CLINICAL TRIALS – GERMAN<>ENGLISH

AN INTRODUCTION TO PROCEDURES
AND ENGLISH<>GERMAN TERMINOLOGY

OUTLINE

I. INTRODUCTION

- Clinical trials are conducted to test the **EFFICACY** and **SAFETY** of medications, medical devices, or other methods of treatment in humans who **VOLUNTARILY** participate in these studies.
- **The terms "study" and "trial" are synonymous**.
- Clinical studies follow **preclinical investigations** that include:
  - in vitro studies (studies performed with cell cultures) and
  - **in vivo studies** (studies with animals).
- Preclinical studies are conducted over several years, and only a small percentage of these studies lead to clinical studies.
- Since results from animal studies cannot be extrapolated to the use in humans, **patients may or may not benefit from participating in a clinical study.**

FOUR MAJOR REQUIREMENTS FOR CLINICAL STUDIES

1. Controlled
2. Randomized
3. Blinded
4. Ethical principles must be followed

1. CLINICAL TRIALS MUST BE <u>CONTROLLED (KONTROLLIERT)</u>

Treatment with study drug versus no treatment OR standard treatment

Study drug, Investigational product Studienpräparat, Prüfpräparat	Treatment group, Investigational group Behandlungsgruppe
Comparator, Comparator product Vergleichspräparat	Control group Kontrollgruppe

2. CLINICAL TRIALS MUST BE <u>RANDOMIZED (RANDOMISIERT)</u>

Random allocation to one or more treatment groups and at least one control group

3. CLINICAL TRIALS MUST BE <u>BLINDED (VERBLINDET)</u>

Double-blind trial Doppelblindstudie	Patient AND physician are "blind"
Single-blind trial Einfachblindstudie	Patient OR physician are "blind"

Placebo: - Pill or liquid without active substances
- looks exactly the same as the study drug
- used as comparator

4. CURRENT ETHICAL PRINCIPLES MUST BE FOLLOWED

- Study participation must be voluntary
- Unnecessary suffering must be avoided
- Informed Consent must be signed by the study participant

II. LANDMARKS IN THE HISTORY OF CLINICAL TRIALS

- **FIRST CONTROLLED TRIAL**
  1747 by James Lind on board of a ship
  Treated disease: scurvy
  Study drug: 2 oranges and 1 lemon/day
  Comparators: cider, vinegar, nutmeg, seawater and others
  Results: Citrus fruits were effective, none of the comparators were effective
- **FIRST RANDOMIZED TRIAL**
  1896/97 by Johannes Fibiger in Denmark
  Treated disease: diphtheria
  Study group: antiserum + standard therapy
  Control group: standard therapy only
  Randomization: allocation of newly admitted patients to the hospital on alternating days to treatment group or control group
  Outcome measure: mortality
  Results: 8 of 239 patients in the treatment group and 30 of 245 patients in the control group died

HISTORY (cont.)

- **FIRST BLINDED TRIAL**
  1948 by the Medical Research Council in London
  Treated disease: Pulmonary tuberculosis
  Study group: Streptomycin + bed-rest
  Control group: Bed-rest only
  Blinding: Radiologists who compared the x-rays before and after treatment were blinded
  Outcome measures: Radiological improvement, mortality
  Results:

	Study Group	Control Group
Radiological Improvement	27 of 55 (51%)	4 of 52 (8%)
Death within 6 months	4 of 55 (7%)	14 of 52 (27%)

HISTORY (cont.)

- **ETHICAL PRINCIPLES**
  First introduced in 1949 by the Nuremberg Code, written after the Nuremberg trials

  Major principles of the Nuremberg Code:
  - The voluntary consent of the subject is essential
  - Unnecessary suffering and injury should be avoided
  - The subject must be free to withdraw from the study at any time and for any reason

  Declaration of Helsinki 1964
  Issued by the World Medical Assembly and amended several times (last time 2002)
  - Ethical principles of the Nuremberg Code were adopted
  - Informed Consent was declared a "major requirement for ethical research"

HISTORY (cont.)

- **Belmont Report**
  - Issued in 1979 in response to the **Tuskegee Syphilis Study** (1932-1972) by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research
  - Tuskegee Study: 399 African American men with syphilis were monitored but did not receive treatment, in particular no penicillin when it became available in the late 1940s.
  - The report includes three principles: Respect for persons, beneficence, justice
  - The report led to the establishment of Institutional Review Boards (Ethics committees)

III. PREPARATION OF A CLINICAL TRIAL

- STUDY PROTOCOL – PRÜFPLAN
- PATIENT INFORMATION AND INFORMED CONSENT – PATIENTENINFORMATION UND EINWILLIGUNGSERKLÄRUNG
- INVESTIGATOR'S BROCHURE – PRÜFARZTBROSCHÜRE
- CASE REPORT FORM (CRF) – PRÜFBOGEN
- ADDITIONAL DOCUMENTS

STUDY PROTOCOL - PRÜFPLAN

1. Study title
2. Sponsor´s name and contact information
3. Investigator´s/principal investigator´s name and contact information
4. Description of the background and objectives of the study
5. Study design
   - Experimental design
   - Study population
   - Inclusion and exclusion criteria
   - Sample size
   - Recruitment procedures
   - Screening procedures
   - Randomization
   - Blinding method
   - Drug administration schedule
   - Study procedures
   - Endpoints
   - Safety monitoring
   - Unblinding
   - Statistical methods

1. Studientitel
2. Name und Kontaktinformation des Sponsors
3. Name und Kontaktinformation des Prüfers/Hauptprüfers
4. Beschreibung des Hintergrunds und der Ziele der Studie
5. Studiendesign
   - Experimentelles Design
   - Studienpopulation
   - Einschluss- und Ausschlusskriterien
   - Fallzahl, Stichprobengröße
   - Rekrutierung
   - Screening
   - Randomisierung
   - Verblindungsmethode
   - Medikamentenverabreichung
   - Studienablauf und Untersuchungsmethoden
   - Endpunkte
   - Erfassung der Sicherheit
   - Entblindung
   - Statistische Methoden

STUDY PROTOCOL (cont.)

Detailed plan of a clinical study and most important document for conducting a clinical study.

1. STUDY TITLE **STUDIENTITEL**

[for example: A randomized, double-blind, placebo-controlled, multicenter study on the treatment of stage III melanoma with XXX]

2. SPONSOR'S NAME AND CONTACT INFORMATION **NAME UND KONTAKTINFORMATION DES SPONSORS**

A sponsor is an individual, company (e.g., pharmaceutical company) or institution that takes the responsibility to initiate, manage, and finance a clinical study

STUDY PROTOCOL (cont.)

3. INVESTIGATOR'S NAME AND CONTACT INFORMATION **NAME UND KONTAKTINFORMATION DES PRÜFARZTES (PRÜFERS)**

The investigator
- must have appropriate qualifications und prove them
- is responsible for writing the protocol
- is responsible for preparing the trial
- is responsible for conducting the trial including medical management of study participants (subjects) **Studienteilnehmer (Probanden)**

If there is more than one investigator, one of them is the leader and is called principal investigator **Hauptprüfer (Leiter der klinischen Prüfung, LKP)**

Investigator Sponsored Trial (IST): Sponsor = Investigator

STUDY PROTOCOL (cont.)

