SPACE FOR ETHICS.

In science and clinical research. Guide for the JKU Faculty of Medicine.

JKU

FACULTY OF MEDICINE

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Preface.

By creating the Faculty of Medicine, the Johannes Kepler University of Linz has committed itself to pursuing and advancing cutting-edge medical research, always keeping pace with the times. One area of particular emphasis at the JKU is conducting responsible and sustainable pre-clinical and clinical research at a scientific hub in Linz in order to meet the needs of science and assuage the concerns of our society.

The high quality of our research is a basic requirement to justify society's trust in our research findings. Complying with the applicable laws, international standards and norms is absolutely essential and in this regard, the JKU is committed to international standards that include Good Scientific Practice (GSP) and Good Clinical Practice (GCP).

In order to meet or surpass international standards, the JKU Faculty of Medicine has developed a first edition ethics guide for scientific and clinical research. This guide builds on the JKU guidelines, serving our university researchers as an instruction manual and a decision-making aid. Intended to support academic integrity and prevent academic misconduct, this guide will be subject to ongoing adaptation in accordance with social, legal and normative circumstances. The guide is available online at jku.at/medizinische-fakultaet/organisation/zentrale-dienste/zentrum-fuer-klinische-forschung.

We would like to express our thanks to everyone who contributed toward the development of this guide.

Univ. Prof. Dr. Meinhard LUKAS
Rector

Mag.ª Dr.in Elgin DRDA
Vice-Rector for Medicine
Director at the JKU Faculty of Medicine

List of abbreviations.

AGES	Agency for Health and Food Safety
AIMED	Active implantable medical device
AMG	Medicines Law
ASchG	Biological Agents Ordinance
AVV	Order processing contract
BASG	Federal Office for Safety in Health Ca
BMBWF	Federal Ministry for Education, Science and Research
CDG	Christian Doppler Research Association
CE	Conformité Européenne (European Conformity)
CRF	Case Report Form
GDPR	General Data Protection Regulati
EMA	European Medicines Agency
EUDAMED	European Database for Medical Devices
EudraCT	European Union Drug Regulating Authorities Clinical Trials
EU-VO	EU regulation
FFG	Austrian Research Promotion Agency
FOG	Research Organization Law
FWF	Austrian Science Fund
FrSV	Release Ordinance
GCP	Good Clinical Practice
GDocP	Good Documentation Practice
GMP	Good Manufacturing Practice
GTG	Genetic Engineering Law
GSP	Good Scientific Practice
GMM	Genetically modified microorganisms
GMO	Genetically modified organisms
IB	Investigator‘s brochure
ICH	International Council for Harmonisation
IMP	Investigational medical product
IMPD	Investigational medical product dossier
IPR	Intellectual property rights
ISO	International Organization for Standardization
IVD	In vitro diagnostics
JKU-EK	Ethics Committee at the Johannes Kepler University of Linz
KAKuG	Hospital and Sanatorium Law
KKS Linz	Competence Center for Clinical Trials in Linz
KUK	Kepler University Hospital Ltd.
LBP	Performance evaluation test
Oö. KAG	Upper Austrian Hospital Law
PIP	Pediatric investigation plan
MED	Faculty of Medicine
MedDRA	Medical Dictionary for Regulatory Activities terminology
MPG	Medical Devices Law
NIS-VO	Regulation on Non-interventional Studies
PatG	Patent Law
SOP	Standard operating procedure
UG	University Act
ZKF	Center for Clinical Research

Foreword from the Linz Center for Clinical Research.

An important component on the path to conducting cutting-edge research was to create the Competence Center for Clinical Trials (KKS Linz) at the Center for Clinical Research (ZKF) at the JKU Faculty of Medicine. KKS Linz is a consultation and service center for all researchers who have questions relating to regulatory standards (e.g., the Medicines Law, data protection, etc.), as well as methodological, statistical and/or administrative aspects of planning and executing clinical research projects. Conceived as an academic contract research institute in November 2019, KKS Linz provides a range of services (e.g., monitoring, GCP audits, statistical analysis, medical writing, data management, etc.) and aims to consistently broaden these services in the future.

In conjunction with our services, this guide will provide valuable support to our researchers at the JKU.

Mag.[a] Dr.[in] Angelika MODER, MSc BSc

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THE 10 GOOD SCIENTIFIC PRACTICE (GSP) RULES.

