation, quartiles, min, max) of total number of days of hospitalization in ICU (see 'Computed variables' chapter);
- distribution of patients by reasons for hospitalization in ICU (i.e. "Hospitalization for" **[F10_RESOURCE_CONS. RES_Hosp_matrix_1__hos_for - RES_Hosp_matrix_10__hos_for]**).

Descriptives and percentages will be computed out of the total number of FAS patients.

Table 23. Hospitalizations in ICU during observation period: details
The table will provide:

- distribution of hospitalizations in ICU by "Type of admission" (**[F10_RESOURCE_CONS. RES_Hosp_matrix_1__Inw - RES_Hosp_matrix_10__Inw]**), considering only hospitalization in ICU according to the field **[RES_Hosp_matrix_x__ICU_YN]**;
- distribution of hospitalizations in ICU by reasons for hospitalization (i.e. "Hospitalization for" **[F10_RESOURCE_CONS. RES_Hosp_matrix_1__hos_for - RES_Hosp_matrix_10__hos_for]**).

Statistics will be computed out of the total number of hospitalizations in ICU during observation period in FAS patients.

Table 24. Emergency room accesses: patients' distribution
The table will provide:

- distribution of patients by number of ER accesses during observation period per patient (see 'Computed variables' chapter);

- descriptive statistics (mean, median, standard deviation, quartiles, min, max) of number of ER accesses during observation period per patient (see 'Computed variables' chapter);
- distribution of patients by reasons of ER admission (i.e. "Admission for" [**F10_RESOURCE_CONS. RES_ER_matrix_1__adm_for - RES_ER_matrix_12__adm_for**]).

Descriptives and percentages will be computed out of the total number of FAS patients.

Table 25. Emergency room accesses: details

The table will provide:

- distribution of reasons of ER accesses during observation period (i.e. "Admission for" [**F10_RESOURCE_CONS. RES_ER_matrix_1__adm_for - RES_ER_matrix_12__adm_for**]).

Statistics computed over the total number of ER accesses during observation period in FAS patients.

Table 26. Specialist outpatient visits: patients' distribution

The table will provide:

- descriptive statistics (mean, median, standard deviation, quartiles, min, max) of the total number of specialist outpatient visits per patient during observation period (see 'Computed variables' chapter);
- distribution of patients by number of specialist outpatient visits per patient during observation period (see 'Computed variables' chapter);
- distribution of patients by type of specialist outpatient visits performed during observation period (i.e. "Specialist "[**F10_RESOURCE_CONS. Specialist**]);
- distribution of patients by reasons of specialist outpatient visit (i.e. "Visit for" [**F10_RESOURCE_CONS. RES_Visit_for**]).

Descriptives and percentages will be computed out of the total number of FAS patients.

Table 27. General practitioner visits: patients' distribution

The table will provide:

- distribution of patients by total number of general practitioner visits per patient during observation period (see 'Computed variables' chapter);
- descriptive statistics (mean, median, standard deviation, quartiles, min, max) of the total number of general practitioner visits per patient during observation period (see 'Computed variables' chapter).

Descriptives and percentages will be computed out of the total number of FAS patients.

Table 28. Laboratory tests: patients' distribution

The table will provide:

- distribution of patients by total number of laboratory test per patient during observation period (see 'Computed variables' chapter);
- descriptive statistics (mean, median, standard deviation, quartiles, min, max) of total number of laboratory test per patient during observation period (see 'Computed variables' chapter);
- distribution of patients by type of test/examination during observation period (i.e. "Test/examination" [**F10_RESOURCE_CONS. RES_Lab_matrix_1_Test - RES_Lab_matrix_20_Test**]);
- distribution of patients by reasons of test/examination (i.e. "Test/examination for" [**F10_RESOURCE_CONS. RES_Lab_matrix_1_for - RES_Lab_matrix_20_for**]).

Descriptives and percentages will be computed out of the total number of FAS patients.

Table 29. Laboratory tests: details

The table will provide:

- frequency of each type of test/examination during observation period (listed in field "Test/examination" [**F10_RESOURCE_CONS. RES_Lab_matrix_1_Test - RES_Lab_matrix_10_Test**] and according to the number of tests recorded in field "N° of tests" [**F10_RESOURCE_CONS. RES_Lab_matrix_1_num - RES_Lab_matrix_20_num**]),
- distribution of reasons of test/examination (i.e. "Test/examination for" [**F10_RESOURCE_CONS. RES_Lab_matrix_1_for - RES_Lab_matrix_20_for**]).

Statistics computed over the total number of Laboratory tests during observation period in FAS patients.

Table 30. Oxygen therapy
The table will provide:
- Absolute and relative frequency of Patients with oxygen therapy during the observational period (see 'Computed variables' chapter)

Percentages will be computed out of the total number of patients evaluable for the FAS.

Table 31. List of oxygen therapies
List of the following variables:
- Patient ID
- "Date of enrollment visit" **[_PatientInfo.Date_enrollment]**
- "Kind of therapy" **[F21_OXYGEN_THERAPY.KIND_OF_THER]**
- "Drug" **[F21_OXYGEN_THERAPY.DRUG]**
- "Flow (L/min)" **[F21_OXYGEN_THERAPY.FLOW]**
- "Hours per day" **[F21_OXYGEN_THERAPY.HOURS]**
- "Start date of therapy" **[F21_OXYGEN_THERAPY.START_DATE_NF]**
- "Ongoing" **[F21_OXYGEN_THERAPY.ONGOING_NF_THER]**
- "End date of therapy" **[F21_OXYGEN_THERAPY.END_DATE_NF]**
- "Therapy for" **[F21_OXYGEN_THERAPY.NF_THER_FOR]**

Only patients evaluable for the FAS will be considered.

Table 32. Patients receiving fixed/non-fixed dose therapies for COPD at enrollment
The table will provide:
- distribution of patients with COPD pharmacological fixed dose therapy at enrollment (see 'Computed variables' chapter);
- distribution of patients with COPD pharmacological non-fixed dose therapy at enrollment (see 'Computed variables' chapter);
- distribution of patients receiving both COPD pharmacological fixed and non-fixed therapy at enrollment (see 'Computed variables' chapter).

Percentages will be computed out of the total number of patients evaluable for the FAS.

Table 33. COPD pharmacological treatments ongoing at enrollment
The table will provide:
- distribution of COPD pharmacological treatments (classes) ongoing at enrollment (see 'Computed variables' chapter).

Percentages will be computed out of the total number of patients evaluable for the FAS.

Table 34. COPD pharmacological treatments ongoing at 6-month follow-up visit
The table will provide:
- distribution of COPD pharmacological treatments (classes) ongoing at 6-month follow-up visit (see 'Computed variables' chapter)

Percentages will be computed out of the total number of patients evaluable for the FAS.

Table 35. COPD pharmacological treatments ongoing at 12-month follow-up visit
The table will provide:
- distribution of COPD pharmacological treatments (classes) ongoing at 12-month follow-up visit (see 'Computed variables' chapter)

Percentages will be computed out of the total number of patients evaluable for the FAS.

Table 36. Medications for adverse events
The table will provide the distribution of patients according to the field "Therapy for the event" **[F22_AES_AND_ADRS.AE_THERAPY]** (i.e. patients who received medications for adverse events during the study).
Percentages will be computed out of the total number of patients evaluable for the FAS.

4.11 Correlation between patients' satisfaction and resource utilization (secondary objective #4)

Table 37. Correlation between patients' satisfaction and resource utilization (including drugs)

A correlation index (Pearson or Spearman) will be computed between TSQM-9 subscales scores (as defined in "Computed variables" chapter) at 12 month follow-up visit and the number of hospitalizations per patient during observation period (as defined in "Computed variables" chapter); p-value will be provided as well.

A correlation index (Pearson or Spearman) will be computed between TSQM-9 subscales scores (as defined in "Computed variables" chapter) at 12 month follow-up visit and the number of ER accesses per patient during observation period (as defined in "Computed variables" chapter); p-value will be provided as well.

A correlation index (Pearson or Spearman) will be computed between TSQM-9 subscales scores (as defined in "Computed variables" chapter) at 12 month follow-up visit and the number of specialist visits per patient during observation period (as defined in "Computed variables" chapter); p-value will be provided as well.

A correlation index (Pearson or Spearman) will be computed between TSQM-9 subscales scores (as defined in "Computed variables" chapter) at 12 month follow-up visit and the number of general practitioner visits per patient during observation period (as defined in "Computed variables" chapter); p-value will be provided as well.

A correlation index (Pearson or Spearman) will be computed between TSQM-9 subscales scores (as defined in "Computed variables" chapter) at 12 month follow-up visit and the number of laboratory test per patient during observation period (as defined in "Computed variables" chapter); p-value will be provided as well.

A correlation index (Pearson or Spearman) will be computed between TSQM-9 subscales scores (as defined in "Computed variables" chapter) at 12 month follow-up visit and the number of therapies administered for COPD per patient during observation period (as defined in "Computed variables" chapter); p-value will be provided as well.

A correlation index (Pearson or Spearman) will be computed between TSQM-9 subscales scores (as defined in "Computed variables" chapter) at 12 month follow-up visit and the number of therapies administered for COPD-related adverse events and COPD exacerbations per patient during observation period (as defined in "Computed variables" chapter); p-value will be provided as well.

4.12 Exacerbations

Table 38. Exacerbations: patients' distribution

This table will provide:

- the distribution of patients by number of exacerbations per patient during observation period (see 'Computed variables' chapter);
- descriptive statistics (mean, median, standard deviation, quartiles, min, max) of number of exacerbations per patient during observation period (see 'Computed variables' chapter);
- the distribution of patients by exacerbation severity [**F08_EXACERBATIONS. Ex_Exacer_1_severity - Ex_Exacer_10_severity**];
- the distribution of patients by changes in COPD therapy due to exacerbations (i.e. "Any new therapy or any change to an ongoing one required*?" [**F08_EXACERBATIONS. Ex_Exacer_1_change - Ex_Exacer_10_change**]).

Percentages will be computed out of the total number of patients evaluable for the FAS.

Table 39. Exacerbations: details

This table will provide:

- the distribution of exacerbations by exacerbation severity [**F08_EXACERBATIONS. Ex_Exacer_1_severity - Ex_Exacer_10_severity**];
- the distribution of exacerbations by changes in COPD therapy due to exacerbations (i.e. "Any new therapy or any change to an ongoing one required*?" [**F08_EXACERBATIONS. Ex_Exacer_1_change - Ex_Exacer_10_change**]).

Percentages will be computed out of the total number of exacerbations occurred during observation period in FAS patients.