4. DESCRIPTION OF THE BACKGROUND AND OBJECTIVES OF THE STUDY
BESCHREIBUNG DES HINTERGRUNDS UND DER ZIELE DER STUDIE

including

- a literature overview of the symptoms and course of the treated disease
- currently available treatment

STUDY PROTOCOL (cont.)

5. STUDY DESIGN **STUDIENDESIGN**
Plan for procedures before, during and after the study

_ **Experimental design** **Experimentelles Design**

_ **Study population** **Studienpopulation**
Defined by inclusion and exclusion criteria

_ **Inclusion and exclusion critieria** **Einschluss- und Ausschlusskriterien**
Determine eligibility of a patient. Criteria include among others:
- Age range
- Gender
- Stage of disease
- Concomitant diseases
- Previous treatments

STUDY PROTOCOL (cont.)

_ **Sample size** **Fallzahl, Stichprobengröße**
Number of participating subjects calculated with statistical methods taking expected results into account

_ **Recruitment procedures** **Rekrutierung**
- Public listings (e.g., Internet)
- Public notices in newspapers and journals,
- Announcements on radio and TV
- Through the patient's physician or other health care providers

Potential patients receive a Patient Brochure **Patientenbroschüre**
(= Patient Information Sheet)
The broschure includes:
- investigator's name and contact information
- information about the tested drug, risks and potential benefits, screening, randomization and blinding, and other procedures before and during the study.

STUDY PROTOCOL (cont.)

- Screening procedures — Screening
  Determination of eligibility of a potential subject for a specific study using inclusion and exclusion criteria
  Procedures Include:
  - History and physical examination
  - Laboratory tests
  - Imaging procedures

- Randomization method — Randomisierungsmethode
  Most common methods include:
  - Simple randomization: Equivalent to tossing coins for each subject
  - Block randomization: Patients are divided into two or more blocks of equal size and the blocks are randomized to treatments.
  - Stratified randomization: Patients are divided into blocks according to certain characteristics such as age range or gender, and the blocks are randomized to treatments.

STUDY PROTOCOL(cont.)

- Blinding method — Verblindungsmethode

- Single-blind
- Double-blind
- Triple-blind — Dreifachblind

Double blind study, in which data management staff and/or physicians (e.g., radiologists) and/or statisticians interpreting and analyzing results are also blinded

STUDY PROTOCOL (cont.)

- Dosages, administration schedule, and route of administration of the investigational product and comparator(s) — Dosierung, Applikationsart

- Study Procedures (Study activities) — Studienablauf und Untersuchungsmethoden

For example:
- Method of dispensing medications to the patient
- Schedule of baseline and follow-up visits and procedures at each visit (e.g., physical examination, laboratory tests, imaging procedures, ECG)
- Methods for evaluation of results:
  a. Data acquisition and collection methods
  b. Statistical methods

STUDY PROTOCOL (cont.)

- Endpoints: — Endpunkte:

Outcome measures (Zielkriterien) related to EFFICACY and SAFETY

Primary endpoints (Primare Endpunkte): direct measures of the response to treatment (e.g., remission) or lack of response (e.g., tumor progression).

Secondary endpoints (Sekundäre Endpunkte): measures related to primary endpoints such as quality of life, duration of remission, survival, or laboratory values.

STUDY PROTOCOL (cont.)

_ Safety Monitoring	_ Erfassung der Sicherheit
1. Adverse Events (AE) Any medical event (including intercurrent diseases and accidents - that occurs under treatment with a medicinal product and - does not necessarily have a causal relationship with the treatment.	1. Unerwünschte Ereignisse (UE) Jedes unerwünschte medizinische Ereignis (einschließlich interkurrenter Erkrankungen und Unfälle), - das unter Behandlung mit einem Arzneimittels auftritt und - nicht unbedingt in ursächlichem Zusammenhang mit dieser Behandlung steht.

STUDY PROTOCOL(cont.)

_ Safety Monitoring	_ Erfassung der Sicherheit
2. Adverse Drug Reactions (ADR) Any unintended, harmful or unpleasant response to a medicinal product that occurs under treatment with a medicinal product at any dose used for ▪ diagnosis, prophylaxis or treatment of diseases or ▪ modification of physiological functions The response is such that there is a reasonable possibility that the adverse reaction was caused by the medicinal product.	2. Unerwünschte Arzneimittelwirkungen (UAW) Alle unbeabsichtigten, schädlichen bzw. unangenehmen Arzneimittelwirkungen unabhängig von der Dosis bei Anwendung des Arzneimittels zur ▪ Diagnose, Prophylaxe oder Behandlung einer Krankheit oder ▪ zur Modifikation physiologischer Funktionen, wobei ein kausaler Zusammenhang mit dem Arzneimittel angenommen werden kann.

STUDY PROTOCOL (cont.)

_ Safety Monitoring	_ Erfassung der Sicherheit
3, Serious Adverse Events (sAE) and Serious Adverse Drug Reactions (sADR) Any adverse experience at any dose that ▪ is fatal or life threatening, ▪ is permanently disabling, ▪ results in hospitalization or prolongation of hospitalization ▪ results in a persistent or significant disability/incapacity, or a congenital anomaly/birth defect (ICH).	3. Schwerwiegende unerwünschte Ereignisse (SUE) und schwerwiegende unerwünschte Arzneimittelwirkungen (schwerwiedende UAW) Jedes unerwünschte Ereignis, das unabhängig von der Dosis ▪ tödlich oder lebensbedrohlich ist ▪ eine stationäre Behandlung oder deren Verlängerung erforderlich macht, ▪ zu einer bleibenden oder schwerwiegenden Behinderung oder Invalidität führt oder eine angeborene Missbildung bzw. eine angeborene Anomalie darstellt (ICH).

STUDY PROTOCOL (cont.)

- **Safety Monitoring** • **Erfassung der Sicherheit**

THE FOLLOWING MUST BE DETERMINED:

- **Methods for monitoring safety**
- **Person who is responsible for identifying, recording, and reporting AEs, ADRs, sAEs, and sADRs**
- **Frequency of reporting ADR and AE**
- **Criteria for discontinuing a patient due to an ADR**
- **Criteria for terminating a study due to an ADR**

STUDY PROTOCOL (cont.)

_ Unblinding **_ Entblindung**

a. Unblinding after completion of the study
Identification of the treatment code and revealing the treatment to the subject, the investigator, and the study staff.

b. Unblinding before completion of the study
- not allowed unless knowledge of the administered drug is absolutely necessary for treatment of adverse reactions or intercurrent diseases.
- The premature unblinding procedures described in the protocol must be followed.
- In most cases, the sponsor must be informed and will give permission if necessary.