1. **Each and every scientist is responsible for learning and following the guidelines relevant to their activities and the applicable legal provisions.**

2. **Every clinical science project must be documented using a study protocol.**

3. **Every research project on humans undertaken for the purpose of gaining knowledge must be submitted to an ethics committee for assessment.**

4. **Animal experiments generally require the approval of the Federal Ministry of Science, Research and Economy (BMWFW) after prior consultation with the university's Animal Trials Committee.**

5. **Collecting, storing, transferring and using data must be carried out exclusively in accordance with the applicable national and international legal standards.**

6. **For an individual to be listed as an author, the following points are required:**
   - Substantial contribution to the study development and design, and/or collection, processing and interpretation of the data
   - Compose and/or perform critical review(s) of the manuscript
   - Approval of the manuscript's final version prior to publication

   Those who meet these three criteria may be named as an author.

7. **Being named as an author for a scientific paper is associated with active intellectual and practical or procedural participation. "Honorary" authorship is not permitted.**

8. **Scientific misconduct can result in legal consequences. Examples of scientific misconduct include:**
   - Fabricating data
   - Falsifying and/or manipulating data
   - Theft of intellectual property (plagiarism)

9. **In addition to applicable national and international regulations, the following guidelines must be observed when cooperating with external industry:**
   - Industry contracts must be submitted to the legal department for review.
   - If there is an industrial cooperation and/or an industrial contract, a simultaneous private consultancy as part of a secondary job for the company concerned must be disclosed (potential conflict of interest).
   - Commissions by industry sectors containing potentially harmful content may be prohibited.

10. **In regard to the context of a research project, full disclosure is required in the event of any potential conflicts of interest.**

QUOTE

The Austrian philosopher Lisz Hirn aptly describes the essence of scientific thought and action: "True science is characterized by humility before the limits of the finite and by curiosity about the infinite beyond these limits." With this quote in mind, there is actually little room for a scientist to act in a way that deviates from good scientific practices.

Univ.-Prof. Dr. Andreas Gruber
Faculty Director for Research
at JKU MED

THE 13 GOOD CLINICAL PRACTICE (GCP) PRINCIPLES.

1. Clinical trials are to be conducted in accordance with the ethical principles as outlined in the Declaration of Helsinki which are consistent with both Good Clinical Practices and pertinent legal requirements.

2. Before beginning a clinical trial, any foreseeable risks and issues should be weighed against the expected benefits for the individual trial participants and society.

3. The rights, safety, and well-being of trial participants are paramount and take precedence over the interests of science and society.

4. The available pre-clinical and clinical information about an investigational product or medical procedure must adequately support the proposed clinical trial.

5. Clinical trials should be scientifically sound and de scribed in a clearly formulated, detailed study protocol.

6. A clinical trial should be conducted in accordance with the study protocol previously approved by the board and an independent ethics committee.

7. A qualified physician should always be responsible for the medical care of the trial participants and the medical decisions made on their behalf.

8. Every person involved in conducting a clinical trial should be qualified to perform their task(s) through education, training and professional experience.

9. Before participating in a clinical trial, each participant must voluntarily submit a declaration of consent that includes comprehensive trial information.

10. All clinical trial data is to be recorded, processed, and stored in a way to best ensure correct reporting, interpretation and review.

11. In compliance with legal regulations, any records that could potentially identify trial participants are to be kept strictly confidential.

12. Any production, handling and storage of investigational products are to be carried out in accordance with the applicable Good Manufacturing Practices (GMP) and used in accordance with the approved study protocol.

13. Systems and measures must be put in place to ensure the quality of every aspect of the clinical trial.

CLINICAL STUDIES.

Study Protocol.


Medication History Record

General Information

The study protocol (alternatively test protocol, test plan or study plan) is an essential part of clinical scientific research projects as it describes the key aspects of the proposed research. It must always be drafted before the start of a clinical study in coordination with the investigators and/or sponsor(s) involved. According to ICH-GCP, ISO 14155, Medicines Law and/or Medical Devices Law, the study protocol must be reviewed by the national authority (BASG) and/or international authorities (e.g.: European Medicines Agency, EMA) and the responsible ethics committee. Together with other documents (e.g.: investigator information), the study protocol also forms the basis for review by the ethics committee and responsible authorities. Regarding pediatric studies, a "pediatric investigation plan" (PIP) must be drawn up instead of - or in conjunction with - the study protocol.

In addition, clinical studies must be registered in the EudraCT (European Union Drug Regulating Authorities Clinical Trials). EudraCT is operated by the European Medicines Agency and is used by the Member States' authorities to approve and monitor clinical trials. As part of the registration procedure, portions of the study protocol must be disclosed, and some will be made publicly available. This also applies to medical device studies that must be entered in the Austrian Medical Devices Registry (MD) and the European Database for Medical Devices (EUDAMED).