4.13 Safety

Table 40. Overall Summary of Adverse Events and Adverse Event Reactions
This table will provide:

- the absolute and relative frequency of patients with at least one adverse event (AE) (see 'Computed variables' chapter),
- the absolute and relative frequency of patients with at least one Serious Adverse Event (SAE) (see 'Computed variables' chapter), and
- the patients distribution by "Seriousness Category" [**F22_AES_AND_ADRS. AE_SERIOUSNESS_CAT**], and
- the absolute and relative frequency of patients with at least one Adverse Drug Reaction (ADR) to one of the products marketed by Boheringer Ingelheim (namely: Spiriva Handihaler, Spiriva Respimat, Striverdi Respimat, Spiolto Respimat, Oxivent, Dosberotec, Duovent) (see 'Computed variables' chapter), and
- the patients distribution by "Product" [**F22_AES_AND_ADRS. AE_BI_Product**]

over the total number of evaluable patients for the Safety set.

Table 41. Patients' distribution by type of adverse event
This table will provide the patients distribution by type of adverse events (i.e. "AE brief description (in English)" **[F22_AES_AND_ADRS.AE_DSCRPT]**.
Percentages will be computed over the total number of evaluable patients for the Safety set.

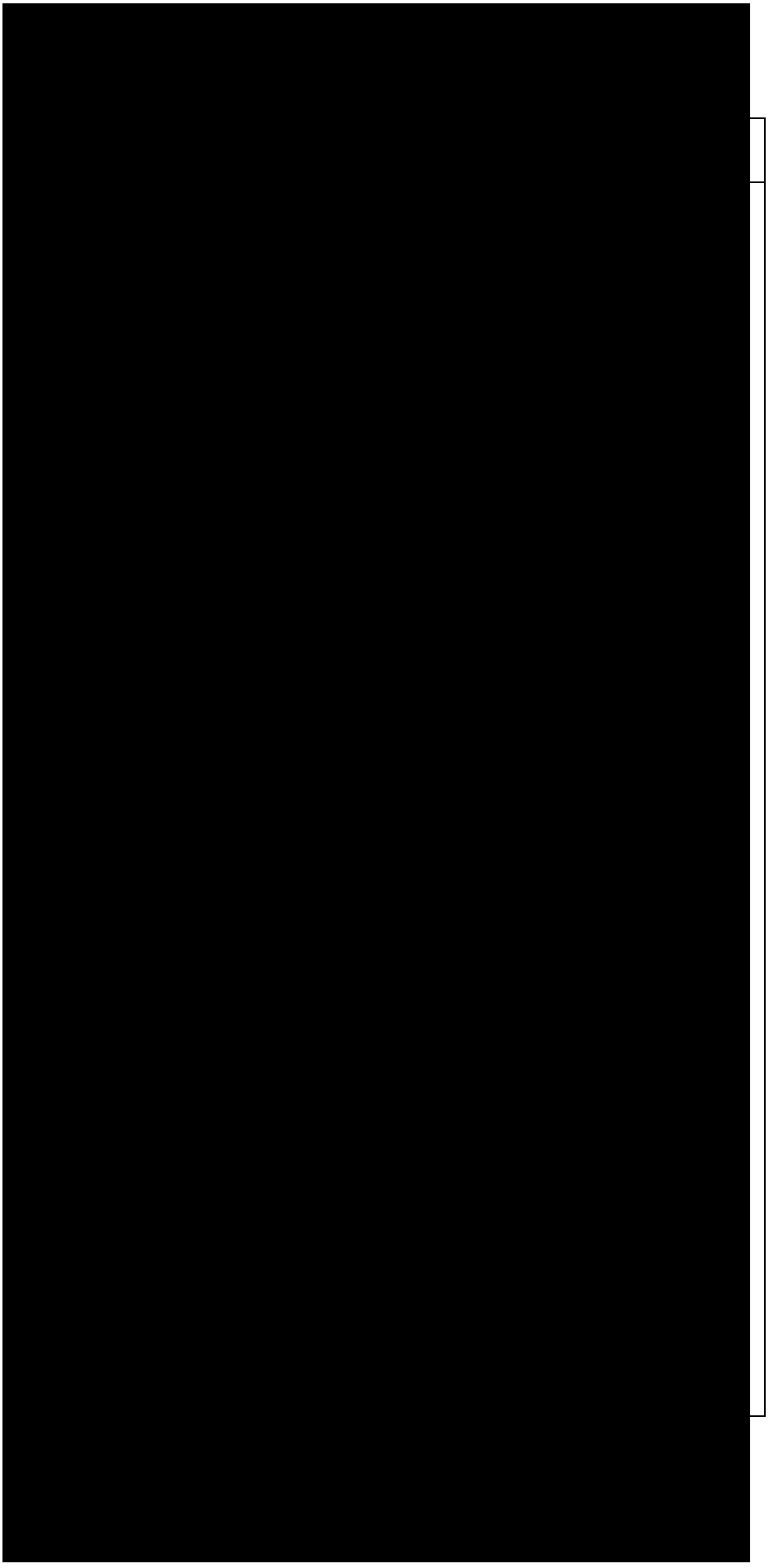
Table 42. Distribution of type of adverse event: details
This table will provide the frequency of each type of adverse events (i.e. "AE brief description (in English)" **[F22_AES_AND_ADRS.AE_DSCRPT]**.
Percentages will be computed over the total number of AEs occurred in the Safety set.

Table 43. List of adverse events
The list of all adverse events occurred in the Safety set will be reported. The following variables will be described:

- Patient ID
- "Date of enrollment visit" **[_PatientInfo.Date_enrollment]**
- "AE brief description (in English)" **[F22_AES_AND_ADRS.AE_DSCRPT]**
- "Date of onset" **[F22_AES_AND_ADRS.AE_ONSET]**
- "Is it ongoing at the end of the study?" **[F22_AES_AND_ADRS.AE_ONGOING]**
- "End date" **[F22_AES_AND_ADRS.AE_END_DATE]**
- "Is it a serious AE" **[F22_AES_AND_ADRS.AE_1]**
- "Seriousness category" **[F22_AES_AND_ADRS.AE_SERIOUSNESS_CAT]**
- "Is there a reasonable causal relationship with one of the products marketed by BI?" **[F22_AES_AND_ADRS.AE_2]**
- "Product" **[F22_AES_AND_ADRS.AE_BI_PRODUCT]**
- "Action taken with BI drug" **[F22_AES_AND_ADRS.AE_ACTION]**
- "Therapy for the event" **[F22_AES_AND_ADRS.AE_THERAPY]**
- "Outcome of the event" **[F22_AES_AND_ADRS.AE_OUTCOME]**

Table 44. Pregnancies: patients' distribution
This table will provide the patients distribution according to the field "Pregnancy" **[F23_PREGNANCY. PREGNANCY_1]** over the total number of evaluable patients for the Safety set.

[redacted]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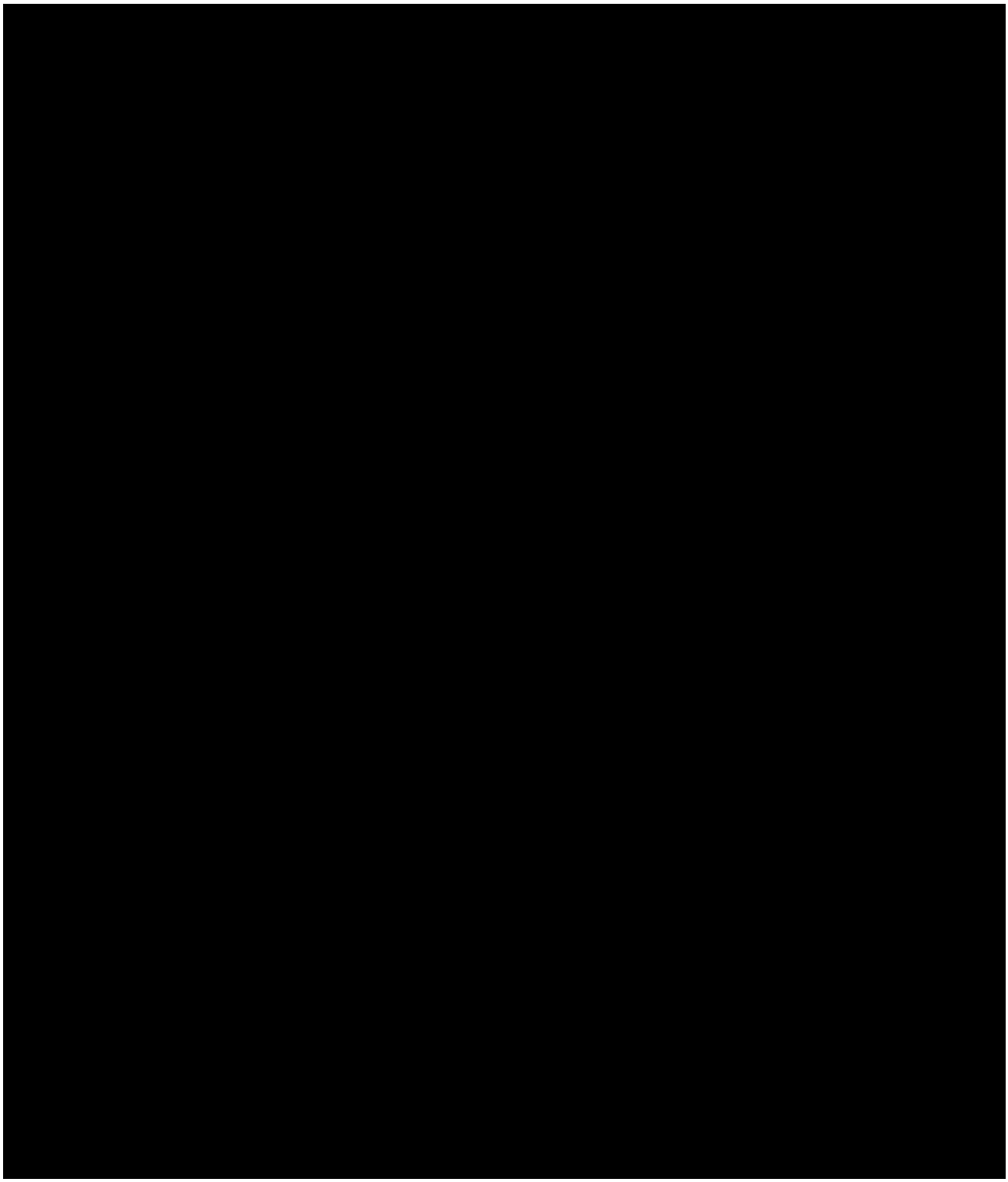