_ Analysis and assessment of study results **_ Analyse und Beurteilung der Studienergebnisse**
I
including methods of statistical analysis

INFORMED CONSENT – EINWILLIGUNGSERKLÄRUNG

Presented and explained to the patient during the screening or a separate visit. Verification of the patient's voluntary participation in the study after receiving information about the trial including:

_ Purpose of the study	_ Zweck der Studie
_ Description of the study	_ Beschreibung (Ablauf) der Studie
_ Potential risks and discomforts	_ Potenzielle Risiken und Beschwerden
_ Potential benefits	_ Potenzielle Nutzen
_ Alternative treatments	_ Alternative Behandlungen
_ Right to withdraw from the study at any time	_ Recht aus der Studie jederzeit auszuscheiden
_ Costs, reimbursement, compensation	_ Kosten, Kostenersatz, Vergütung
_ Confidentiality agreement	_ Wahrung der Vertraulichkeit (Schweigepflicht)
_ Signature of the study participant or his legal guardian and the investigator	_ Unterschrift des Studienteilnehmers oder seine gesetzlichen Vormundes und des Prüfers

INVESTIGATOR'S BROCHURE - PRÜFARZTBROSCHÜRE

The brochure is provided to the Investigator before initiation of the study and must contain the following:

Description of the study drug and its formulation	Beschreibung des Studienpräparates und seiner Formulierung
Pharmacological and toxic effects of the study drug in animal experiments	Pharmakologische und toxische Wirkungen des Studienpräparates in Tierexperimenten
Anticipated possible risks and adverse reactions	Erwartete Risiken und unerwünschte Arzneimittelwirkungen

As soon as **clinical data** on risks, safety, and efficacy are available, they must be **included** in the Investigator's Brochure **before** further clinical investigations are conducted.

CASE REPORT FORM (CRF) - PRÜFBOGEN

- A printed or electronic questionnaire
- Designed by the sponsor
- Purpose: To report to the sponsor all information on each subject as outlined in the protocol

The CRF contains but is not limited to:

Contact information of the investigator	Kontaktinformation des Prüfers
Contact information of the subject (patient)	Kontaktinformation des Probanden (Patienten)
History of the subject	Anamnese (Krankengeschichte)
Physical examination at baseline and follow-up visits	Körperliche Untersuchung bei der Baseline- und weiteren Klinikbesuchen (Visiten)
Laboratory values at baseline and follow-up visits	Laborwerte bei der Baseline- und weiteren Klinikbesuchen
Results of imaging procedures at baseline and follow-up visits	Ergebnisse bildgebender Verfahren bei der Baseline- und weiteren Klinikbesuchen
Adverse events and adverse reactions	Unerwünschte Ereignisse und unerwünschte Arzneimittelreaktionen

ADDITIONAL DOCUMENTS (Examples)

- Data acquisition, collection and management procedures
- Manual of study activities (procedures)
- Guidelines for collaborating with the laboratory, radiology department and other involved departments
- Guidelines for collaborating with the pharmacy, including distribution and dispensing of medications
- Guidelines for interactions between the participating centers
- Computer programs for scheduling appointments for follow-up visits
- Training material for clinic staff and other staff involved in the study

IV. ETHICAL ASPECTS A. CONDUCTION OF THE STUDY

INTERNATIONAL CONFERENCE ON HARMONIZATION (ICH)	INTERNATIONALE HARMONISIERUNGSKONFERENZ
GOOD CLINICAL PRACTICE (GCP)	GUTE KLINISCHE PRAXIS
STANDARD OPERATING PROCEDURES (GCP)	STANDARDARBEITSANWEISUNGEN

The **ICH** is an International body that
- Issues **GOOD CLINICAL PRACTICE (GCP)** RECOMMENDATIONS
- Defines **STANDARD OPERATING PROCEDURES (SOPs).** The ICH GCP recommendations are defined in the **Harmonized ICH Guidelines for the EU, Japan and the US**

- In Germany, compliance with GCP is regulated by the drug law (**Arzneimittelgesetz**, AMG)
- American GCP are codified in the **Code of Federal Regulations**

ETHICAL ASPECTS (cont.) A. CONDUCTION OF THE STUDY (cont.)

GOOD CLINICAL PRACTICE (GCP):
International standard for ethical and scientific quality of clinical trials
Includes standards for:
- Design
- Conduct
- Monitoring
- Recording
- Analysis of results

STANDARD OPERATING PROCEDURES (SOPs):
"Detailed written instructions to achieve uniformity of the performance of a specific function" (ICH definition)

SOPs must be prepared for each individual or group of individuals with the same function, including (but not limited to):
- Sponsor
- Monitor
- Investigator
- Clinic staff
- Institutional Review Board (Ethics Committee)

ETHICAL ASPECTS (cont.) A. CONDUCTION OF THE STUDY (cont.)

STANDARD OPERATING PROCEDURES (SOPs) (cont.)
- SOPs must be prepared by the institution that conducts the trial, in cooperation with the sponsor
- SOPs must be prepared according to GCP recommendations

EXAMPLE: The **SOPs for the Investigator** include (but are not limited to):

- Review the investigator's brochure and the literature on the investigational product
- Review and discuss Good Clinical Practice (GCP) guidelines and the study protocol with the monitor
- Ensure that procedures described in the protocol are applicable to the study center
- Ensure that there is enough staff available for study procedures and emergencies
- Ensure safety conditions for subjects
- Ensure availability of needed equipment

ETHICAL ASPECTS (cont.) B. EVALUATION OF DOCUMENTS AND CONDUCTION OF THE STUDY

INSTITUTIONAL REVIEW BOARDS (IRBs) = INDEPENDENT ETHICS COMMITTEES (IECs)	INSTITUTIONELLE PRÜFUNGSKOMMISSIONEN = UNABHÄNGIGE ETHIKKOMMISSIONEN
FOOD AND DRUG ADMINISTRATION (FDA)	AMERIKANISCHE ZULASSUNGSBEHÖRDE FÜR LEBENSMITTEL UND ARZNEIMITTEL
GERMAN FEDERAL INSTITUTE FOR DRUGS AND MEDICAL DEVICES	BUNDESINSTITUT FÜR ARZNEIMITTEL UND MEDIZINPRODUKTE (BfArM)
EUORPEAN MEDICINES AGENCY (EMEA)	EUROPÄISCHE ARZNEIMITTELAGENTUR

ETHICAL ASPECTS (cont.) B. EVALUATION OF DOCUMENTS AND THE CONDUCTION OF THE STUDY (cont.)

INSTITUTIONAL REVIEW BOARDS (IRBs)/INDEPENDEN ETHICS COMMITTEES

IRBs are responsible for the **ETHICAL CONDUCT OF CLINICAL TRIALS ACCORDING TO GOOD CLINICAL PRACTICE (GCP)**

IRBs consist of:
- Physicians
- Researchers
- Statisticians
- Community advocates

In the **US**, IRBs are regulated by the **Office for Human Research Protection** which is part of the **Department of Health and Human Services (DHHS)**

In **Germany**, IRBSs are accredited and registered by the **Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM)**

ETHICAL ASPECTS (cont.)
B. EVALUATION OF DOCUMENTS AND THE CONDUCTION OF THE STUDY (cont.)