What content should a study protocol contain?

General project information – Synopsis

- Title and identification number (e.g.: EudraCT) of the study protocol and date. Any change to the study protocol should also be documented with the modified number and date
- Sponsor's name and address
- Name and address of the study center and the Principal Investigator
- Project outline

Scientific and medical background information about the project

- Summary of observations from pre-clinical studies that may be of clinical significance
- Information about the pharmacokinetics and metabolism of the investigational product or technical information about the investigational product
- Objectives and purpose of the clinical trial
- Description of the trial design (e.g., double-blind, randomized, placebo-controlled)
- Clearly formulated inclusion/exclusion criteria
- Precise specification of the main endpoints and, if applicable, the secondary endpoints
- Treatment strategy for the trial participants
- Definition of the efficacy endpoints

Data management and statistics

- Information about data processing including data protection, description of the planned statistical methods including the timing for planned interim evaluations
- The sample size of trial participants. In the case of multi-center studies, the number of subjects should be specified for each study center
- The level of significance used for hypothesis testing
- Criteria for terminating the clinical trial
- Rules to address missing, unused and questionable data
- Definition of how deviations from the original statistical planning should be reported
- Selection of the data included in the analyses

Ethical considerations
- Description of the ethical considerations related to the clinical trial
- Overview of any known and/or potential risks or benefits to the study participants, if applicable

Safety Assessment
- Definition of safety endpoints
- Methods and times to assess, record and evaluate safety endpoints
- Description of the procedure for querying, recording and reporting adverse events and disorders occurring to the trial participants
- Description of the type and duration of follow-up observation of the trial participants after adverse events

Quality control and quality assurance
- Description of the monitoring strategy (frequency, scope and methodology)
- Data checks by data management (centralized monitoring)
- Information about planned audits

Guidelines and legal principles

JKU MED is committed to the principles of the Declaration of Helsinki and Good Clinical Practice (GCP) for any medical research involving human subjects. Accordingly, study protocols must be submitted to an independent ethics committee for assessment and eventual approval. In addition, existing legal provisions must also be observed. As corresponding EU regulations (e.g.: EU Regulation No. 536/2014 on clinical medicine studies and EU Regulation No. 745/2017 in regard to medical device studies) will be enacted, applying ICH-GCP and ISO 14155 will also become legally mandatory in Austria.

When creating study protocols, particularly for pediatric research projects, use templates established by the Forum of Austrian Ethics Committees (www.ethikkommissionen.at) or the respective, locally responsible ethics committee. In addition, researchers at JKU MED can draw on advising services offered by the Competence Center for Clinical Studies (KKS Linz) at any time.

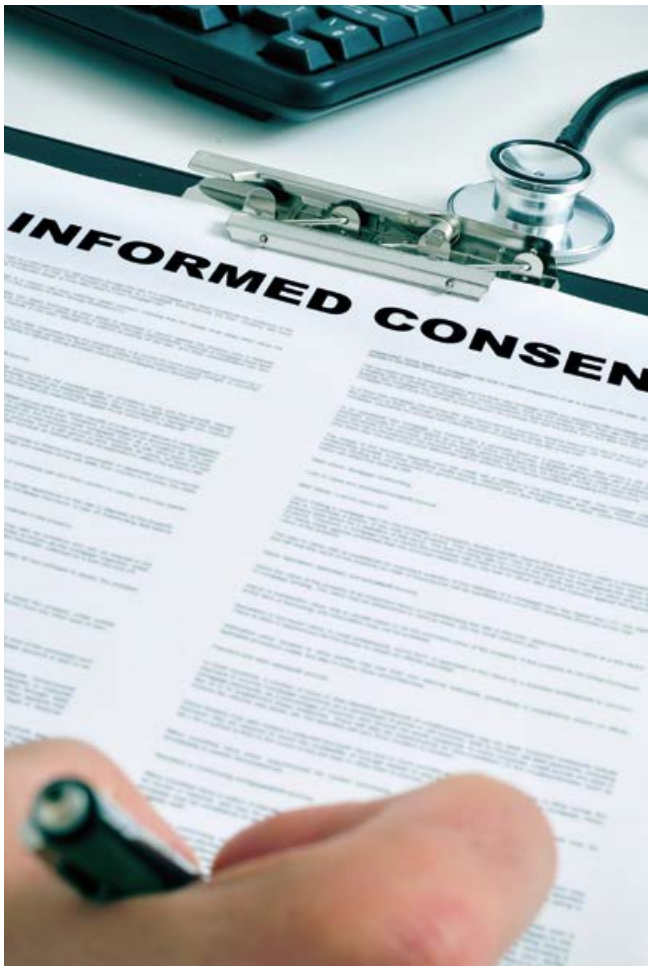
CLINICAL TRIALS.