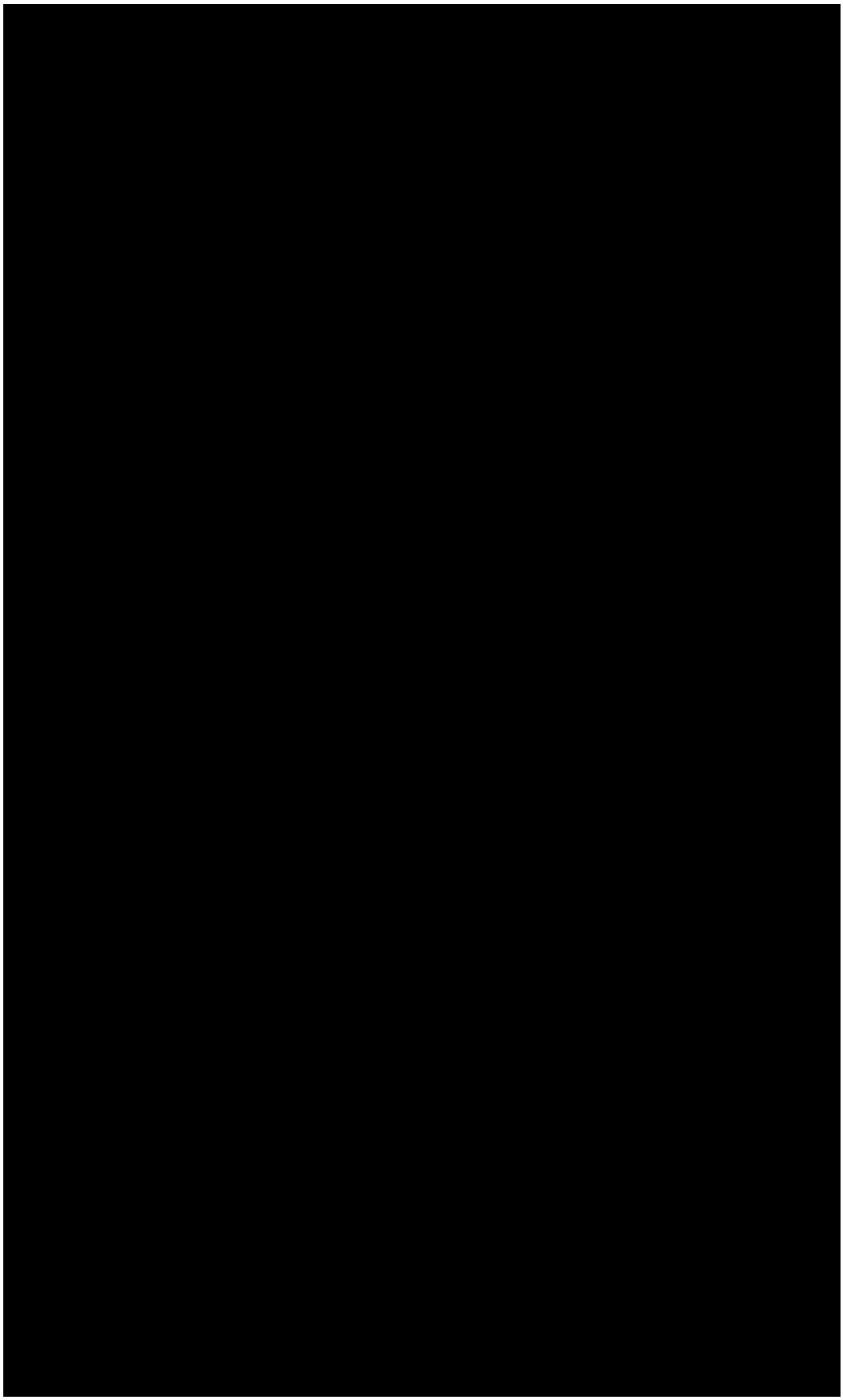

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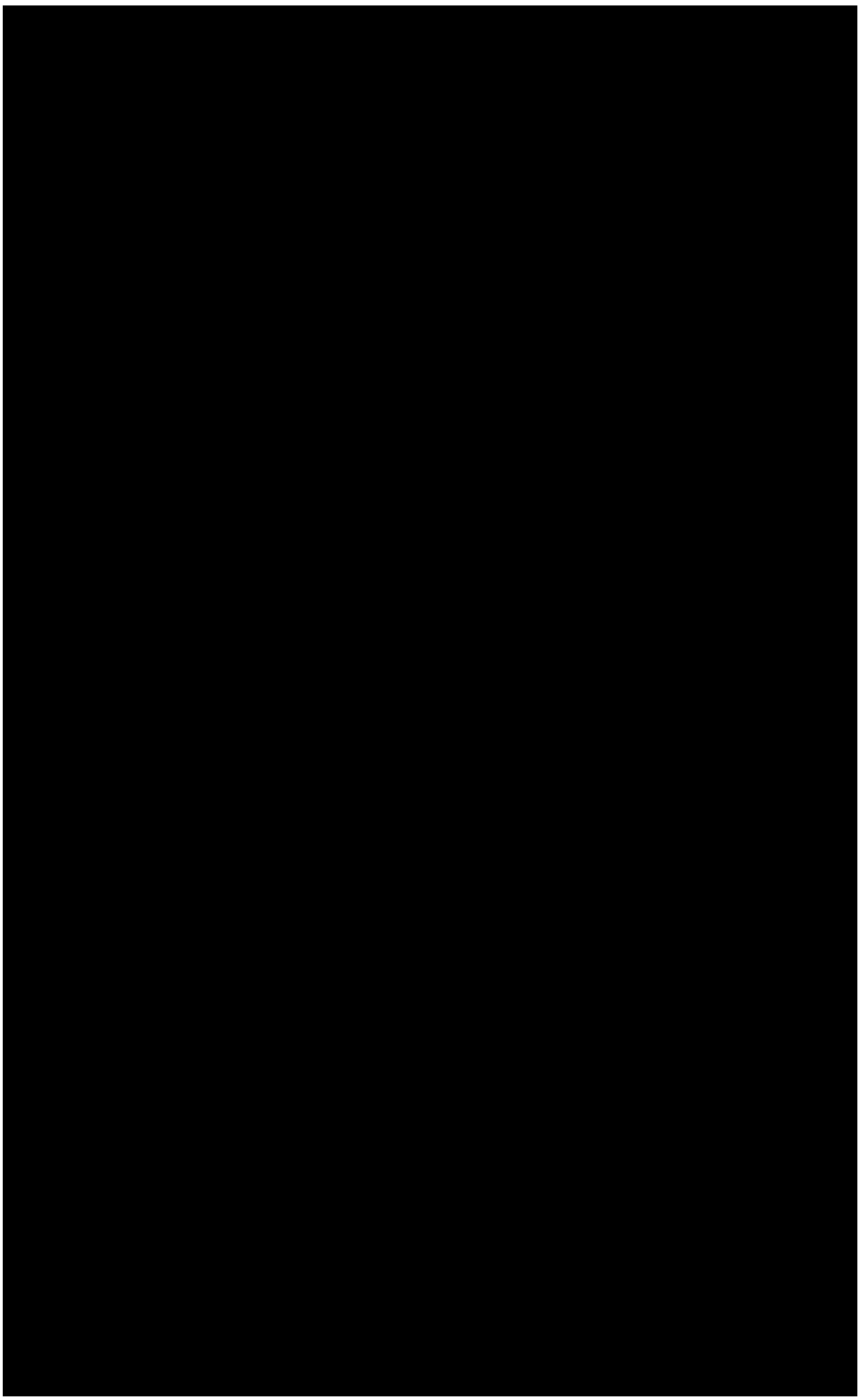