FOOD AND DRUG ADMINISTRATION (FDA)

- An agency of the Department of Health and Human Services (DHHS)
- Responsible for regulating foods, drugs, and other dietary and medicinal products, including monitoring the safety of drugs, and their approval

BUNDESINSTITUT FÜR ARZNEIMITTEL UND MEDIZINPRODUKTE (BfArM)

- Ein Bundeinstitut (eine selbständige Bundesoberbehörde) im Geschäftsbereich des Bundesministeriums für Gesundheit mit Sitz in Bonn
- Responsible for approval of drugs, improving the safety of drugs, monitoring and reducing risks of medicinal products

ETHICAL ASPECTS (cont.)
B. EVALUATION OF DOCUMENTS AND THE CONDUCTION OF THE STUDY (cont.)

EUROPEAN MEDICINES AGENCY (EMEA)

- A decentralized body of the European Union
- Responsible for monitoring the safety of drugs and approval of drugs
- If a drug receives approval from a country-specific agency before it is approved by EMEA, the drug can be marketed in this specific country.
- Drugs for treatment of AIDS, cancer, diabetes, and neurodegenerative diseases must be approved by the EMEA

ETHICAL ASPECTS (cont.)
B. EVALUATION OF DOCUMENTS AND THE CONDUCTION OF THE STUDY (cont.)

The **Institutional Review Board** (**IRB**)/the **Independent Ethics Committee** (**IEC**) **AND** the **Food and Drug Administration** (**FDA**/the **Bundesinstitut für Arzneimittel und Medizinprodukte** (**BfArM**)

- Review and approve or disapprove the following documents:
  - Study protocol
  - Informed consent
  - Subject recruitment procedures
  - Patient's Brochure
  - Investigator's Brochure
  - Investigator's curriculum vitae
- Evaluate the conduct of the study (audits)

The major objectives of reviews and evaluations are:
- To assess the scientific merit of the study
- To promote fully informed and voluntary participation of subjects
- To optimize the safety of subjects
- To assure compliance with the study protocol

Both the IRB/IEC and the FDA/BfArM may request modifications before the clinical trial is initiated.

V. PHASES OF CLINICAL TRIALS

PHASE I

- Not controlled
- Small number of subjects (20-80), most often healthy volunteers
- Duration: several weeks
- Objectives:
  - Pharmacokinetics (distribution, metabolization, elimination of the drug)
  - Tolerability and safety (side effects)
  - Best route of administration
  - Dose range with acceptable tolerability

PHASES OF CLINICAL TRIALS (cont.)

PHASE II

- **Controlled or not controlled, randomized or not randomized**
- **Several hundred subjects with a specific disease**
- **Duration: Several weeks to months**
- **Objectives:**
  - **Efficacy**
  - **Safety**
  - **Best dosage**

Phase IIa: Proof-of-concept studies – Überprüfung des Therapiekonzepts
Phase IIb: Dose-finding studies - Dosisfindungsstudien

PHASES OF CLINICAL TRIALS (cont.)

PHASE III

- Double-blind, controlled, randomized
- Several hundred to several thousand subjects
- Duration: Months to years
- Objectives:
  - Further investigation of efficacy and safety
  - Dose adjustments
- After completion, the sponsor applies to the Food and Drug administration (FDA) or the Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM) for approval to market the drug

PHASES OF CLINICAL TRIALS (cont.)

PHASE IV

- Double-blind, controlled, randomized
- Large number (several thousand)
- Duration: Years
- Objectives:
  - Rare and long-term side effects
  - Drug interactions
- May result in drug withdrawal or restrictions (example: Vioxx)

VI. CONDUCTION OF THE CLINICAL STUDY ACCORDING TO THE PROTOCOL

WHAT IS INVOLVED FOR THE **PARTICIPATING SUBJECT (TEILNEHMER)**?

- **BASELINE VISIT (BASELINE-VISITE, AUSGANGSUNTERSUCHUNG):**
  Visit before treatment (combined with or after the screening visit)
  - History
  - Physical examination
  - Laboratory tests
  - Imaging tests
  - Subject receives medication (if taken or administered at home) for a certain period of time
  - Subject receives information about dosage and administration schedule
  - Subject receives schedule of follow-up visits
  - Subject receives additional information if needed, for example, on diet, exercise, keeping a diary

CONDUCTION OF THE CLINICAL STUDY ACCORDING TO THE PROTOCOL (cont.)

- FOLLOW-UP VISITS (KLINIKBESUCHE [VISITEN] IM VERLAUF DER STUDIE)

  - Some or all examinations as at the baseline visit
  - Additional examinations and/or tests
  - Subject receives medication
  - Subject delivers his/her diary

CONDUCTION OF THE CLINICAL STUDY ACCORDING TO THE PROTOCOL (cont.)

RESPONSIBILITIES OF THE **INVESTIGATOR (PRÜFER)**

- Ensures that all study procedures are performed according the protocol
- Completes the Case Report Forms (CRF) at each patient visit
- Meets with the **monitor** at regular intervals. The **monitor** is a person who is employed by the sponsor and reviews study records to determine whether a study is being conducted in accordance with the protocol.
- Reports adverse events (AEs) to
  - the Investigational Review Board (IRB)/Independent Ethics Committee (IEC)
  - the FDA/BfArM
  - the sponsor.

Specific forms for AEs (part of the CRF) must be completed.

VII. QUALITY MANAGEMENT

The QUALITY of

- **study related documents**
- **the conduct of the study**
- **the evaluation of results**

must be monitored using STANDARD PROCEDURES

QUALITY MANAGEMENT (cont.)

QUALITY ASSURANCE (QA) **QUALITÄTSSICHERUNG (QS)**

Regulations and requirements established to ensure that

- **the trial is conducted in compliance with Good Clinical Practice (GCP)**
- **data are generated, documented and reported in compliance with Good Clinical Practice (GCP)**

QUALITY CONTROL (QC) **QUALITÄTSKONTROLLE (QK)**

Techniques and activities undertaken within the quality assurance system to verify that the requirements for quality of the trial-related activities are fulfilled.

QUALITY MANAGEMENT (cont.)

AUDITS **AUDITS**

Who performs an audit?
- **an employee (who is not involved in the study) or hired consultant of the Sponsor**
- **Institutional Review Boards (IRBs)/Independent Ethics Committees (IECs)**
- **the Food and Drug Administration (FDA)**

The person performing the audit is the AUDITOR.

The FDA uses INSPECTION for audit and INSPECTOR for auditor.

QUALITY MANAGEMENT (cont.)

What is an audit?
A systematic and independent examination of
- **trial-related activities**
- **trial-related documents**

What is the purpose of the audit?
TO DETERMINE WHETHER the trial-related activities are/were conducted and the trial-related documents are/were recorded, analyzed and reported in accordance with
- **the study protocol**
- **Standard Operating Procedures (SOPs)**
- **Good Clinical Practice (GCP)**
- **federal regulations**

QUALITY MANAGEMENT (cont.)