Patient informed consent.

General Information

The informed consent process is the procedure by which patients declare their willingness to participate voluntarily in a particular clinical trial. A prerequisite for this is a comprehensive explanation by the investigator in accordance with all applicable legal provisions, GCP and the Declaration of Helsinki. The consent is then documented by means of a written, personally signed and dated declaration of consent (informed consent).

As with the study protocol itself, the text of the informed consent document must also be examined by the ethics committee before the clinical study begins. The corresponding templates can be found, among other places, on the homepage (jku.at/index.php?id=16729&no_ cache=1) of the JKU ethics committee or the forum of Austrian ethics committees (www.ethikkommissionen.at).



What content should the patient information and declaration of consent include?

Section 1 – Patient information

- Declaration that participation in the study is absolutely voluntary
- A description of the clinical study's purpose written in a manner accessible to a layperson
- Information about alternative treatment options
- Description of the course of the clinical trial and the planned measures (e.g.: blood samples, imaging procedures, biopsies etc.)
- Description of the investigational medicinal product or medical device
- Information about the expected benefits, possible risks, complaints and side effects
- Information regarding handling and storing biological samples
- Other lifestyle implications and obligations for the patient
- Reference to the concomitant intake/use of medications or medical devices
- Information about insurance coverage for patients
- Special information for women of childbearing potential and fertile men
- Information regarding any costs, reimbursement of costs or remuneration
- Description of the procedure for premature termination of the clinical trial

Section 2 – Data protection declaration in accordance with GDPR

- Exact list of all personal data collected about the trial participant
- Description of how the collected data is pseudonymized
- Information on the purpose, scope, location and duration of the data processing
- List of data subject rights
- Contact details of the data protection officer at JKU or KUK and the data protection authority

Section 3 – Declaration of consent

- Trial participant's name and date of birth
- Signed declaration by the patient/subject of voluntary participation in the study
- Declaration by the trial participant that the investigator has provided the required information
- Consent of the trial participant regarding use of collected data
- Trial participant's signature and current date
- Date, name and signature of the responsible investigator
- Acknowledgment that the trial participant has received a copy of the patient information and consent form

Important Information regarding vulnerable subjects

Informed consent by underage trial participants
Clinical examinations involving minors require the written consent of a parent/guardian or the legal representative after an appropriate explanation. In addition, the minor's written consent is required if they can understand the investigation's content and scope. The declaration of consent must therefore contain two signature sections. It is also important to ensure that the patient information is linguistically and visually adapted to the age of the underage patient. This may require different versions of the document.

Informed consent by participants with mental illness or disabilities
The consent of a trial participant with a mental illness or disability is permitted only if the individual understands the nature, significance, scope and risks of the clinical trial and voluntarily chooses to participate. If necessary, relatives (immediate or extended) or confidants may be engaged to support the trial participant's decision.
If co-consent to enroll in the clinical trial is to be provided by a healthcare agent (or adult representative) for medical matters, the healthcare agent or adult representative must provide a detailed explanation of the trial and written consent in addition to the trial participant's consent. In the event of dissent (patient refuses, adult representative/ health care agent agrees or vice versa), the approval of the guardianship court must be obtained.

Clinical trials in emergency situations
Inclusion in a clinical trial when in an emergency situation wherein the consent of the affected individual or their legal representative cannot be obtained within a reasonable amount of time is only permitted if:

- research data can only be collected in emergency situations
- there are no indications that the trial participant has rejected or would reject the clinical trial
- administering the medicine being tested is advisable according to the knowledge of medical science
- the clinical trial has been approved by an independent ethics committee
- in case of doubt, the interests of the trial participant always take precedence over public interests and the interests of science
- the public is appropriately informed about the execution of the study; this can be done directly via the respective patient representative or by posting a notice at certain locations in the individual study centers that are accessible to patients or their relatives or on the study center's homepage

Once the trial participant concerned has regained the capacity to consent, he/she is to be informed immediately that a clinical trial has been or is being conducted due to an emergency. The clinical trial may only proceed once informed consent is provided.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STATISTICS.

Research quality at the Faculty of Medicine is largely determined by the quality and integrity of data, its documentation and the statistical analysis. Biometric planning and statistical analysis of clinical studies is conducted at the JKU Faculty of Medicine in accordance with the ICH E9 guideline "Statistical Principles for Clinical Trials".