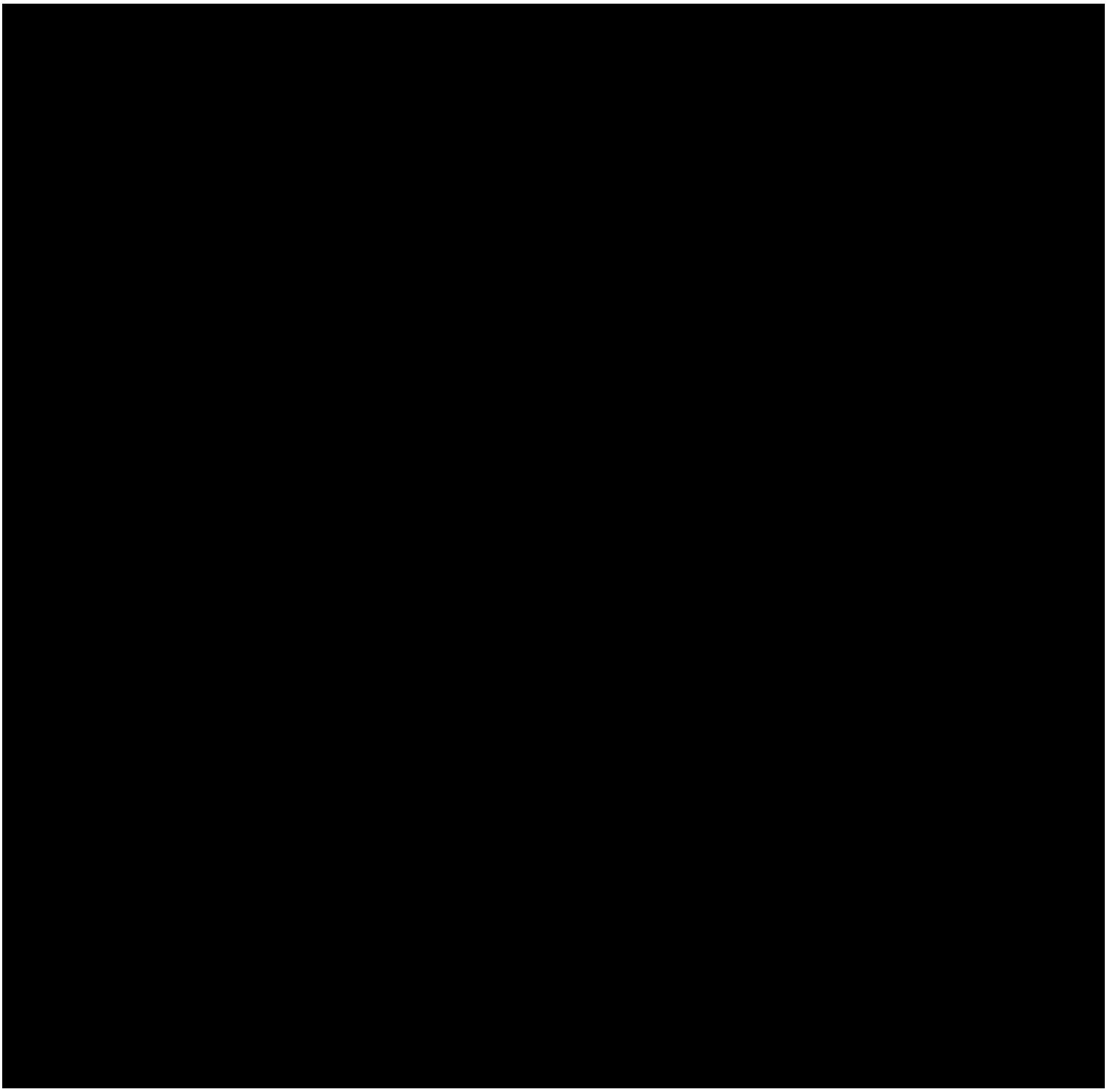

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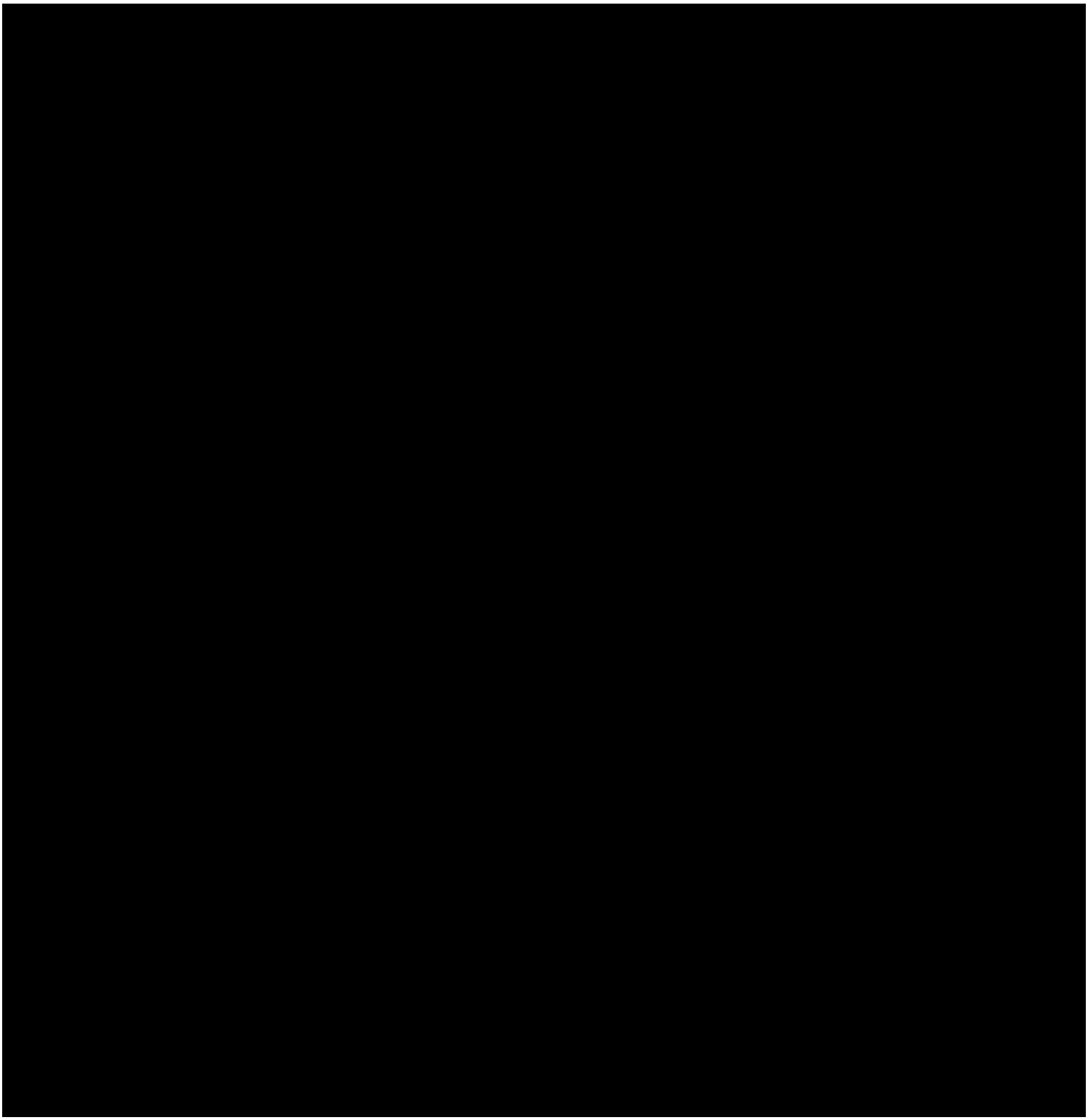

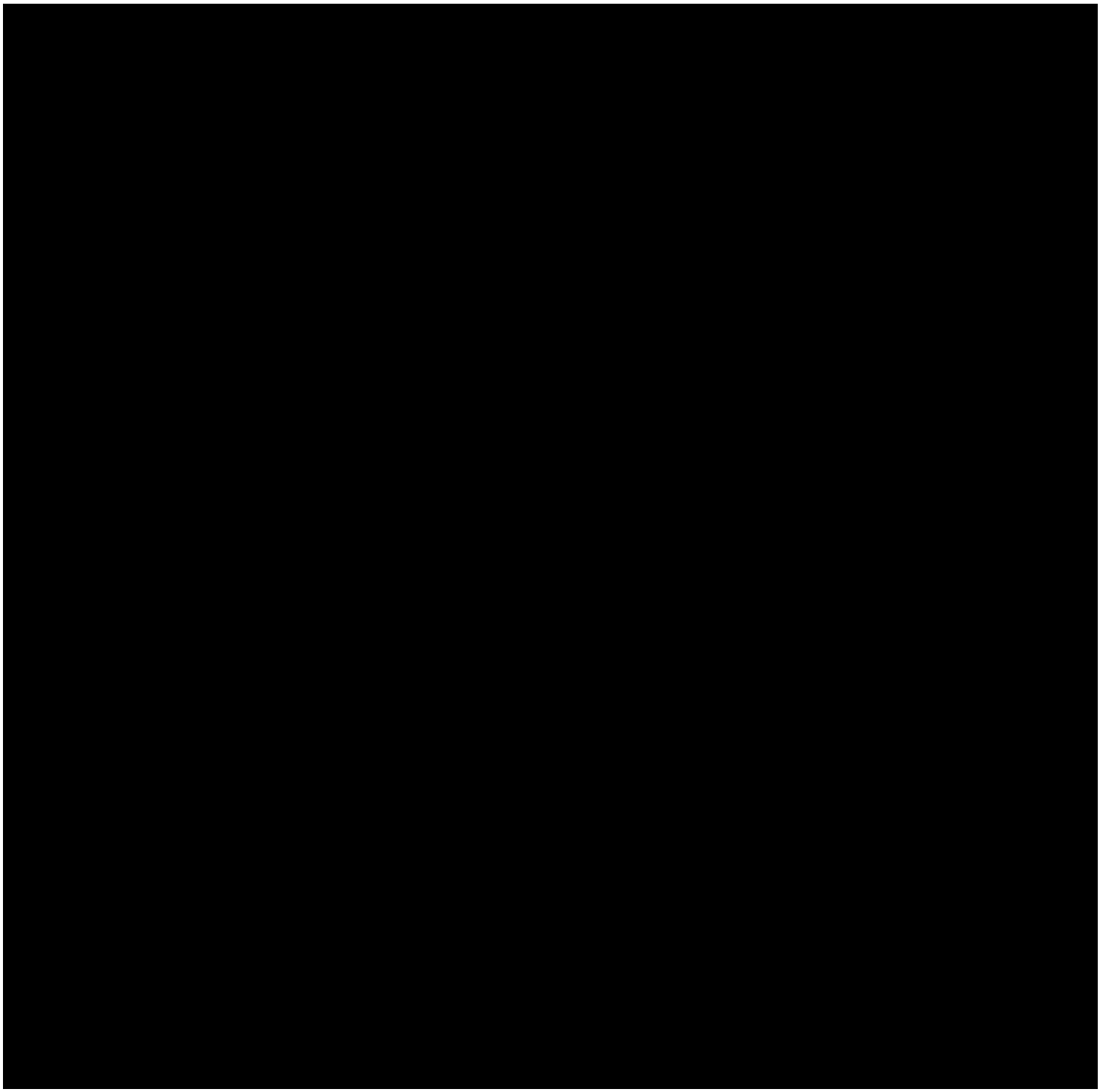

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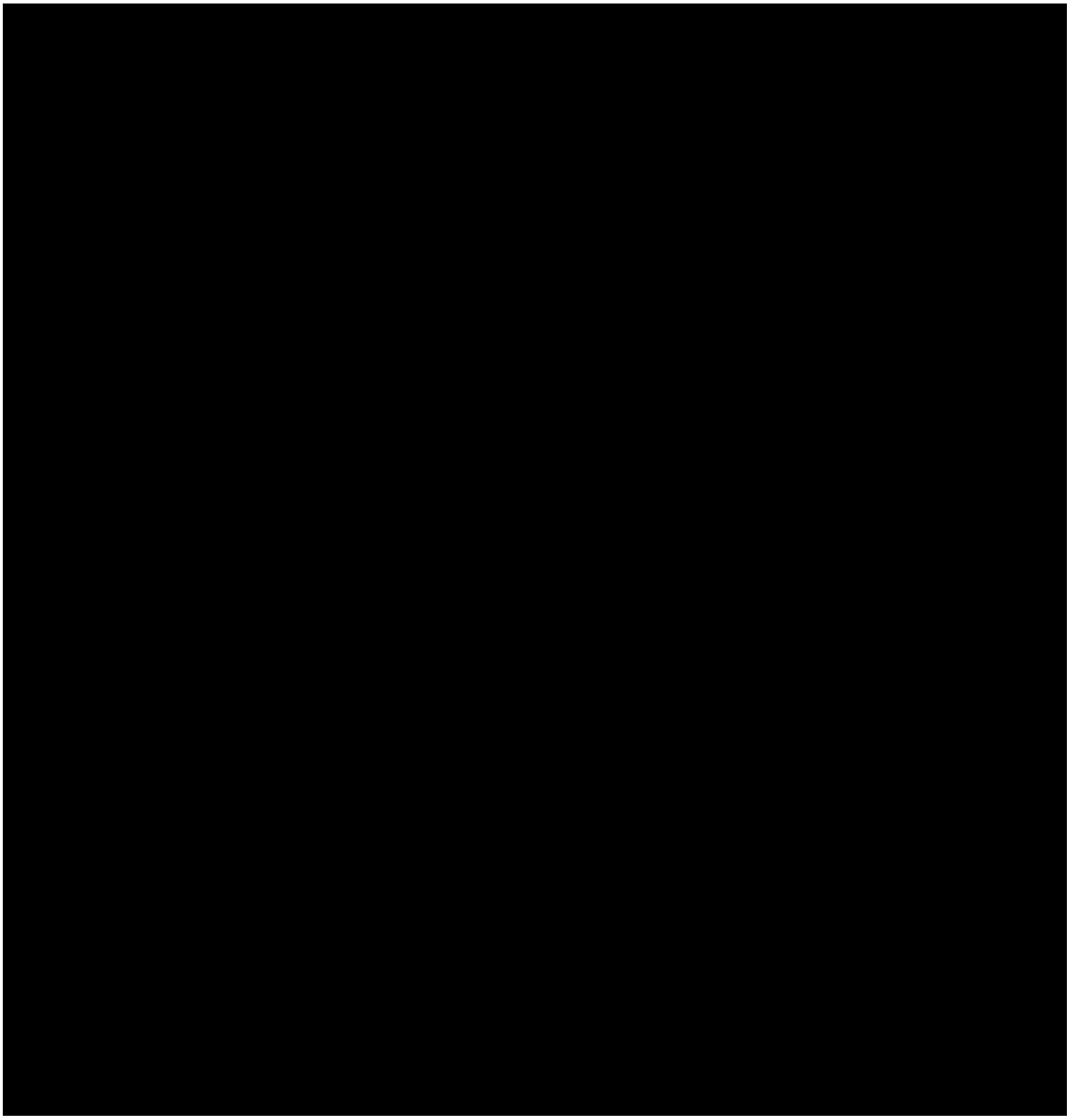