When is an audit performed?

- **as a routine (routine audit)**
- **if there is reason for potential fraud or misinterpretation of data (for cause audit)**
- **after a marketing application has been filed by the sponsor**

QUALITY MANAGEMENT (cont.)

MONITORING **MONITORING**

Who performs the monitoring?

- **An employee of the Sponsor or**
- **An Independent Clinical Research Associate (CRA)**

The person or institution performing the monitoring is the MONITOR.

What is monitoring?
- **Overseeing the progress of a clinical trial**
- **Assisting the investigator and his staff in performing their activities**

QUALITY MANAGEMENT (cont.)

What is the purpose of monitoring?
TO ENSURE THAT the trial-related activities are conducted and the trial-related documents are recorded, analyzed and reported in accordance with
- **the study protocol**
- **Standard Operating Procedures (SOPs)**
- **Good Clinical Practice (GCP)**
- **federal regulations**

When is the monitoring performed?
- **In regular intervals during the course of the study**

VIII. DATA ACQUISITION, COLLECTION AND ANALYSIS

Study procedures, data, and results are electronically collected, processed, and analyzed by various systems and computer programs.

EXAMPLES:

INTERACTIVE VOICE RESPONSE SYSTEMS (IVRS)
- Data are entered into a database using a touchtone phone
- The **investigator** may enter, for example
  - patient demographics
  - randomization of individual patients
  - dosing
  - dispensing medications (date and amount) to individual patients
- The **subject** may enter, for example:
  - symptoms during a certain period of time
  - effects of the study drug
  - side effects of the study drug

DATA ACQUISITION, COLLECTION AND ANALYSIS (cont.)

ELECTRONIC DATA CAPTURE (EDC)

- Systems for collecting patient data electronically and transmitting the data over the Internet
- The data are automatically checked against predefined rules and corrected if necessary

IX. PUBLISHING AN ARTICLE

- **Introduction**: Description of the treated disease and its current standard treatment
- **Material and Methods:**
  - Patients: Demographics, pretreatment, treated disease and stage of disease
  - Methods: Dosage, administration schedule, examinations and tests, statistical analysis and other methods of evaluation
- **Results**: Response rate, types of responses (complete, incomplete), test results, adverse events, statistical analysis
- **Discussion**: Interpretation of results and comparison with conventional treatment, influence of the investigational product on prognosis of treated disease, and recommendations

CLINICAL TRIALS - GLOSSARY		KLINISCHE STUDIEN - GLOSSAR	
Admission (enrollment) criteria	Criteria used to select the target population for a particular clinical trial. All studies must have both a list of inclusion criteria and exclusion criteria which patients have to meet to be eligible for the study.	Aufnahmekriterien	Kriterien für die Auswahl der Zielpopulation einer bestimmten Studie. Für alle Studien muss eine Liste der Einschluss- und Ausschlusskriterien vorliegen. Patienten müssen diese Kriterien erfüllen, um für die Studie in Frage zu kommen.
Adverse drug reaction (ADR)	Any unintended, harmful or unpleasant response to a medicinal product at any dose, used for diagnosis, prophylaxis or treatment of diseases or modifications of physiological functions. The response is such that there is a reasonable possibility that the adverse reaction was caused by the medicinal product.	Unerwünschte Arzneimittelwirkung (UAW)	Alle unbeabsichtigten, schädlichen bzw. unangenehmen Arzneimittelwirkungen unabhängig von der Dosis bei Anwendung des Arzneimittels zur Diagnose, Prophylaxe oder Behandlung einer Krankheit oder zur Modifikation physiologischer Funktionen, wobei ein kausaler Zusammenhang mit dem Arzneimittel angenommen werden kann. **Definition im Arzneimittelgesetz (AMG):** Eine schädliche, unbeabsichtigte Reaktion, die beim bestimmungsgemäßen Gebrauch eines Arzneimittels auftritt.
Adverse event (AE)	Any medical event (including intercurrent diseases and accidents) that occurs under treatment with a medicinal product that does not necessarily have a causal relationship with the treatment	Unerwünschtes Ereignis (UE)	Jedes unerwünschte medizinische Ereignis (einschließlich interkurrenter Erkrankungen und Unfälle), das unter Behandlung mit einem (nach Verabreichung eines) Arzneimittel(s) auftritt und nicht unbedingt in ursächlichem Zusammenhang mit dieser Behandlung steht. **Definition im Arzneimittelgesetz (AMG):** Jedes schädliche Vorkommnis, das einem Patienten nach Verabreichung eines Arzneimittels widerfährt,

			unabhängig davon, ob ein kausaler Zusammenhang mit dieser Behandlung vermutet worden wird.
Baseline	Values, findings etc. before treatment	Ausgangs-, Baseline(-)	Werte, Befunde etc. vor Behandlung
Bias	Systemic distortion of the estimated intervention away from the "truth", caused by inadequacies in the design, conduct or analysis of the trial (ICH).	(der) Bias (systematischer Fehler)	Tendenz der Studienergebnisse, von den „wahren" Ergebnissen abzuweichen. Die Ursachen liegen im Design, der Durchführung oder Analyse der Studie.
Blinding	The process through which study participants and the study team are unaware of the treatment assignment	Verblindung	Vorgang, durch den Studienteilnehmer und das Studienpersonal an der Kenntnis der Behandlungszuordnung verhindert werden.
Case Report Form (CRF)	Printed or electronic document with all protocol-required information to be reported to the sponsor for each subject	Prüfbogen	Schriftliches oder elektronisches Dokument für jeden Studienteilnehmer mit allen im Prüfplan angeführten Informationen, die dem Sponsor mitgeteilt werden müssen.
Clinical study = clinical trial	Clinical trials are studies for testing the efficacy, and safety of medications, medical devices, or other types of treatment in humans who voluntarily participate in these studies. In studies with medications, the determination of pharmacokinetic parameters may also be part of the study. "Trial" or "study" is used for investigations testing medications or other means of treatment. "Study" is used for long-term observations including epidemiological investigations.	Klinische Studie = klinische Prüfung	Untersuchung der Wirkung und Sicherheit von Arzneimitteln und Medizinprodukten sowie anderen Behandlungsmethoden an freiwillig teilnehmenden Personen. In Studien mit Arzneimitteln werden u.U. auch pharmakokinetische Parameter bestimmt werden. „Klinische Prüfung" entspricht „Clinical Trial"; „Klinische Studie" entspricht „Clinical Study
Comparator (product)	Any product including placebo used for comparison to the investigational product	Vergleichspräparat	Präparat (einschließlich Placebo), das zum Vergleich mit dem Prüfpräparat verwendet wird
Contract Research	A person or an organization (commercial,	Auftragsforschungsinstitut	Ein Dienstleistungsunternehmen, an das