Study Objectives

A clinical study's objective is always determined according to the latest scientific developments. A distinction is made between the following types of study:

- A confirmatory study tests an a priori generated hypothesis. Careful planning in regard to the number of trial participants (number of cases) and subsequent statistical evaluations is required so the study can provide adequate evidence. A confirmatory study should be carried out as a controlled, randomized, double-blind study.
- An exploratory study aims to examine a specific research question. The information acquired is then used to generate a hypothesis which can be tested in a subsequent confirmatory study.

A pilot study is a special case serving as the basis for sample size estimation and the feasibility of future confirmatory studies. Guidelines governing pilot studies are available at: medunigraz.at/ethikkommission/richtlinien-gesetze.

Study design

A clinical study focuses on comparing different interventions or treatment regimens. The study is to be designed in a way that permits collecting corresponding information without bias. Appropriate strategies to avoid bias are **randomization,** i.e., randomly assigning trial participants to different treatment groups, and **blinding** (masking), where the latter is based on the trial participant and/or the investigator being unaware of the respective treatment group. Depending on whether this information is known to the trial participants and/or the investigators, a distinction is made between open, blind, double-blind and observer-blind design.

The parallel group design – common for controlled studies – assigns patients to one of several treatment groups, at least one of which receives the intervention to be tested while the control group receives the standard treatment or a placebo.
In crossover designs, each patient is randomly assigned to a sequence of one or more treatments. Each patient thus acts as his or her own control. Carry-over effects are to be avoided.

The factorial design randomly assigns the patient to one of the treatment combinations to be examined to (e.g.: only A, only B, A and B, neither A nor B).

While prospective studies use newly collected data, preexisting data are the basis for retrospective studies. The gold standard to prove the efficacy of investigational medicinal products is the prospective, randomized, controlled, double-blind study.

Another important aspect in trial design is the definition of the study population via clearly formulated inclusion and exclusion criteria. In order to allow for an accurate estimate of treatment effects, in a confirmatory study the patient cohorts should be sufficiently homogeneous. In addition, the study population should be representative for the target population in terms of relevant covariates (e.g.: age, sex). Multi-center studies typically provide a better basis to generalize results as there is a broader pool of trial participants and a wider range of clinical circumstances.

When planning the study, the variables to be ascertained as well as their scale level and any coding must also be specified.

Sample size estimation

Sample size estimation, i.e. the number of subjects that need to be enrolled in a prospective confirmatory trial, is key to assure sufficient statistical power. Based on the study's main outcome, a null and an alternative hypothesis has to be formulated. Additionally, the kind of test has to be specified (i.e. one- or two-sided, equivalence or superiority).
To calculate the required number of trial participants (sample size) so that an effect can be proven in the study, provided it exists, the following parameters must be specified:

- Type 1 error (i.e., the maximum probability of rejecting the null hypothesis although it is correct)
- The (clinically relevant) size of the effect to be demonstrated
- Desired power (i.e., the probability of rejecting the null hypothesis for the effect size to be demonstrated if the alternative hypothesis is correct)

If several hypotheses are being tested, a correction for multiple testing (e.g.: Bonferroni, Bonferroni-Holm or Benjamini-Hochberg) must be made. In addition, information about the expected number of study dropouts in follow-up examinations must be considered.
Sample size estimation is also possible and recommended for exploratory studies, provided that adequate information is available.

Statistical analyses

When planning a clinical study, key components in the statistical data analysis must be specified. In case of poor adherence to the study protocol, it has to be stated whether the analysis is based on the intent-to-treat or per-protocol principle, or if interim evaluations are required. Apart from that, criteria that will lead to termination of the study have to be specified.

As part of planning phase, a detailed statistical analysis plan must also be developed. In general, this plan will not only contain the test for the research hypothesis, but also univariate analyses of the ascertained variables. Frequency distributions can be shown in tables and graphs, measures can be determined, and relationships between other variables and the main target variable can be analyzed.

Quality criteria for statistical analysis

For publications, a complete record of corrections, calculations and statistical data analysis is required so that the findings are completely reproducible. The analysis should always be conducted using reliable and validated statistical software packages and has to be reproduced upon request (e.g., in the form of program codes).
It is the researcher's responsibility to present the analyses findings in full and interpret them accurately in keeping with the utilized statistical method.