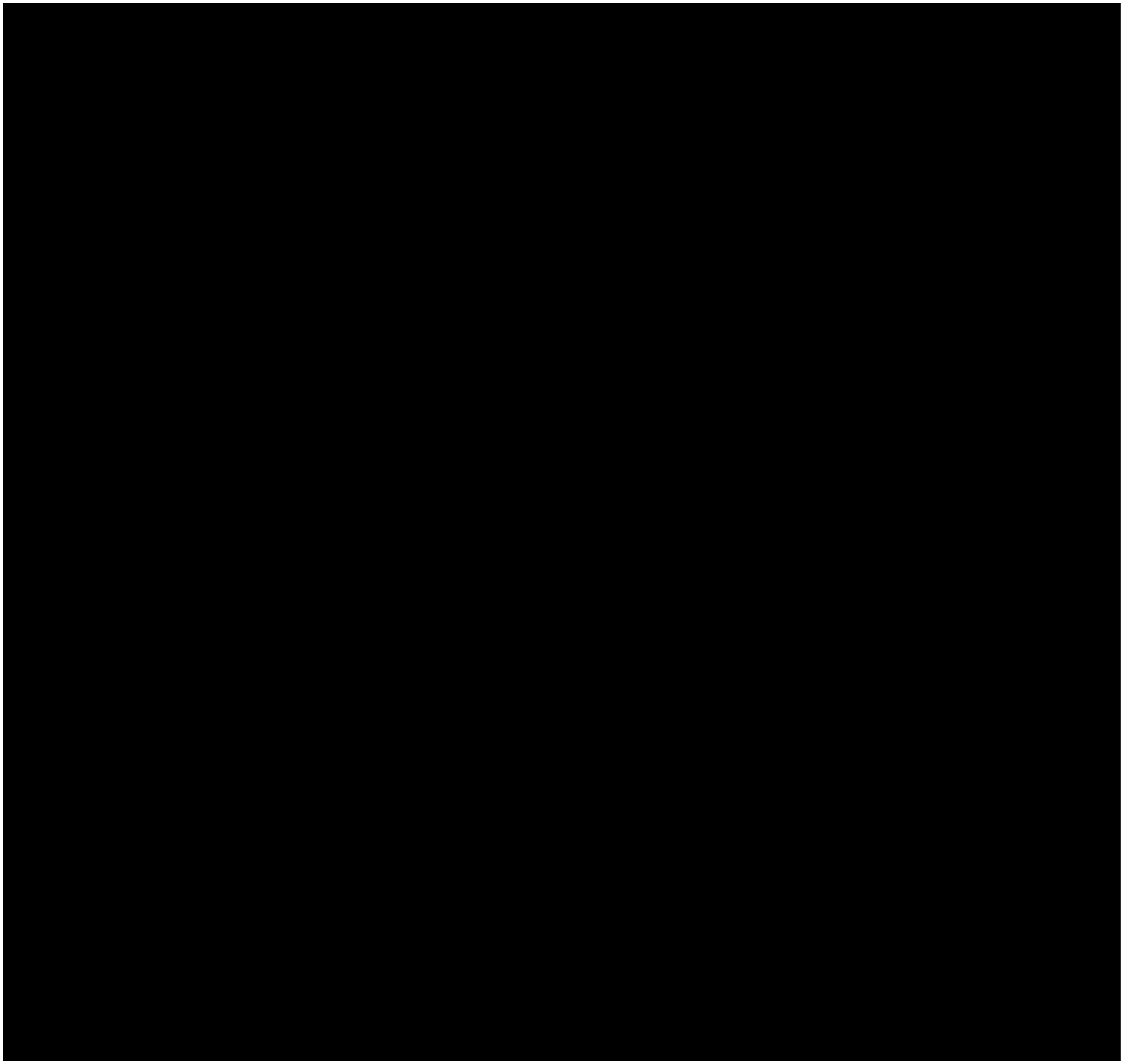

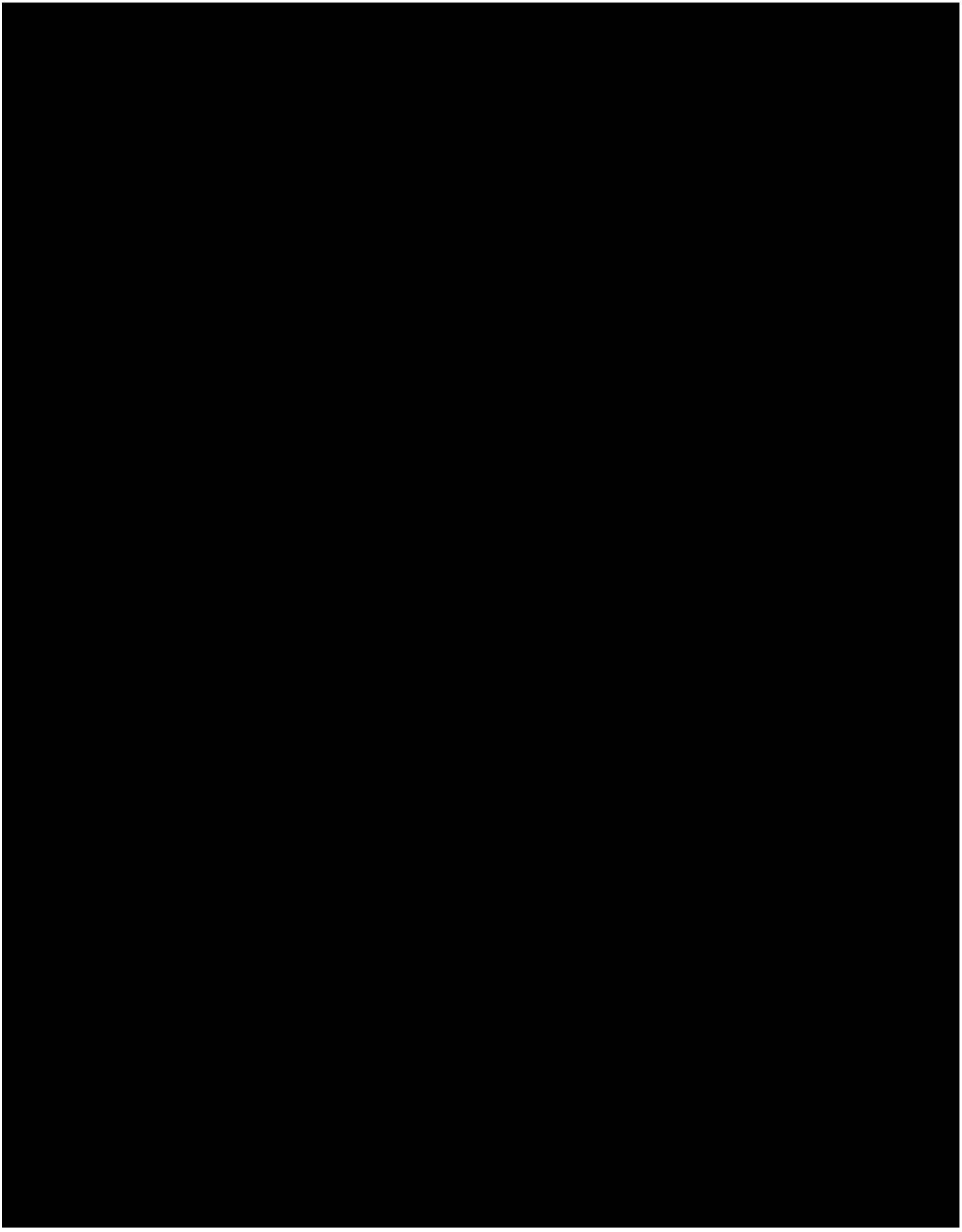

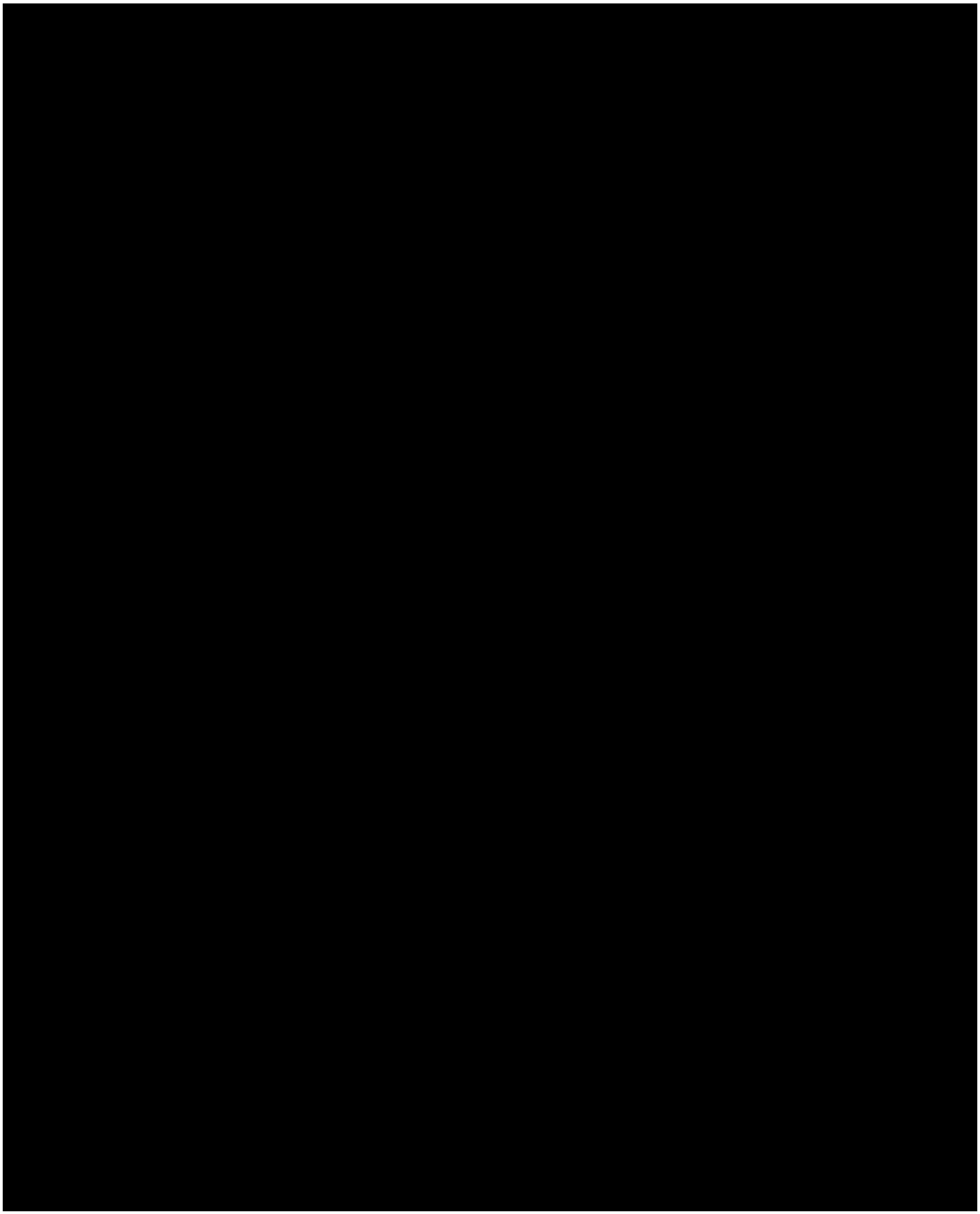

[redacted]

[redacted]

[redacted]

6 QUALITY CHECKS ON THE STATISTICAL REPORT

The statistical analysis of the SAT study will be managed by 3 main figures in [redacted]: the Biostatistician (BS), the Clinical Data Manager (CDM) and the Manager of Data Management and Statistics unit (R-DMS). In particular, in this context, CDM is the owner of data cleaning, database creation, management and lock, while BS is the owner of Statistical Analysis Plan and Statistical Report redaction.