Organization (CRO)	academic or other) contracted by the sponsor to perform study related duties and functions	(CRO)	der Sponsor Aufgaben und Verpflichtungen im Rahmen der Studie vertraglich delegiert
Control group, control arm	Group of subjects that receives no treatment, placebo or standard therapy	Kontrollgruppe, Kontrollarm	Gruppe aus Studienteilnehmern, die nicht behandelt wird, Placebo oder Standardtherapie erhält
Discontinuation	The act of concluding participation in a clinical trial prior to completion of all protocol-required elements. There are four categories: 1. dropout: active discontinuation by a subject, 2. Investigator-initiated (i.e., for a cause), 3. loss to follow-up, 4. Sponsor-initiated. Discontinuation does not imply exclusion of subject data from analysis.	Vorzeitiges Ausscheiden aus der Studie	Beenden der Teilnahme an der Studie vor Abschluss der nach dem Protokoll (Prüfplan) geforderten Elemente. Vier Kategorien: 1. Dropout: aktives Ausscheiden (Entschluss des Patienten), 2. Entschluss des Prüfarztes (vorhandener Grund), 3. nicht zu Untersuchungen erschienen, 4. Entschluss des Sponsors.
Endpoints	Outcome measures used for analysis of the study, related to efficacy and safety **Primary (true) endpoints:** direct measures of the response to treatment (e.g., remission) or lack of response (e.g., tumor progression). **Secondary (surrogate) endpoints:** measures related to primary endpoints such as quality of life, duration of remission, survival, or laboratory values	Endpunkte	Zielkriterien, anhand derer die Studie beurteilt wird und die sich auf Wirkung und Sicherheit beziehen **Primäre (wahre, patientenrelevante) Endpunkte:** Ansprechen oder fehlendes Ansprechen auf die Behandlung. Parameter, die die klinisch relevanteste Beurteilung ermöglichen **Sekundäre Endpunkte (Surrogatendpunkte, intermediäre Endpunkte):** Zielgrößen, die für die Beurteilung der Ergebnisse von Bedeutung sind; z.B. Laborwerte, Blutdruck, Überlebenszeit
Exclusion criteria	Characteristics that exclude a potential subject from participating in a study	Ausschlusskriterien	Eigenschaften, die einen potenziellen Kandidaten von einer Studienteilnahme ausschließen
Food and Drug	Agency of the United States Department of	Food and Drug	Amerikanische Zulassungsbehörde für

Administration (FDA)	Health and Human Services, responsible for regulating foods, drugs, and other dietary and medical products	Administration (FDA)	Medizinprodukte und Lebensmittel
Good Clinical Practice (GCP)	A standard for the design, conduct, monitoring, recording, analyzing and reporting clinical studies. GCP ensures that the reported data are accurate and that the subjects' rights and confidentiality are protected.	Good Clinical Practice, Gute Klinische Praxis (GCP)	Standard für Design, Durchführung, Dokumentation, Analyse und Berichterstattung klinischer Studien. Mithilfe der GCP wird sichergestellt, dass die Rechte der Studienteilnehmer und die Vertraulichkeit der Identität geschützt werden.
Inclusion criteria	Characteristics that a potential subject must meet to be eligible for participation in the study	Einschlusskriterien	Eigenschaften, die ein potenzieller Kandidat erfüllen muss, um sich für eine Studie zu eignen
Informed consent	Agreement of the subject to participate in a study after receiving information about the study.	Einwilligungserklärung	Einwilligung einer Person an einer Studie nach Aufklärung über dieselbe teilzunehmen.
Intention to treat	Inclusion of all patients in the study analysis according to their original treatment group allocation, regardless of whether they completed the treatment or withdrew from the study (or were terminated) prematurely, i.e. did not complete treatment or did not receive any treatment.	Intention-to-Treat	Berücksichtigung aller Patienten nach ihrer ursprünglichen Gruppenzuteilung in der Ergebnisauswertung, unabhängig davon, ob sie die zugeordnete Behandlung abgeschlossen haben oder vorzeitig aus der Studie ausgeschieden sind bzw. ausgeschlossen wurden und daher die Behandlung nicht abgeschlossen oder nicht erhalten haben.
International Conference of Harmonization (ICH)	An international body that issues recommendations for Good Clinical Practice (GCP) and Standard Operating Procedures (SOPs)	International Conference of Harmonization, Internationale Harmonisierungskonferenz (ICH)	Internationales Gremium, das Richtlinien zur "Guten Klinischen Praxis" and Standardarbeitsanweisungen (Standard Operational Procedures, SOPs) empfiehlt
Institutional Review Board (IRB), Independent Ethics	An independent body that is responsible for the ethical conduct of clinical studies according to Good Clinical Practice	Institutional Review Board (IRB), Institutionelle Prüfungskommission,	Ein unabhängiges Gremium, das für die ethische Durchführung von Studien nach Guter Klinischer Praxis (Good Clinical

Committee (IEC)	(GCP). In the US, IRBs are regulated by the Office for Human Research Protection which is part of the Department of Health and Human Services (DHHS).	Unabhängige Ethikkommission	Practice, GCP) verantwortlich ist. In Deutschland müssen die für klinische Studien zuständigen Ethikkommissionen beim Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM) registriert sein.
Investigational product, study drug	A pharmaceutical product with an active substance, being tested in a clinical trial	Prüfpräparat, Studienpräparat, Verum	Pharmazeutische Form eines Wirkstoffes, die in einer klinischen Studie untersucht wird.
Investigational group, treatment group, arm	Group of subjects who are treated with the investigational product	Behandlungsgruppe, Arm	Gruppe von Personen (Patienten, Probanden), die mit dem Prüfpräparat behandelt werden.
Investigator	Person responsible for conducting the clinical study at the study site	Prüfer, Prüfarzt	Person, die für die Durchführung der Studie in einer Prüfstelle (= einem Zentrum) verantwortlich ist.
Investigator's brochure	A compilation of pharmacological, preclinical and clinical data on the investigational product which are relevant for the investigation of the investigational product in human subjects.	Prüfarztbroschüre	Eine Zusammenstellung der pharmakologischen, vorklinischen und klinischen Daten über das Prüfpräparat, die für die Prüfung des Prüfpräparates am Menschen relevant sind.
Monitor	Person employed by the sponsor or a CRO who reviews study records to determine whether a study is being conducted in accordance with the protocol. A monitor's duties may include, but are not limited to, helping to plan and initiate a study, assessing the conduct of a study, and assisting in data analysis.	Monitor	Person, die vom Sponsor oder einem Auftragsforschungsinstitut angestellt wird und dafür verantwortlich ist, dass die Studie protokollgemäß verläuft. Er startet und beendet die Studie, erstellt Berichte über den Fortgang der Studie und überprüft die Datenanalyse.
Placebo	Placebo is Latin and means literally "I will please". A pharmaceutical preparation with no active substance that looks and tastes exactly like to investigational product	Placebo	Wörtlich: „Ich werde gefallen". Inaktive Substanz (Scheinmedikament) mit dem Aussehen und dem Geschmack des Prüfpräparates
Principal investigator	If there is more than one investigator at a site, the principal investigator is the	Hauptprüfer, Leiter der klinischen Prüfung (LKP)	Wird eine Prüfung in einer Prüfstelle (einem Zentrum) von mehreren Prüfern

