

## ***PROTOCOL TEMPLATE - OBSERVATIONAL Trial***

*The protocol template is a tool to facilitate rapid protocol development. Any sections that do not apply to a specific study should contain the statement “not applicable. New section can be added if appropriate as sub-headings of the predefined sections.*

*All protocol template instructions and prompts are in blue and italics. As you complete the information requested, please delete the blue italicized text.*

*<Title>*

*The title should describe essential aspects of the study.*

Product Identifiers: *< name and/or code>*

Protocol Number: *(Assigned by the sponsor)*

EudraCT Number: *(Applicable in EU countries)*

Protocol Version (Date): *v. XX; (dd/mm/yyyy)*

*In case of amendment(s) list here the different protocol versions with relative dates*

Protocol including the amendment: *N. xx (dd/mm/yyyy)*

Sponsor: *<name>*

*This document contains confidential information belonging to Sponsor. Except as may be otherwise agreed to in writing, by accepting or reviewing these materials, you agree to hold such information in confidence and not to disclose it to others (except where required by applicable law), nor to use it for unauthorized purposes. In the event of actual or suspected breach of this obligation Sponsor should be promptly notified.*

## SIGNATURES PAGE

### SPONSOR SIGNATURE

\_\_\_\_\_  
Printed name

\_\_\_\_\_  
Role & Department

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Date

## SIGNATURES PAGE

### CENTRE SIGNATURE – PRINCIPAL INVESTIGATOR

I have read this Protocol Amendment relevant to the study entitled “<Protocol Title>” and I agree to conduct the study as detailed herein and in compliance with guidelines for Good Clinical Practice and applicable regulatory requirements. I will provide all study personnel under my supervision with all information provided by the Sponsor and I will inform them about their responsibilities and obligations.

\_\_\_\_\_  
Printed name

\_\_\_\_\_  
Role & Department

\_\_\_\_\_  
Address

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Date

## GLOSSARY OF ABBREVIATIONS

Abbreviation	
EC	Ethics Committee
GCP	Good Clinical Practice

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## 1. SYNOPSIS

(limit to 1-2 pages)

<b>Title</b>	
<b>Sponsor</b>	
<b>Study coordinator</b>	
<b>Protocol Code</b>	
<b>Protocol version; date</b>	
<b>Background and rationale</b>	<i>Explanation of the main research question along with a justification for the study and discussion of its feasibility. Summarize the rationale for the study overall and its relevance to the research area</i>
<b>Objectives</b>	<i>Summarize the primary and, if applicable, secondary objectives that will be evaluated in the clinical study.</i>
<b>Endpoints (when applicable)</b>	
<b>Study design and procedures</b>	<i>Include a brief description of the study design including the setting in which the research will be conducted and procedures</i>
<b>Population and patient selection criteria</b>	<i>Describe the subject population in terms of sex, race, ethnicity, age, etc. Identify the criteria for inclusion or exclusion. Specify the sample size.</i>
<b>Data collection</b>	<i>In an Observational study by definition procedures are focused on data collection: include a brief description of system (es. eCRF) used and on kind of data collected (es. pre-existing data of medical records...or prospective data coming from observation of patients)</i>
<b>Assessment(s) (when applicable)</b>	<i>Include a brief description of standard criteria, scales, risk scores etc used for assessment of endpoints: Es. RECIST criteria</i>
<b>Statistical methods, data analysis</b>	<i>Insert the calculation of the sample size and the description of the statistical methods to be employed</i>
<b>Study timetable</b>	Project starting date: Project completion of data collection: Project data analysis: Project presentation of scientific report:

## 2. BACKGROUND AND INTRODUCTION

*The background should include a clear explanation of the main research question along with a full literature review, a detailed justification for the study and discussion of its feasibility.*

- *Background on the disease to be studied, focusing on the need for new therapy development. Inventory of the treatments known to be active.*
- *Give a brief overview of the incidence, therapeutic policies and outcome of the disease type(s) addressed in the study.*
- *Precise details of the literature search: your review should make reference to relevant papers, unpublished works as well as clinical experience.*
- *A statement indicating the size of the problem (and effect on the health service) and why the study is appropriate*
- *Discuss the feasibility of the study in terms of subject and data availability as well as length.*

## 3. RATIONALE OF THE STUDY

*Describe the rationale for the study overall and its relevance to the research area. Explain the potential benefits to the health service and what your study will add to the body of evidence already available.*

## 4. OBJECTIVES OF THE STUDY

*This section has to be written by the study coordinator after discussion with the statistician.*

### 4.1 General objectives

*A detailed description of the primary and secondary or explanatory objectives of the study should be included in this section. Distinguish primary and secondary objectives.*

### 4.2 Endpoints

#### 4.2.1 Primary endpoint

*Specify which primary endpoint (outcome measures) will be used to evaluate the principal objective of the study. The principal endpoint should be objectively measurable in all eligible patients. It will form the basis of the statistical design and sample size computation.*

#### 4.2.2 Secondary endpoint

## 5. PATIENT SELECTION CRITERIA

*The following items are generally used in the definition of selection (eligibility) criteria:*

### 5.1 Inclusion criteria

- *age, gender, race*
- *diagnosis, method of diagnosis, diagnostic test result requirements*
- *prior treatments required / allowed / not allowed*
- *disease type (severity of symptoms and signs of the disease)*