BS and CDM of the SAT study have performed an annual training of at least 30 hours and an induction training concerning knowledge and skills required for the management of observational studies with a focus on their role. Furthermore they are coordinated by R-DMS who possesses qualifications necessary for [redacted] job.

Moreover, regarding instruments, database management and data analysis will be performed using SAS Enterprise Guide v. 7.1 and SAS 9.4.

Actions to improve the quality of data are taken in different moments during the study and using various tools, as described in [redacted] Standard Operating Procedures concerning data cleaning and statistical analysis.

Data validation (see Data Validation Plan) foresees both on-line (electronic CRF allows to verify data at the moment they are entered by means of automated edit checks, out of range controls, etc.) and off-line checks. Subsequently, quality control continues at the moment of the database lock when, as requested by [redacted] procedure, the CDM can lock the database only if, among other conditions, BS and Sponsor approve the quality of data (i.e In defining if the obtained quality of data is sufficient, the impact of possible missing/inconsistent data remained after all possible efforts to fix are done, will be based on the impact of these data on the primary and the secondary study objectives).

Finally, a quality control of the data analysis process focused on the detection of possible calculation errors or inconsistent data is performed. To observe the recommendation about the detection of priorities in order to make the process more efficient, the type of statistical report quality control is defined on the basis of the risk analysis conducted for the study.

The following quality controls will be performed on the statistical report of the SAT study.

- All the tables described in this document will be programmed and verified by a BS.
- R-DMS will perform an overall conceptual review of results, in order to evaluate their coherence and plausibility. Moreover, all the tables in this report will be independently reviewed to verify their consistency.
- Moreover, the following tables will be reprogrammed or independently verified (by another BS or CDM):
  - **Table 93. Enrolled and evaluable patients:** 100% of patients will be checked by a CDM or another BS in order to assess whether the evaluability variables are correctly computed according to the algorithm described in the SAP.
  - **Table 2. Reasons for non-eligibility to analyses:** 100% of patients will be checked by a CDM or another BS in order to assess whether the evaluability variables are correctly computed according to the algorithm described in the SAP.
  - **Table 3. Premature study termination:** 100% of patients will be checked by a CDM or another BS in order to verify the number of completed/discontinued patients and frequency of cause of drop-out.
  - **Table 4. Socio-demographic characteristics at enrollment:** Table output will be verified by another BS or CDM
  - **Table 5. Smoke habilts at enrollment:** Table output will be verified by another BS or CDM ; moreover, smoking duration will be verified by CDM/another BS in order to assess if it is computed according to the algorithm described in the SAP
  - **Table 6. COPD medical history at enrollment**: Table output will be verified by another BS or CDM ; moreover, COPD duration and age at COPD diagnosis will be verified by CDM/another BS in order to assess if it is computed according to the algorithm described in the SAP
  - **Table 7. Comorbidities at enrollment:** Table output will be verified by another BS or CDM
  - **Table 8. Vital signs at enrollment:** Table output will be verified by another BS or CDM
  - **Table 11. Patients' satisfaction for medical treatment (TSQM-9 subscales) at each study visit**: another BS/CDM will verify 100% of evaluable patients in order to assess that the TSQM-9 subscales scores are calculated according to the algorithm described in the SAP
  - **Table 12. Patients' disease perception (B-IPQ) at each study visit**: randomly chosen patients (50% of evaluable patients) will be checked by a CDM or another BS in order to assess whether B-IPQ total score is correctly computed according to the algorithm described in the SAP.
  - **Table 13. Patients' adherence to COPD treatment (MMAS-4) at each study visit**: Table output will be verified by another BS or CDM ; moreover, randomly chosen patients (50% of evaluable patients) will be checked by a CDM or another BS in order to assess whether MMAS-4 total score is correctly computed according to the algorithm described in the SAP.
  - **Table 14. Patients' health status (CAT) at each study visit:** randomly chosen patients (50% of evaluable patients) will be checked by a CDM or another BS in order to assess whether CAT total score is correctly computed according to the algorithm described in the SAP.
  - **Table 16. Patients' COPD awareness (Awareness structured interview) each study visit**: randomly chosen patients (50% of evaluable patients) will be checked by a CDM or another BS in order to assess whether COPD awareness questionnaire's composite scores are correctly computed according to the algorithm described in the SAP.
  - **Table 19. Relation between treatment satisfaction and demographic/clinical parameters and PROs during 12 month observation period (Repeated measures regression models) – Global satisfaction domain**: another BS will verify the results obtained from the mixed model for repeated measures

- **Table 20. Hospitalizations not in ICU during observation period: patients' distribution**: Table output will be verified by another BS or CDM ; moreover, randomly chosen patients (20% of evaluable patients) will be checked by a CDM or another BS in order to assess whether Number of hospitalization not in ICU during observation period per patient and Number of days of hospitalization not in ICU per patient are correctly computed according to the algorithm described in the SAP
- **Table 23. Hospitalizations in ICU during observation period: details**: Table output will be verified by another BS or CDM
- **Table 24. Emergency room accesses: patients' distribution**: Table output will be verified by another BS or CDM ; moreover, randomly chosen patients (20% of evaluable patients) will be checked by a CDM or another BS in order to assess whether Number of ER accesses during observation period per patient is correctly computed according to the algorithm described in the SAP
- **Table 26. Specialist outpatient visits: patients' distribution**: Table output will be verified by another BS or CDM ; moreover, randomly chosen patients (20% of evaluable patients) will be checked by a CDM or another BS in order to assess whether Number of specialist outpatient visits per patient during observation period is correctly computed according to the algorithm described in the SAP
- **Table 27. General practitioner visits: patients' distribution**: Table output will be verified by another BS or CDM ; moreover, randomly chosen patients (20% of evaluable patients) will be checked by a CDM or another BS in order to assess whether Number of general practitioner visits per patient during observation period is correctly computed according to the algorithm described in the SAP
- **Table 28. Laboratory tests: patients' distribution**: Table output will be verified by another BS or CDM ; moreover, randomly chosen patients (20% of evaluable patients) will be checked by a CDM or another BS in order to assess whether Number of laboratory tests/examinations per patient during observation period is correctly computed according to the algorithm described in the SAP
- **Table 30. Oxygen therapy**: Table output will be verified by another BS or CDM ; moreover, randomly chosen patients (10% of evaluable patients) will be checked by a CDM or another BS in order to assess whether Patients with oxygen therapy during the observational period were correctly identified according to the algorithm described in the SAP
- **Table 31. List of oxygen therapies**: 3 patients will be verified with respect to DB content
- **Table 32. Patients receiving fixed/non-fixed dose therapies for COPD ongoing at enrollment**: randomly chosen patients (10% of evaluable patients) will be checked by a CDM or another BS in order to assess whether patients with COPD pharmacological fixed and/or non-fixed dose therapy ongoing at enrollment were correctly identified according to the algorithm described in the SAP
- **Table 33. COPD pharmacological treatments ongoing at enrollment:** randomly chosen patients (10 for each COPD pharmacological treatment cathegory) will be checked by a CDM or another BS in order to assess whether the patient was correctly classified according to the algorithm described in the SAP.
- **Table 37. Correlation between patients' satisfaction and resource utilization (including drugs)**: another BS will verify the correlations coefficients and p-values
- **Table 38. Exacerbations: patients' distribution**: Table output will be verified by another BS or CDM ; moreover, randomly chosen patients (20% of evaluable patients) will be checked by a CDM or another BS in order to assess whether Number of exacerbations per patient during observation period is correctly computed according to the algorithm described in the SAP
- **Table 40. Overall Summary of Adverse Events and Adverse Event Reactions**: Table output will be verified by another BS or CDM ; moreover, randomly chosen patients (10% of evaluable patients) will be checked by a CDM or another BS in order to assess whether patients with at least one AE/SAE/ADR were correctly identified accordingto the algorithm described in the SAP
- **Table 43. List of adverse events**: 3 patients will be verified with respect to DB content
- **Table 45. Patients' satisfaction for medical treatment (TSQM-9 items) at each study visit - Switchers vs non-switchers**: randomly chosen patients (50% of evaluable patients) will be checked by a CDM or another BS in order to assess whether they were correctly classified as switchers/non-switchers.

7 REVISION HISTORY

Table (N° and title)	SAP version and date	Change description	Applicant	Note
All applicable tables	Vers.1.0, 16/09/2016	Analysis modified according to the changes agreed with Sponsor during the conference call held on the 27/09/2016	BI	
All applicable tables	Vers.1.0, 16/09/2016	General review of the document and proposed analyses	[redacted]	
Whole document	Vers.1.1, 10/07/2017	General review of the document	BI Global	
Tables 4-6	Vers. 1.2, 25/07/2017	Descriptive analyses on non-evaluable patients removed	BI Global	
Tables 20-22	Vers. 1.2, 25/07/2017	Regression model characteristics further specified	BI Global, [redacted]	
Whole document	Vers. 1.3, 15/09/2017	General review of the document	BI Global	
Table 14	Vers. 1.4, 21/09/2017	Analysis on CAT score categories added	BI Global	

8 APPENDICES

8.1 COPD awareness questionnaire scoring system

The following table specifies the score that is to be given to the single answer options of each COPD awareness questionnaire's item.