	responsible leader of the investigator team		vorgenommen, ist der verantwortliche Leiter der Gruppe der Hauptprüfer.
Randomization	Random allocation of subjects to the treatment group(s) or the control group(s)	Randomisierung	Zuordnung der Studienteilnehmer nach dem Zufallsprinzip zur (zu den) Behandlungsgruppe(n) oder zur (zu den) Kontrollgruppe(n)
Sample size	Number of subjects in a clinical trial	Stichprobengröße, Fallzahl	Anzahl der Teilnehmer an einer Studie
Screening	Evaluation of subjects for participation in a clinical trial according to inclusion and exclusion criteria	Screening	Beurteilung von Personen (Patienten, Probanden) zur Eignung für eine klinische Studie mithilfe der Einschluss- und Ausschlusskriterien
Screen failure	Subject who does not meet all criteria for participation in a clinical trial	Screen failure	Person (Patient, Proband), der die Kriterien zur Teilnahme an einer klinischen Studie nicht erfüllt
Serious adverse events (SAE) or serious adverse drug reaction (serious ADR)	Any adverse experience at any dose that results in any of the following outcomes: death, a life-threatening adverse experience, hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect (ICH).	Schwerwiegendes unerwünschtes Ereignis (SUE) oder schwerwiegende unerwünschte Arzneimittelwirkung (schwerwiegende UAW)	Jedes unerwünschte Ereignis, das unabhängig von der Dosis tödlich oder lebensbedrohlich ist, eine stationäre Behandlung oder deren Verlängerung erforderlich macht, zu einer bleibenden oder schwerwiegenden Behinderung oder Invalidität führt oder eine angeborene Missbildung bzw. eine angeborene Anomalie darstellt (ICH).
Sponsor	An individual, company, institution or organization taking responsibility for initiation, management, and financing of a clinical study.	Sponsor, Auftraggeber	Auftraggeber einer klinischen Prüfung. Person, Unternehmen, Institution oder Organisation, die/das die Verantwortung für die Planung, das Management und die Finanzierung einer klinischen Prüfung übernimmt.
Standard Operating Procedure (SOP)	Detailed written instructions to achieve uniformity of the performance of a specific function. SOPs must be prepared for each individual or group of individuals with the	Standard Operating Procedure (SOP), Standardarbeitsanweisung, Verfahrensvorschrift	Detaillierte, schriftliche, standardisierte Arbeitsanweisungen für Personen oder Gruppen von Personen mit derselben Funktion (Sponsor, Monitor, Institutional

	same function, participating in the procedures of the clinical trial, including the sponsor, the monitor, the Institutional Review Board, the investigator, and all clinic staff.		Review Board, Prüfer und Klinikpersonal). Diese Arbeitsanweisungen müssen für alle Aktivitäten, die im Rahmen der klinischen Studie notwendig sind, erstellt werden.
Standard treatment	Currently accepted treatment for a specific disease	Standardtherapie	Allgemein anerkannte Behandlung einer bestimmten Krankheit
Study protocol	Document that describes the background and rationale of the study, as well as the objectives, design, methodology, organization, and statistical evaluation of the study	Prüfplan, Studienprotokoll	Dokument, in dem Hintergrund der Studie und Gründe für die Durchführung der Studie sowie Zielsetzungen, Design, Methodik, Organisation und statistische Methoden der Studie beschrieben werden.
Study (trial) site (center)	Institution where the study is conducted.	Studienzentrum, Prüfzentrum	Ort (Klinik, Praxis), an dem die Studie durchgeführt wird.
Subject, study participant	Patient or healthy volunteer participating in a study	Studienteilnehmer, Prüfungsteilnehmer, Proband	Patient oder gesunder Freiwilliger, der an einer Studie teilnimmt
Termination of subject	Premature withdrawal of a patient from the study. Should no longer be used (see Discontinuation)	Vorzeitiger Ausschluss eines Patienten aus der Studie	Ausschluss eines Patienten aus der Studie vor dem geplanten Zeitpunkt
Termination of trial	Premature discontinuation of a trial (prior to plan)	Vorzeitiger Abbruch der Studie	Abbruch der Studie vor dem geplanten Zeitpunkt
Unblinding	Identification of the treatment code	Entblindung	Offenlegung der Identität eines verblindeten Prüfpräparates

TYPES OF CLINICAL STUDIES (TRIALS)		**ARTEN KLINISCHER STUDIEN (PRÜFUNGEN)**	
Case-control study	An epidemiological study in which the potential risk factors of a disease are determined by investigating two groups – one group with the disease (cases) and one group without the disease (controls). If exposure to a certain substance was significantly more common or at	Fall-Kontroll-Studie, Fallkontrollstudie	Eine epidemiologische Studie, in der potenzielle Risikofaktoren in zwei Gruppen untersucht werden – eine Gruppe mit einer bestimmten Krankheit (Fälle) und eine Gruppe ohne diese Krankheit (Kontrollen). Wenn die „Fälle“ signifikant häufiger bzw. in signifikant

	significantly higher doses in the “case” group, it can be assumed that the substance is a risk factor for the disease. A case-control study is always a retrospective study.		höheren Dosen einer bestimmten Substanz ausgesetzt waren als die „Kontrollen“, kann davon ausgegangen werden, dass die Substanz ein Risikofaktor für die Krankheit ist. Fall-Kontroll-Studien sind immer retrospektive Studien.
Cohort study	Study in which a defined group of patients with a certain common condition or certain common features (a cohort) is followed over time and may be compared with a cohort who does not have these features. A cohort study is a longitudinal study.	Kohortenstudie	Eine Studie, in der eine definierte Patientengruppe mit bestimmten Eigenschaften oder einer bestimmten Krankheit (Kohorte) über längere Zeit beobachtet wird und u.U. mit einer Gruppe, die diese Eigenschaften nicht hat, verglichen wird. Sonderform der Längsschnittstudie
Controlled study	A study in which the investigational product is compared with no treatment, placebo, or standard treatment	Kontrollierte Studie	Eine Studie, in der die Gruppe, die mit dem Prüfpräparat behandelt wird, mit einer unbehandelten Gruppe, einer mit Placebo behandelten Gruppe oder einer mit Standardtherapie behandelten Gruppe verglichen wird.
Cross-over study	A controlled, usually double-blind study during which Patients receive both the study drug and the placebo or another drug in a consequential manner.	Cross-over-Studie	Kontrollierte, meist doppelblinde Studie, in der die Patienten das Studienpräparat und Placebo oder ein anderes Präparat nacheinander über einen bestimmten Zeitraum erhalten.
Cross-sectional study	An epidemiological study of a defined group of people at one point in time to determine whether a potential risk factor is associated with the occurrence of a disease.	Querschnittsstudie	Eine epidemiologische Studie einer definierten Personengruppe zu einem bestimmten Zeitpunkt zur Bestimmung potenzieller Risikofaktoren einer bestimmten Krankheit.
Diagnostic study	A study in which diagnostic tests are evaluated in patients with a specific	Diagnostische Studie, Diagnosestudie	Studie, in der diagnostische Verfahren bei Patienten mit einer bestimmten Krankheit

