|  |  |
| --- | --- |
| Checklist: Non-interventional Study Protocol  (Secondary 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 |

# TABLE OF CONTENTS

1. LIST OF ABBREVIATIONS 4

2. Responsible Parties 5

3. Synopsis 6

4. Amendments and updates 7

5. Milestones 7

6. Rationale and Background 7

7. Research Question and Objectives 8

8. Research methods 8

8.1 Study Design 8

8.2 SETTING 8

8.3 Variables 8

8.3.1 Primary Variables 8

8.3.2 Secondary Variables 8

8.4 Data Sources 9

8.5 Study Size 9

8.6 Data Management 9

8.7 Data Analysis 9

8.7.1 Effectiveness Analyses 10

8.7.2 Safety Analyses 10

8.7.3 Other Analyses 10

8.7.4 Interim and Final Analyses and Timing of Analyses 10

8.7.5 Determination of Sample size 10

8.8 Quality Control 10

8.9 Limitations of the research method 10

8.10 Other aspects 10

9. Protection of Study Participants 11

9.1 Informed Consent 11

9.2 Institutional Review Board or Ethics Committee 11

10. Management and Reporting of Adverse Events 11

11. Plans for disseminating  
and communicating study results 11

12. References 11

# LIST OF ABBREVIATIONS

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

# Responsible Parties

# 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 |  |

# Amendments and updates

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Number | Date | Section of  study protocol | Amendment  or update | Reason |
| 1 | Date | Text | Text | Text |
| 2 | Date | Text | Text | Text |
| … | Date | Text | Text | Text |

# Milestones

Planned dates for study milestones should be indicated in a table as indicated below. Start of data collection and End of data collection are defined in Module VIII of the GVP. Other important timelines can be added.

|  |  |
| --- | --- |
| Milestone | Planned Date |
| First Data Extraction |  |
| Last Data Extraction |  |
| Interim report |  |
| Final report of study results (CSR) |  |
| Publication submission |  |

# Rationale and Background

Short description of the study background and short critical review of available published and unpublished data to explain gaps in knowledge that the study is intended to fill. The review may encompass relevant animal and human experiments, clinical studies, vital statistics and previous epidemiologic studies. The review should cite the findings of similar studies, and the expected contribution of the current study.

# Research Question and Objectives

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 organised as primary or secondary objectives where applicable.

# Research methods

## Study Design

Overall research design and rationale for this choice. 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.

## SETTING

Setting and study population defined in terms of persons, place, study time period, and selection criteria, including the rationale for any exclusion criteria and their impact on the number of subjects 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. Where the study design is a systematic review or a meta-analysis, the criteria for the selection and eligibility of studies should be explained.

## 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

Strategies and data sources for determining exposures, outcomes and all other variables relevant to the study objectives, such as potential confounding variables and effect modifiers. Where the study is based on secondary analysis an existing data source, such as electronic health records or claims databases, any information on the validity of the recording and coding of the data should be reported. For exposures or outcomes not previously validated, validation performed in the study should be described or otherwise addressed. Linkage methods between data sources should be described as appropriate. If data collection methods or instruments are tested in a pilot study, plans for the pilot study should be presented. If a pilot study has already been performed, a summary of the results should be reported. Involvement of any expert committees to validate diagnoses should be stated. In case of a systematic review or meta-analysis, the search strategy and processes and any methods for confirming data from investigators should be described.

## Study Size

Any projected study size, precision sought for study estimates and any calculation of the sample size that can minimally detect a pre-specified risk with a pre-specified statistical precision. All assumptions used to calculate the study size or precision of the study should be presented and justified.

## Data Management

Data management and statistical software(s) to be used in the study, including procedures for data collection, retrieval, collection and preparation.

Data collection methods and tools (e.g. paper-based or electronic case reporting forms, monitoring if any and supervision) can be summarised in this section and fully described or presented in an Annex.

## Data Analysis

Rationale for the choice of statistical techniques and major steps that lead from raw data to a final result, including methods used to correct inconsistencies or errors, impute values, modify raw data, categorise, analyse 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.

### 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.

## Quality Control

Description of any mechanisms and procedures to ensure data quality and integrity, including accuracy and legibility of collected data and original documents, extent of source data verification and validation of endpoints, storage of records and archiving of the statistical programming performed to generate the results. As appropriate, certificationand/or qualifications of any supporting laboratory or research groups should be included.

## Limitations of the research method

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

## Other aspects

Any other aspect of the research method not covered by the previous sections.

# Protection of Study Participants

Safeguards in order to comply with national and European Union requirements for ensuring the well-being and rights of participants in non-interventional studies.

## Informed Consent

## Institutional Review Board or Ethics Committee

# Management and Reporting of Adverse Events

Procedures for the collection, management and reporting of individual cases of adverse events/adverse reactions (see GVP Module VI) and of any new information that might influence the evaluation of the benefit-risk balance of the product while the study is being conducted if applicable.

# Plans for disseminating and communicating study results

# References