		Domain	**Per nulla d'accordo**	**Poco d'accordo**	**Abbastanza d'accordo**	**Molto d'accordo**
1.	Dovrò assumere i farmaci inalatori per sempre	*Knowledge of disease*	0	1	2	3
2.	Penso che la BPCO tenda a peggiorare con il passare del tempo	*Knowledge of disease*	0	1	2	3
3.	I farmaci per la BPCO mi permettono di svolgere le normali attività quotidiane	-	0	1	2	3
4.	I farmaci presi regolarmente permettono di muoversi con minor fatica	*Awareness of treatment needs*	0	1	2	3
5.	Penso che la BPCO sia una malattia poco grave, infatti viene curata con farmaci per inalazione	*Disease perception*	3	2	1	0
6.	Il fumo è la causa principale della BPCO	-	0	1	2	3
7.	Faccio fatica ad accettare di avere la BPCO	*Acknowledgement of disease*	3	2	1	0
8.	I farmaci somministrati per via inalatoria sono meno potenti delle pillole, compresse o altre medicine prese per bocca	*Disease perception*	3	2	1	0
9.	I farmaci per la BPCO vanno presi regolarmente	*Awareness of treatment needs*	0	1	2	3
10.	Preferisco ignorare i sintomi della BPCO	*Disease perception*	3	2	1	0
11.	I farmaci inalatori possono essere sospesi quando i sintomi migliorano	-	3	2	1	0
12.	La terapia regolare riduce i peggioramenti improvvisi	*Awareness of treatment needs*	0	1	2	3
13.	E' normale, alla mia età, avere problemi respiratori	-	3	2	1	0
14.	I farmaci assunti per via inalatoria consentono di migliorare la fatica a respirare	*Awareness of treatment needs*	0	1	2	3
15.	Sono preoccupato per la mia BPCO	*Acknowledgement of disease*	3	2	1	0
16.	Da quando ho la BPCO faccio fatica a sentirmi me stesso	-	3	2	1	0
17.	La sospensione della terapia inalatoria aumenta i peggioramenti	-	0	1	2	3
18.	La spirometria è un esame fondamentale per giungere alla diagnosi di BPCO	*Awareness of treatment needs*	0	1	2	3
19.	Penso che la mia BPCO non guarirà mai	*Knowledge of disease*	0	1	2	3
20.	Penso che la mia BPCO non guarirà mai perché non ci sono farmaci efficaci	*Disease perception*	3	2	1	0
21.	Preferisco non pensare al fatto di avere la BPCO	*Disease perception*	3	2	1	0
22.	L'idea di soffrire di BPCO mi fa arrabbiare	*Acknowledgement of disease*	3	2	1	0
23.	I farmaci per la BPCO migliorano i sintomi	*Awareness of treatment needs*	0	1	2	3
24.	Faccio fatica a convivere con i sintomi della BPCO	*Acknowledgement of disease*	3	2	1	0
25.	Mi chiedo perché questa malattia sia capitata proprio a me	*Acknowledgement of disease*	3	2	1	0
26.	La BPCO è una malattia cronica, cioè non guarisce	*Knowledge of disease*	0	1	2	3
27.	Tutti i fumatori soffrono di BPCO	-	3	2	1	0

Here below, the meaning of each question and answer option in English language (which is not an official, validated translation) is provided:

	Domain	**I totally disagree**	**I agree a little**	**I somewhat agree**	**I totally agree**
1. I need to be treated with inhaled drugs forever	*Knowledge of disease*	0	1	2	3
2. I believe that COPD tends to worsen over time	*Knowledge of disease*	0	1	2	3
3. Treatments for COPD allow me to carry out normal daily activities	-	0	1	2	3
4. A regular administration of drugs allows me to move with less effort	*Awareness of treatment needs*	0	1	2	3
5. I think that COPD is a mild disease since it is treated with inhaled drugs	*Disease perception*	3	2	1	0
6. Smoke is the main cause of COPD	-	0	1	2	3
7. I cannot easily accept to have COPD	*Acknowledgement of disease*	3	2	1	0
8. Inhaled drugs are less effective than pills, tablets or other oral medications	*Disease perception*	3	2	1	0
9. Treatments for COPD must be taken regularly	*Awareness of treatment needs*	0	1	2	3
10. I prefer to ignore COPD symptoms	*Disease perception*	3	2	1	0
11. Inhaled drugs can be interrupted if symptoms improve	-	3	2	1	0
12. A regular therapy reduces the risk of sudden worsening	*Awareness of treatment needs*	0	1	2	3
13. It is common to have respiratory problems at my age	-	3	2	1	0
14. Inhaled drugs help improving the fatigue in breathing	*Awareness of treatment needs*	0	1	2	3
15. I am worried about my COPD	*Acknowledgement of disease*	3	2	1	0
16. I have been finding it hard to feel like myself since I suffer from COPD	-	3	2	1	0
17. Interrupting the inhaled therapy increases the risk of COPD worsening	-	0	1	2	3
18. Spirometry is a fundamental examination for the COPD diagnosis	*Awareness of treatment needs*	0	1	2	3
19. I will never heal from my COPD	*Knowledge of disease*	0	1	2	3
20. I think I will never heal from my COPD because there is lack of effective drugs	*Disease perception*	3	2	1	0
21. I prefer not to think about my COPD	*Disease perception*	3	2	1	0
22. I am angry because of my COPD	*Acknowledgement of disease*	3	2	1	0
23. Drugs for COPD improve my symptoms	*Awareness of treatment needs*	0	1	2	3
24. I am having difficulty living with COPD symptoms	*Acknowledgement of disease*	3	2	1	0
25. I wonder why COPD happened to me	*Acknowledgement of disease*	3	2	1	0
26. COPD is a chronic disease and it is not possible to heal from it	*Knowledge of disease*	0	1	2	3
27. All smokers suffer from COPD	-	3	2	1	0

8.2 Modified Medical Research Council (mMRC) dyspnoea scale

- Italian version (used in the SAT study)

Scala modificata del Medical Research Council (mMRC) per la valutazione della dispnea

Grado

0 "Mi manca il fiato solo in occasione di attività fisica intensa"

1 "Mi manca il fiato se cammino in piano a passo veloce o se percorro una lieve salita a piedi"

2 "A causa della mancanza di fiato, cammino in piano più lentamente dei miei coetanei, oppure mi devo fermare per respirare quando cammino in piano al mio passo abituale"

3 "Mi devo fermare per respirare dopo aver camminato in piano per circa 100 metri o per pochi minuti"

4 "La mia mancanza di fiato è talmente intensa da impedirmi di uscire di casa", o "mi manca il fiato mentre mi vesto"

NB: La scala MRC modificata utilizza gli stessi descrittori della scala MRC originale, nella quale i descrittori sono numerati da 1 a 5. La scala MRC modificata (0-4) è utilizzata per il calcolo dell'indice BODE.

- English version

Table 2.5. Modified MRC dyspnea scale[a]	
PLEASE TICK IN THE BOX THAT APPLIES TO YOU (ONE BOX ONLY) (Grades 0–4)	
mMRC Grade 0. I only get breathless with strenuous exercise.	❑
mMRC Grade 1. I get short of breath when hurrying on the level or walking up a slight hill.	❑
mMRC Grade 2. I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level.	❑
mMRC Grade 3. I stop for breath after walking about 100 meters or after a few minutes on the level.	❑
mMRC Grade 4. I am too breathless to leave the house or I am breathless when dressing or undressing.	❑

[a] Fletcher CM. BMJ 1960; 2: 1662.

8.3 Treatment Satisfaction Questionnaire for Medication (TSQM-9)

- Italian version (used in the SAT study)

TSQM-9 *(italiano)*

Questionario sulla soddisfazione riguardo al farmaco

Istruzioni – Rifletta sul suo livello di soddisfazione o insoddisfazione riguardo al farmaco che le viene prescritto in questa sperimentazione clinica. Vorremmo la sua opinione sull'efficacia, gli effetti collaterali e la praticità del farmaco durante le ultime 2-3 settimane o dall'ultima volta che lo ha usato. Per ogni domanda, contrassegni solo la risposta che meglio corrisponde alle sue esperienze.

1. Quanto è soddisfatto/a o insoddisfatto/a della capacità del farmaco di prevenire o trattare il suo disturbo?

☐1 Estremamente insoddisfatto/a
☐2 Molto insoddisfatto/a
☐3 Insoddisfatto/a
☐4 Moderatamente soddisfatto/a
☐5 Soddisfatto/a
☐6 Molto soddisfatto/a
☐7 Estremamente soddisfatto/a

2. Quanto è soddisfatto/a o insoddisfatto/a del modo in cui il farmaco allevia i suoi sintomi?

☐1 Estremamente insoddisfatto/a
☐2 Molto insoddisfatto/a
☐3 Insoddisfatto/a
☐4 Moderatamente soddisfatto/a
☐5 Soddisfatto/a
☐6 Molto soddisfatto/a
☐7 Estremamente soddisfatto/a

3. Quanto è soddisfatto/a o insoddisfatto/a del tempo che il farmaco impiega ad agire?

☐1 Estremamente insoddisfatto/a
☐2 Molto insoddisfatto/a
☐3 Insoddisfatto/a
☐4 Moderatamente soddisfatto/a
☐5 Soddisfatto/a
☐6 Molto soddisfatto/a
☐7 Estremamente soddisfatto/a

4. Quanto facile o difficile è l'impiego del farmaco nella sua forma attuale?

☐1 Estremamente difficile
☐2 Molto difficile
☐3 Difficile
☐4 Relativamente facile
☐5 Facile
☐6 Molto facile
☐7 Estremamente facile

5. Quanto è facile o difficile pianificare quando usare il farmaco ogni volta?

☐1 Estremamente difficile
☐2 Molto difficile
☐3 Difficile
☐4 Relativamente facile
☐5 Facile
☐6 Molto facile
☐7 Estremamente facile

6. Quanto è comodo o scomodo seguire le istruzioni per l'impiego del farmaco?

☐1 Estremamente scomodo
☐2 Molto scomodo
☐3 Scomodo
☐4 Relativamente comodo
☐5 Comodo
☐6 Molto comodo
☐7 Estremamente comodo

7. Complessivamente, quanto è sicuro/a che il farmaco le sia di giovamento?

☐1 Per niente sicuro/a
☐2 Poco sicuro/a
☐3 Abbastanza sicuro/a
☐4 Molto sicuro/a
☐5 Estremamente sicuro/a

8. Quanto è sicuro/a che i vantaggi offerti dal farmaco superino gli svantaggi?

☐1 Per niente sicuro/a
☐2 Poco sicuro/a
☐3 Abbastanza sicuro/a
☐4 Molto sicuro/a
☐5 Estremamente sicuro/a

9. Tutto considerato, quanto è soddisfatto/a o insoddisfatto/a del farmaco?

☐1 Estremamente insoddisfatto/a
☐2 Molto insoddisfatto/a
☐3 Insoddisfatto/a
☐4 Moderatamente soddisfatto/a
☐5 Soddisfatto/a
☐6 Molto soddisfatto/a
☐7 Estremamente soddisfatto/a

- English version

TSQM-9

Abbreviated Treatment Satisfaction Questionnaire for Medication

Instructions: Please take some time to think about your level of satisfaction or dissatisfaction with the medication you are taking in this clinical trial. We are interested in your evaluation of the effectiveness, side effects, and convenience of the medication *over the last two to three weeks, or since you last used it*. For each question, please place a single check mark next to the response that most closely corresponds to your own experiences.