Additional information about presenting and representing findings are provided in the ICH E3 guideline "Structure and Content of Clinical Study Reports". For submissions to ethics committees, we refer to the "Statistics Checklist" under the guidelines and principles section provided by the JKU ethics committee: jku.at/index.php?id=17271


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REPORTING TO ETHICS COMMITTEES AND AUTHORITIES.

General Information

The JKU ethics committee is responsible for clinical trials of medicines and medical devices, as well as assessing the use of new medical methods, including non-interventional studies (NIS) and medical research applied to humans. The ethics committee's tasks also include assessing the execution of nursing research projects and implementing new nursing and treatment methods. The panel additionally assesses the ethical and legal soundness of each prospective project. The committee's decision making process is steered largely by the Declaration of Helsinki, the EC-GCP and the ICH-GCP.

The JKU Ethics Committee's legal and ethical assessment must verify the patients' informed consent, the study's scientific nature with respect to planning and execution, the patient's benefit to risk ratio, the termination criteria, and insurance coverage. An assessment will be made as to whether the research project complies with the prescribed standards and whether the study is ethically sound. The patient's participation in a clinical trial/study is voluntary following a detailed explanation by the investigator and after signing a declaration of consent.

Submitting applications to the JKU ethics committee

An ethics committee (JKU-EK) was created at the Faculty of Medicine at the Johannes Kepler University in accordance with § 30 (1) of the 2002 Austrian Universities Act in conjunction with § 8c KAKuG, § 18 Oö. KAG 1997 and the Central Ethics Committee Regulation to create an Ethics Commission (JKU-EK) to act on the basis of corresponding legal provisions in Austria and abroad. The announcement was made in the Vienna Official Gazette. The JKU-EK's scope of activity extends not only to areas of federal enforcement, but also to areas of enforcement by the state of Upper Austria.

As of 10/26/2017, new applications must be submitted via the electronic ECS submission system (ecs.kuk-ooe. at). The deadline for submission is always the monthly JKU-EK meeting so that the study can be scheduled for the next meeting.

Which documents must be submitted?

- Cover letter (possibly also a cover letter to locally responsible ethics committees)
- EudraCT form
- Study protocol with synopsis in German
- Patient information and declaration(s) of consent
- List of center-specific contact details
- List of centers and local ethics committee which received the study prospectus
- Insurance confirmation/insurance policy, including general insurance conditions in accordance with Medicines Law (applicability of Austrian law, Austrian jurisdiction, amount of the sum insured, description of the study, etc.)
- Investigator's brochure (investigator information)
- Case report form (CRF)
- Curriculum vitae including proof of the Principal Investigator's qualifications, list of publications, specialist medical certificate, etc. (signed, dated and not older than one year)
- Curriculum vitae of all responsible employees (signed, dated and not older than one year)
  - CE certificate(s) and product brochure (only for studies according to MPG)
  - Application for exemption from fees (for academic studies, Bachelor's, Master's, and Diploma degree theses and dissertations)
  - Technical information (only for NIS according to AMG)
- Votes from other ethics committees (if any)
- Documents according to EU Directive 2001/20/EC
- Conflict of interest statement
- Investigator's protocol signature page

Additional information about the required documents and the meeting dates can be found on the JKU-EK homepage (jku.at/index.php?id=16744&no_cache=1).

QUOTE

"Science needs confident, scholarly, and well-educated women and men who can put vanity and arrogance aside. This is an irreducible truth."

Univ.-Prof. Dr. Johannes Fischer
Chairman of the JKU ethics committee

Reporting to the authorities

All clinical trials in accordance with AMG, all medical device trials in accordance with MPG, and all non-interventional studies in accordance with NIS-VO are to be reported to the Federal Office of Safety in Health Care (BASG) or the Agency for Health and Food Safety (AGES). When EU Regulation No. 536/2014 comes into effect (expected 2022), clinical trials will need to be submitted to the European Medicines Agency (EMA) via an online EU portal. The EU portal is then used to forward the information to national authorities and the responsible ethics committees.