- *ability to give informed consent.*
- *other criteria related to the safety*

## **5.2 Exclusion criteria**

- *previous medical history*
- *pregnancy, childbearing potential*
- *current or past therapy*
- *severity of disease*
- *current medical conditions*
- *a minimum of time since the last clinical study*
- *upper/lower limits of laboratory tests that will disqualify potential subjects should be provided*

## **6. STATISTICAL CONSIDERATIONS**

*This section has to be written by the statistician of the study.*

### **6.1 Sample size**

- *Details of the precision or power calculation used to estimate the required sample size based on primary outcome*
- *Statistical assumptions regarding distribution*
- *Estimates of difference to be detected along with appropriate justification*
- *Chosen levels of significance and power.*
- *Reference or details of method/formula used for the calculation*

### **6.2 Analysis**

- *Describe which variables will be used to assess groups comparability and how they will be reported (e.g. means, proportions)*
- *Description of primary and secondary analyses including summary measures used, methods of analysis (e.g. t-test, logistic regression) and how the results will be reported (e.g. odds ratios with 95% confidence intervals)*
- *Details of adjustments for predefined confounders.*
- *Approach used to deal with missing data and loss to follow-up.*
- *When will the analysis be done and by whom*
- *Details of how any planned subgroup analyses will be done*

## **7. FORMS AND PROCEDURES FOR COLLECTING DATA AND DATA MANAGING**

- *Describe procedures for data collection and recording (software to be used, location of the data etc)*



- *Detail methods implemented to ensure validity and quality of data (e.g. double entry, cross validation etc, Security / storage of data and records retention (duration and location)*

*Data to be collected should be identified early in the protocol development phase.*

*CRF is the primary data collection instruments for the study. All data requested on the CRF must be recorded, and any missing data must be explained. If a space is left blank because the procedure was not done or the question was not asked, "N/D" must be noted. If the item is not applicable to the individual case "N/A" must be noted.*

## 8. ETHICAL CONSIDERATIONS

### 8.1 Patient protection

The responsible investigator will ensure that this study is conducted in agreement with either the Declaration of Helsinki, Good Clinical Practice and the regulations of the country.

The protocol and its annexes are subject to review and approval by the competent Ethics Committee(s).

### 8.2 Subject identification – Personal Data protection

A specific (computerized) system is set up to collect data in order to ensure privacy of patients included in the study. Patients will be identified in the study by the unique progressive number (UPN). This number will be used instead of the internal code of the hospital or other sensible identification data. All data records and study reports will be treated anonymously by coordinating data center, where no personal data to identify patient will be recorded. The mapping from anonymized code and patient information is resolved in a table of the database, but accessible only with specific authorizations.

Combined identification codes/passwords before access is granted to the computerized system and at the start of a data entry session. SSL connection is used to assure secure data transactions.

To guarantee the secrecy of the data, but also to avoid manipulation and loss of data, precautionary action (hardware and software) are taken.

In particular:

1. Access to data collected from the participating centres is reserved only to authorized personnel designed by the Sponsor
2. The data-collection network is protected by a firewall
3. The internet connection is encrypted with a digital certificate (SSL technology)
4. The database is located on a server that is protected with a password, that is changed periodically
5. Access to the database is protected with a password and is only accessible by responsible persons designed by the Sponsor
6. Periodical back-ups will guarantee secure copies, to allow retrieval of both stored data and the data collection system
7. The patient is registered and identifiable with a code, to guarantee anonymity

All information regarding study supplied by Sponsor (*FROM – E.T.S. or ASST*) to the investigator is privileged and confidential information. The investigator agrees to use this information to accomplish the study and will not use it for other purposes without consent from Sponsor(*FROM – E.T.S. or ASST*).

The investigator agrees to keep in confidence all the results obtained from the study. Such information shall not be disclosed to third parties without prior written permission from Sponsor, except to regulatory authority(ies), when requested.

### 8.3 Informed consent

Documented informed consent concerning the use of data and privacy protection will be obtained for all patients alive and actively followed-up at time of research starting. The consent will be compliant to the European General Data Protection Regulation (GDPR) 2016/679

## 9. DATA OWNERSHIP

According to the ICH Guidelines on Good Clinical Practice the sponsor of a study is the owner of the data resulting therefrom. All centers and investigators participating in the study should be made aware of such circumstance and invited not to disseminate information or data without the Institution's prior express consent.

## 10. PUBLICATION POLICY

After completion of the study, the Coordinating Investigator will prepare a Clinical Study report. In addition, the Coordinating Investigator will prepare a draft manuscript containing the study results on the basis of the statistical analysis. The manuscript will be reviewed by the co-authors for comments and after revision sent to a scientific journal.

All publications, abstracts, presentations, manuscripts and slides including data from the present study will be submitted to and reviewed by the Study Coordinator

*Specific advance periods for submission and review may be specified in the protocol.*

## 11. STUDY TIMETABLE

*Duration of enrolment:*

*Expected FPI:*

*Expected LPO:*

*Expected LPLV:*

## 1. REFERENCES

*This is the bibliography section for any information and publications cited in the protocol. It should be organized as any standard bibliography page.*

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*List of ANNEXES to be attached to the protocol*