|  |  |
| --- | --- |
| Checklist: Non-interventional Study Protocol (Primary Data Collection)  Diese Checkliste für die Erstellung eines Studienprotokolls dient lediglich zur Information. Gerne dürfen Sie diese Checkliste für die Erstellung Ihres Studienprotokolls nutzen. Selbstverständlich steht es Ihnen frei Ihre eigenen Dokumente zu verwenden. | |
| **TITLE:** |  |
| PROTOCOL NUMBER: | incl. Roche number |
| VERSION NUMBER: |  |
| DATE FINAL: |  |
| STUDIED MEDICINAL PRODUCT{S}: |  |
| STUDY INITIATOR: |  |
| AUTHOR: |  |
| RESEARCH QUESTION AND OBJECTIVES: |  |

|  |
| --- |
|  |
| Signatures |

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# LIST OF ABBREVIATIONS

| Abbreviation | Definition |
| --- | --- |
|  |  |

# 

# Synopsis

|  |  |
| --- | --- |
| **TITLE** |  |
| PROTOCOL NUMBER |  |
| VERSION NUMBER |  |
| DATE OF SYNOPSIS |  |
| STUDIED MEDICINAL PRODUCT{S} |  |
| INDICATION: |  |
| STUDY INITIATOR: |  |
| RATIONALE AND BACKGROUND |  |
| RESEARCH QUESTION AND OBJECTIVES |  |
| STUDY DESIGN |  |
| DATA SOURCES |  |
| POPULATION |  |
| VARIABLES |  |
| STUDY SIZE |  |
| DATA ANALYSIS |  |
| MILESTONES |  |

# PROTOCOL Amendments and updates

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Amendment/ Update Number | Date | Section of Study Protocol | Amendment  or Update | Reason |
| 1 | {Date} | {Section no.} | {Short description} | {Reason} |
| 2 | {Date} | {Section no.} | {Short description} | {Reason} |
| {Number} | {Date} | {Section no.} | {Short description} | {Reason} |

# Rationale and Background

Brief paragraph describing the disease and current therapies.

A critical and thorough review of the literature usually aims at evaluating the pertinent information and at identifying gaps in knowledge. The findings of similar studies should be mentioned and gaps in knowledge that the study is intended to fill should be described.

Short description of the scientific rationale that led to the initiation of the study and a short critical review of available published and unpublished data to explain gaps in knowledge that the study is intended to fill. Include references to relevant literature.

Brief paragraph describing the disease and current therapies. Describe unmet needs related to the disease.

# Research question and Objectives

## Research Question

Define a research question that explains how the study will address the issue which led to the study being initiated or imposed, and research objectives, including any pre-specified hypotheses and main summary measures. Objectives should be organized as primary or secondary objectives where applicable.

## Objectives

The objectives need to be detailed enough to define the specific scientific questions being studied. General statements such as “determination of safety and effectiveness” are not adequate objectives.

# Research methods

## Study Design

Describe the overall research design and rationale for this choice. specifying the study design proposed (e.g. cohort, case-control, etc.) and any comparison groups. The primary and secondary endpoints and the main measure(s) of effect should be mentioned. The strength of the study design to answer the research question may be explained in this section.

### Overview of Study Design

Include key design features:

Indicate the scope of the study

Name the target population

Specify medicine and mention that its use according to national labeling and local standard of care will be observed. Justification for off-label use is mandatory.

Identify and give the length of the study periods (e.g., treatment, follow-up). Indicate the study duration for each patient, as well as an approximate length of the entire study, from first data collection to “end of study.”

Specify the approximate number and general location of sites (e.g., United States, Europe).

Indicate if patient and/or site recruitment will be done in stages. If so, consider the strategy of opening a few sites at the beginning, before expansion is considered.

For complex studies, it is useful to provide a table or a diagram of the study design (i.e., study schema).

Do not include details regarding the study population, study variables, or statistical analyses because these will be extensively described in other sections.

### Number of Patients Observed in the Study

Provide number of patients to be included.

## Population

Describe study population defined in terms of persons, study time period, and selection criteria, including the rationale for any inclusion and exclusion criteria and their impact on the number of patients available for analysis.

Plans for baseline visits and follow-up visits should be described. Representativeness of the study population as regards the source population should be addressed. Where any sampling from a source population is undertaken, description of the source population and details of sampling methods should be provided.

## Variables

Definition of exposures, outcomes, and other variables including measured risk factors, co-morbidities, co-medications, etc., with operational definitions and measurement; potential confounding variables and effect modifiers should be specified.

### Primary Variables

### Secondary Variables

## Data Sources

Describe strategies and data sources for determining exposures, outcomes and all other variables relevant to the study objectives.

## Data Management

Describe data management and data checking programs to be used in the study, including procedures for data collection, retrieval, collection, and preparation.

Provide description of any mechanisms and procedures to ensure data quality and integrity, including accuracy and legibility of collected data and original documents, extent of SDV and validation of endpoints, storage of records and archiving of statistical programs. As appropriate, certification and/or qualifications of any supporting laboratory or research groups should be included.

### Data Quality Assurance

### Electronic Case Report Forms

### Source Data Documentation

## Statistical Considerations

Describe the major steps that lead from raw data to a final result, including methods used to correct inconsistencies or errors, impute values, modify raw data, categorize, analyze and present results, and procedures to control sources of bias and their influence on results; statistical procedures to be applied to the data to obtain point estimates and confidence intervals of measures of occurrence or association, and sensitivity analyses. The primary analyses should be clearly differentiated from sub-group analyses and secondary analyses.

This section must be consistent with the Data Analysis section of the synopsis, but it may contain more detail.

### Effectiveness Analyses

Specify definitions of outcome measures/variables in effectiveness analyses and how they will be analyzed: either all enrolled patients as described in the protocol or all enrolled patients as described in the protocol and have at least one post-baseline outcome/ variable/ measurement.

### Safety Analyses

Specify definitions of outcome measures/variables in safety analyses and how they will be analyzed.

### Other Analyses [If applicable]

Specify other types of analyses, e.g., analysis of patient subgroups or exploratory statistical modeling work addressing additional questions, patient disposition, patient demographics, Quality of Life analyses...

### Interim and Final Analyses and Timing of Analyses

Specify reasons for interim analyses and their timing. Mention if interim analyses are planned.

### Determination of Sample size

Provide number of patients to be included and if applicable the number of treatments (in case more than one medicinal product is included). Determination of sample size or different scenarios for sample size under different assumptions must be in the document.

## Study Documentation, Monitoring, and Administration

### Study Documentation

### Site Audits and Inspections

### Retention of Records

### Administrative Structure

## Limitations of the Research Method

Describe any potential limitations of the study design, data sources, and analytical methods, including issues relating to confounding, bias, generalizability, and random error. The likely success of efforts taken to reduce errors should be discussed.

# Protection of human subjects

Provide safeguards in order to comply with national and European Union requirements for ensuring the well-being and rights of participants in non‑interventional post-authorization safety studies.

## Compliance with Laws and Regulations

## Informed Consent

## Institutional Review Board or Ethics Committee

## Confidentiality

# Management and Reporting of Adverse Events/ Adverse Reactions

Describe procedures for the collection, management and reporting of individual cases of adverse events/adverse reactions and other medically important events while the study is being conducted that might influence the evaluation of the benefit-risk balance of the studied medicinal product while the study is being conducted.

## Safety Parameters and Definitions

## Methods and Timing for Capturing and Assessing Safety Parameters

### Adverse Event Reporting Period

### Procedures for Recording Adverse Events

# Publication of Data

# References