1. How satisfied or dissatisfied are you with the ability of the medication to prevent or treat your condition?
- ☐1 Extremely Dissatisfied
- ☐2 Very Dissatisfied
- ☐3 Dissatisfied
- ☐4 Somewhat Satisfied
- ☐5 Satisfied
- ☐6 Very Satisfied
- ☐7 Extremely Satisfied

2. How satisfied or dissatisfied are you with the way the medication relieves your symptoms?
- ☐1 Extremely Dissatisfied
- ☐2 Very Dissatisfied
- ☐3 Dissatisfied
- ☐4 Somewhat Satisfied
- ☐5 Satisfied
- ☐6 Very Satisfied
- ☐7 Extremely Satisfied

3. How satisfied or dissatisfied are you with the amount of time it takes the medication to start working?
- ☐1 Extremely Dissatisfied
- ☐2 Very Dissatisfied
- ☐3 Dissatisfied
- ☐4 Somewhat Satisfied
- ☐5 Satisfied
- ☐6 Very Satisfied
- ☐7 Extremely Satisfied

4. How easy or difficult is it to use the medication in its current form?
- ☐1 Extremely Difficult
- ☐2 Very Difficult
- ☐3 Difficult
- ☐4 Somewhat Easy
- ☐5 Easy
- ☐6 Very Easy
- ☐7 Extremely Easy

5. How easy or difficult is it to plan when you will use the medication each time?

☐1 Extremely Difficult
☐2 Very Difficult
☐3 Difficult
☐4 Somewhat Easy
☐5 Easy
☐6 Very Easy
☐7 Extremely Easy

6. How convenient or inconvenient is it to take the medication as instructed?
☐1 Extremely Inconvenient
☐2 Very Inconvenient
☐3 Inconvenient
☐4 Somewhat Convenient
☐5 Convenient
☐6 Very Convenient
☐7 Extremely Convenient

7. Overall, how confident are you that taking this medication is a good thing for you?
☐1 Not at All Confident
☐2 A Little Confident
☐3 Somewhat Confident
☐4 Very Confident
☐5 Extremely Confident

8. How certain are you that the good things about your medication outweigh the bad things?
☐1 Not at All Certain
☐2 A Little Certain
☐3 Somewhat Certain
☐4 Very Certain
☐5 Extremely Certain

9. Taking all things into account, how satisfied or dissatisfied are you with this medication?
☐1 Extremely Dissatisfied
☐2 Very Dissatisfied
☐3 Dissatisfied
☐4 Somewhat Satisfied
☐5 Satisfied
☐6 Very Satisfied
☐7 Extremely Satisfied

8.4 COPD Assessment Test (CAT)

- Italian version (used in the SAT study)

Nome:

Data di oggi:

CAT
COPD Assessment Test

Come va la Sua broncopneumopatia cronica ostruttiva (BPCO)? Esegua il COPD Assessment Test™ (test di valutazione della BPCO) (CAT)

Questo questionario denominato CAT - **C**OPD **A**ssessment **T**est™ (che significa test per la valutazione della (BPCO)), aiuterà sia Lei che l'operatore sanitario a misurare l'impatto della BPCO sul Suo benessere e sulla Sua vita quotidiana. Le Sue risposte e punteggi del test possono essere utilizzati sia da Lei che dall'operatore sanitario per migliorare la gestione della Sua BPCO e per ottenere i massimi vantaggi dal trattamento.

Per ogni affermazione riportata di seguito, inserisca un segno (X) nella casella che meglio descrive la Sua situazione attuale. Può selezionare solo una risposta per ogni domanda.

Esempio: Sono molto contento 0 X 2 3 4 5 Sono molto triste

			PUNTEGGIO
Non tossisco mai	0 1 2 3 4 5	**Tossisco sempre**	
Il mio petto è completamente libero da catarro (muco)	0 1 2 3 4 5	**Il mio petto è tutto pieno di catarro (muco)**	
Non avverto alcuna sensazione di costrizione al petto	0 1 2 3 4 5	**Avverto una forte sensazione di costrizione al petto**	
Quando cammino in salita o salgo una rampa di scale non avverto mancanza di fiato	0 1 2 3 4 5	**Quando cammino in salita o salgo una rampa di scale avverto una forte mancanza di fiato**	
Non avverto limitazioni nello svolgere qualsiasi attività in casa	0 1 2 3 4 5	**Avverto gravi limitazioni nello svolgere qualsiasi attività in casa**	
Mi sento tranquillo ad uscire di casa nonostante la mia malattia polmonare	0 1 2 3 4 5	**Non mi sento affatto tranquillo ad uscire di casa a causa della mia malattia polmonare**	
Dormo profondamente	0 1 2 3 4 5	**Non riesco a dormire profondamente a causa della mia malattia polmonare**	
Ho molta energia	0 1 2 3 4 5	**Non ho nessuna energia**	
		PUNTEGGIO TOTALE	

- English version

Your name:_____

Today's date:_____

How is your COPD? Take the COPD Assessment Test™ (CAT)

This questionnaire will help you and your healthcare professional measure the impact COPD (Chronic Obstructive Pulmonary Disease) is having on your wellbeing and daily life. Your answers, and test score, can be used by you and your healthcare professional to help improve the management of your COPD and get the greatest benefit from treatment.

For each item below, place a mark (X) in the box that best describes you currently. Be sure to only select one response for each question.

Example: I am very happy [0] [X] [2] [3] [4] [5] I am very sad

			SCORE
I never cough	[0] [1] [2] [3] [4] [5]	I cough all the time	☐
I have no phlegm (mucus) in my chest at all	[0] [1] [2] [3] [4] [5]	My chest is completely full of phlegm (mucus)	☐
My chest does not feel tight at all	[0] [1] [2] [3] [4] [5]	My chest feels very tight	☐
When I walk up a hill or one flight of stairs I am not breathless	[0] [1] [2] [3] [4] [5]	When I walk up a hill or one flight of stairs I am very breathless	☐
I am not limited doing any activities at home	[0] [1] [2] [3] [4] [5]	I am very limited doing activities at home	☐
I am confident leaving my home despite my lung condition	[0] [1] [2] [3] [4] [5]	I am not at all confident leaving my home because of my lung condition	☐
I sleep soundly	[0] [1] [2] [3] [4] [5]	I don't sleep soundly because of my lung condition	☐
I have lots of energy	[0] [1] [2] [3] [4] [5]	I have no energy at all	☐

TOTAL SCORE ☐☐

8.5 Brief Illness Perception Questionnaire (B-IPQ)

- Italian version (used in the SAT study)

Per le seguenti domande, per favore cerchi il numero che meglio corrisponde al suo punto di vista.

Quanto la sua malattia influenza la sua vita?

1	2	3	4	5	6	7	8	9	10
Non l'influenza per nulla									la influenza gravemente

Per quanto tempo pensa la sua malattia continuerà?

1	2	3	4	5	6	7	8	9	10
Per un tempo molto breve									per sempre

Quanto controllo crede di avere sulla sua malattia?

1	2	3	4	5	6	7	8	9	10
Assolutamente nessun controllo									un controllo assoluto

Quanto pensa che il suo trattamento (pillole, ecc.) possa aiutare la sua malattia?

1	2	3	4	5	6	7	8	9	10
Per nulla									Estremamente di aiuto

Quanto sente i sintomi della sua malattia?

1	2	3	4	5	6	7	8	9	10
Alcun sintomo									Sintomi molto gravi

Quanto è preoccupato per la sua malattia?

1	2	3	4	5	6	7	8	9	10
Per nulla preoccupato									Estremamente preoccupato

Quanto crede di capire bene la sua malattia?

1	2	3	4	5	6	7	8	9	10
Per nulla									Capita molto chiaramente

Quanto la sua malattia ha cambiato le sue emozioni? (ad es. la fa arrabbiare, spaventare, turbare, deprimere?)

1	2	3	4	5	6	7	8	9	10
Non ha cambiato per nulla le emozioni									Ha cambiato estremamente le emozioni

Per favore, elenchi in ordine di importanza i tre fattori principali che hanno causato la sua malattia:

_____

_____

_____

- English version

The Brief Illness Perception Questionnaire

For the following questions, please circle the number that best corresponds to your views:

How much does your illness affect your life?										
0 no affect at all	1	2	3	4	5	6	7	8	9	10 severely affects my life
How long do you think your illness will continue?										
0 a very short time	1	2	3	4	5	6	7	8	9	10 forever
How much control do you feel you have over your illness?										
0 absolutely no control	1	2	3	4	5	6	7	8	9	10 extreme amount of control
How much do you think your treatment can help your illness?										
0 not at all	1	2	3	4	5	6	7	8	9	10 extremely helpful
How much do you experience symptoms from your illness?										
0 no symptoms at all	1	2	3	4	5	6	7	8	9	10 many severe symptoms
How concerned are you about your illness?										
0 not at all concerned	1	2	3	4	5	6	7	8	9	10 extremely concerned
How well do you feel you understand your illness?										
0 don't understand at all	1	2	3	4	5	6	7	8	9	10 understand very clearly
How much does your illness affect you emotionally? (e.g. does it make you angry, scared, upset or depressed?										
0 not at all affected emotionally	1	2	3	4	5	6	7	8	9	10 extremely affected emotionally
Please list in rank-order the three most important factors that you believe caused <u>your illness</u>. *The most important causes for me:-*										
1. _____										
2. _____										
3. _____										

8.6 Morisky Medication Adherence Scale (MMAS-4)

- Italian version (used in the SAT study)

Morisky Medication Adherence Scale (©MMAS-4)

	Sì	*No*
1. Le capita mai di dimenticarsi di prendere i suoi farmaci per la BPCO?	❑	❑
2*. Le capita mai di avere problemi a ricordarsi di prendere i suoi farmaci per la BPCO?	❑	❑
3. Quando si sente meglio, a volte smette di prendere i suoi farmaci per la BPCO?	❑	❑
4. Se a volte si sente peggio quando prende i suoi farmaci per la BPCO, smette di prenderli?	❑	❑

- English version

Morisky Medication Adherence Scale (©MMAS-4)

(Please check one box on each line)

	Yes	*No*
1. Do you ever forget to take your (name of health condition) medicine?	❑	❑
2*. Do you ever have problems remembering to take your (name of health condition) medication?	❑	❑
3. When you feel better, do you sometimes stop taking your (name of health condition) medicine?	❑	❑
4. Sometimes if you feel worse when you take your (name of health condition) medicine, do you stop taking it?	❑	❑

*modified item from original scale appearing in Medical Care 1986