Application to approve a clinical trial
In accordance with § 40 of the Medicines Law (AMG), clinical trials must always be submitted to the authorities for approval. The application must be made electronically and must include the following documents:

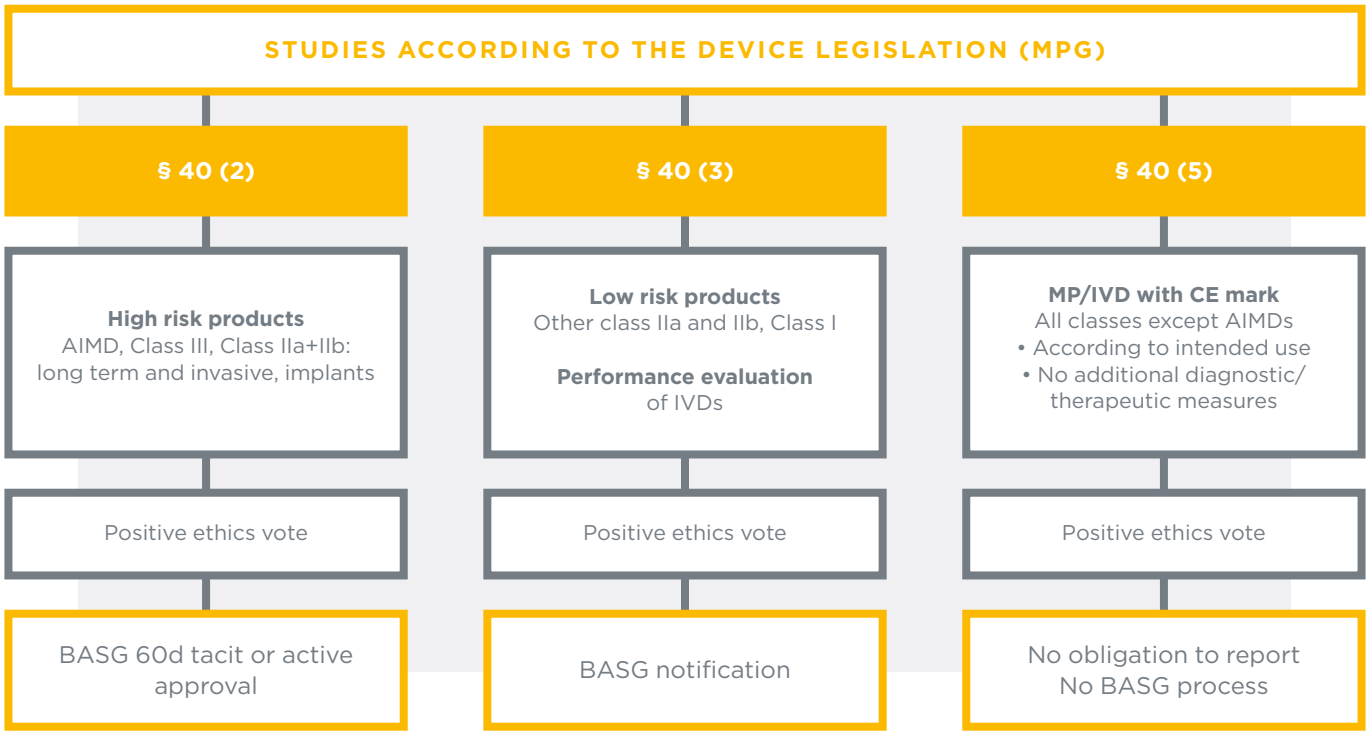
- Cover letter
- EudraCT application form (as pdf and xml version)
- Current version of the protocol, synopsis and the signature pages
- Investigator information (investigator's brochure, IB)
- Product dossier (investigational medical product dossier, IMPD)
- Patient information and declaration of consent
- (informed consent)
- Summary of the pediatric investigation plan
- (if applicable)

Detailed information can be found in the document "List of required documents (L_I211)" (see: basg.gv.at/gesundheitsberufe/klinische-studien/klinische-pruefung-arzneimittel ▸ „Leitfaden und Dokumente").

When is it necessary to report a medical device study to the authorities?
Not all clinical trials that include the use of medical devices need to be reported to the authorities; a **report** is **required** if **one** or more of the following points applies:

a. The investigational product is not CE marked
b. The investigational product is CE-marked but is used in clinical trials beyond the scope of its intended purpose
c. The investigational product is CE-marked and used within the scope of its intended purpose, but the clinical trial requires additional diagnostic or treatment measures
d. The investigational product is an active implantable medical device (AIMD)
e. There is a prototype to be tested and clinical data will be generated
f. The study is a "Pilot" study, "proof-of-concept" study or "basic research"
g. The study's purpose is to generate findings that prove a deviation from the usage instructions or serve as the basis for a modification of the usage instructions

General Information – Named patient use
Currently, no submission or approval by the ethics committee or authorities is required in Austria. According to § 8 (1) item 2 of the AMG, named patient use involves the urgent treatment of specific patients to avert a threat to life or serious damage to health. Systematically collecting data in regard to the safety and efficacy of a medicine in the context of named patient use is thereby not permitted.