	disease		beurteilt werden.
Dose-finding study	A study in which two or more doses of a drug are tested to evaluate which of the doses is most effective and has the fewest side effects	Dosisfindungsstudie	Eine Studie, in der mindestens zwei Dosierungen eines Medikaments untersucht werden, um herauszufinden, welche Dosis am wirksamsten ist und die wenigsten Nebenwirkungen har.
Double-blind (double-masked) study	A study in which neither the subjects nor the investigator or the study team know what treatment (study drug or comparator) the subjects are receiving	Doppelblindstudie, doppelblinde Studie, doppelmaskierte Studie	Eine Studie, bei der weder die Studienteilnehmer noch der Prüfer und das Studienpersonal wissen, womit die Teilnehmer behandelt werden (Studien- oder Vergleichpräparat)
Intervention study, treatment study	A study that investigates whether a new treatment is safe and effective.	Interventionsstudie, Behandlungsstudie	Eine Studie, in der untersucht wird, ob eine neue Behandlung sicher und wirksam ist.
Longitudinal study	A study conducted over a longer period of time	Längsschnittstudie, Longitudinalstudie	Eine über längere Zeit durchgeführte Studie
Monocenter (monocentric) study	Study conducted at one site (center)	Monozenterstudie, Monocenterstudie, monozentrische Studie	In einem Zentrum durchgeführte Studie
Multicenter (multicentric) study	Study conducted at more than one sites (centers) according to one protocol	Multizenterstudie, Multicenterstudie, multizentrische Studie	In mehr als einem Zentrum nach einem Prüfplan durchgeführte Studie
Observational study	Study without experimental intervention in which a group of subject is being observed. The subjects have something in common, e.g., a disease or exposure to a substance.	Beobachtungsstudie	Eine Studie ohne Interventionen, in der eine Gruppe von Probanden beobachtet wird. Die Probanden haben zum Beispiel dieselbe Krankheit oder sind einer bestimmten Substanz ausgesetzt.
Open-label study	A study in which patients and investigators are informed about the administered drug and dosages. These are Phase I and some phase II studies.	Offene Studie, Open-Label-Studie	Eine Studie, bei der Patient und Prüfarzt wissen, welches Präparat verabreicht wird und in welcher Dosierung. Dies sind meist Phase-I- und manche Phase-II-Studien.
Parallel group study,	A randomized study with a treatment and	Parallelgruppenstudie	Eine randomisierte Studie mit einer

parallel trial, parallel design trial	a control group, in which patients receive the same treatment throughout the study		Behandlungs- und einer Kontrollgruppe, in der die behandelten Patienten dieselbe Behandlung während des ganzen Verlaufs der Studie erhalten.
Pilot study	A small study carried out before a large-scale study in order to try out a procedure, or examine a new treatment	Pilotstudie, Leitstudie	Eine Studie mit einer kleinen Anzahl von Teilnehmern, die als Machbarkeitsstudie einer größeren Studie vorausgeht.
Pivotal study	A controlled, randomized, double-blind study with a large number of patients. In the US, the FDA uses data from such studies in their decision about approval of the drug.	Pivotalstudie	Kontrollierte, randomisierte, doppelblinde Studie mit einer großen Anzahl von Teilnehmern. Bei signifikantem Wirkungsnachweis Marktzulassung durch das BfArM.
Placebo-controlled study	A study in which one group receives placebo (placebo group)	Placebokontrollierte Studie	Eine Studie, in der eine Gruppe Placebo erhält (Placebogruppe)
Prevention study	A study in which the prevention of a disease or its recurrence is investigated by medications, diet, or life style changes.	Präventionsstudie, Präventivstudie	Eine Studie, in der Methoden zur Vorbeugung einer Krankheit oder deren Rezidiv untersucht wird. Zur Anwendung kommen Medikamente, Diäten oder Änderungen des Lebensstils.
Prospective study	A study for which subjects are recruited, treated, and monitored according to criteria described in the protocol. Most clinical trials today are prospective studies.	Prospektive Studie, Prospektivstudie	Eine Studie, in der die Teilnehmer nach den im Protokoll beschriebenen Kriterien rekrutiert, behandelt und beobachtet werden, um eine Hypothese der medizinischen Wirksamkeit einer Behandlungsmethode zu überprüfen.
Randomized study	A study in which subjects are randomly assigned to one or more treatment groups and to one or more control groups.	Randomisierte Studie	Eine Studie, für deren Durchführung die Teilnehmer nach dem Zufallsprinzip einer oder mehreren Behandlungsgruppen und einer oder mehreren Kontrollgruppen zugeteilt werden.
Retrospective study	A study based on the medical records of patients, looking backward in time at events that happened in the past. Case-	Retrospektive Studie, Retrospektivstudie	Eine Studie, bei der retrospektiv (zurückschauend), häufig anhand von Krankenblättern, z.B. die Wirkung einer

	control studies are always retrospective, cohort studies can be, and randomized controlled trials are never retrospective.		Behandlung oder das Auftreten einer Krankheit unter bestimmten Bedingungen untersucht wird. Fallkontrollstudien sind immer retrospektiv, Kohortstudien können retrospektiv sein und randomisierte, kontrollierte Studien sind immer prospektiv.
Screening study	A study in which the accuracy and value of a screening test is evaluated.	Screening-Studie	Eine Studie, in der der Wert einer Methode zur Erkennung einer bestimmten Krankheit geprüft wird.
Single-blind (single-masked) study	A study in which only the investigator or the subjects know what treatment (study drug or comparator) the subjects are receiving. In most single-blind studies, the subjects are blinded.	Einfachblindstudie, einfachblinde Studie	Eine Studie, bei der nur der Prüfarzt oder die Studienteilnehmer die den Gruppen zugeteilte Therapie kennen. In den meisten Einfachblindstudien sind die Teilnehmer verblindet.

RECOMMENDED WEBSITES:

www.cirp.org/library/ethics/helsinki (Declaration of Helsinki)
http://en.wikipedia.org/wiki/Clinical_trial
http://de.wikipedia.org/wiki/Klinische_Studie
www.ClinicalTrials.gov
www.answers.com/topic/clinical-trial-1
http://www.cdisc.org/glossary/CDISCGlossaryV5.pdf
http://www.sdisc.org/glossary/CDISCAcronymsV5.pdf
www.krebshilfe.de/fileadmin/Inhalte/Downloads/PDFs/Blaue_Ratgeber/060_klinische_studie.pdf

RECOMMENDED DICTIONARY:

Simon Day; Dictionary for Clinical Trials, Second Edition; John Wiley & Sons, Ltd., 2007 (ISBN 978-0-470-05817-6)