(AGES guidelines for submitting a CT according to MPG dated 03/16/2016, p. 22)

Reporting procedure for a medical device study/performance evaluation test

In general, the responsibility to correctly classify clinical studies lies with the sponsor/applicant and the responsibility to classify the product lies with the manufacturer. Assistance to classify a medical device is available in Annex IX of Directive 93/42/EEC or in Annex II of Directive 98/79/EC for in vitro diagnostics.

The corresponding form for clinical trials (application-form.basg.gv.at/mpgform) from MD/performance evaluation tests from IVDs of the BASG must be used for proper reporting.

Additional documents to be submitted (in contrast to AMG studies)

- German language instructions for medical devices with CE markings
- Manufacturer's declaration of conformity
- Certificate(s) of notified bodies
- Written assurance that the medical device – with the exception of the points that are the subject of the clinical trial – complies with the basic requirements of the relevant directive
- Information about the design/manufacturing process, especially relating to sterilization
- Results of the design calculations, tests, technical tests, etc.
- Results of the risk analysis
- List of fully or partially applied standards
- The risk management measures applied to reduce the risk of infection in the case of products made using animal tissue
- Data regarding tests necessary to assess the safety, quality and benefit of substances or derivatives made from human blood

GENETIC ENGINEERING APPLICATIONS.

All work, methods and procedures at scientific universities or scientific federal institutions that enable targeted interventions in the genetic material and thus in the biochemical control processes of living beings or viral genomes (i.e. genetically modified organisms, "GMOs") must, according to § 19 of the Genetic Engineering Act, be registered with the Federal Ministry for Education, Science and Research (BMBWF) by the operator (thereof a natural or legal person, a partnership or purchasing company that operates a genetic engineering facility or carries out work with GMOs or releases) before the start of the research project. Corresponding projects must also be submitted to the responsible ethics committee (see "Reporting to ethics committees and authorities" starting on page 24).

The following types of work with a GMO must be brought to the attention of the appropriate authorities with respect to safety protocols:

- Initial work with genetically modified microorganisms ("GMM") in a safety level 1 or 2 genetic engineering facility
- Additional work with GMM in a safety level 2 genetic engineering facility
- Initial work with transgenic plants or animals in a genetic engineering facility
- Additional work with transgenic plants or animals in a genetic engineering facility, provided that a safety classification of safety level 1 is not permitted
- Additional work with transgenic vertebrates at safety level 1 in a genetic engineering facility

EXCEPTION: The operator must notify the authorities before starting their work and obtain approval for work carried out with GMMs in a genetic engineering facility at safety levels 3 and 4.

Biological safety committee

In accordance with § 16 of the Genetic Engineering Act, the operator (e.g., a JKU research institute) must also establish a biological safety committee. The operator must provide a detailed description of the genetically modified organism and the cells used for each project. All necessary safety measures and methods for the safe disposal of the GMO must also be described and ensured before the work may be performed. A corresponding classification of the safety level is carried out together with the committee based on this description. This information must be made available to the authorities with the registration and approval application.

Additional information

In addition to the information about the operator, GMO, safety level and disposal, the authorities must receive the following information:

- Description of the parts of the genetic engineering **facility** that are relevant to the work with GMOs and their safety (room numbers, possibly with a map)
- **Name** and **qualification** of the biological safety representative and their deputy (see § 14 GTG)
- Information about **accident prevention measures**

Additional details about genetic engineering applications can be found on the Federal Ministry for Education Science and Research homepage (BMBWF) (bmbwf.gv.at/Themen/Forschung/Forschung-in-%C3%96sterreich/Services/Gentechnik.html).

EXPERIMENTAL RESEARCH IN A LABORATORY.

General Information

In contrast to field studies, working hypotheses are tested under controlled experimental conditions through laboratory study, requiring an artificial environment developed especially for the study and with the advantage of being able to observe all influencing variables and potential confounding variables. As a result, changing a single variable so that changes in a trial group compared to a control group have the same essential characteristics in all (ceteris paribus) and can be attributed to this specific variable is only possible in the laboratory.

Formulating a hypothesis

Although many findings can be traced back to chance observations, typically exclusively descriptive research (collecting data, undirected experiments) is often fruitless. To counteract this situation, the research should enter a hypothesis-driven phase. To this end, a corresponding research project is to be formulated as part of a project plan (similar to clinical studies). Developing a hypothesis is particularly important (see "Statistics" starting on page 20). Creating a project plan should also target project funding. Even if the research will not receive external funding, a fully formulated project plan is still required.

Data management

In order to guarantee the data's quality and integrity, recording the data in a correct and complete way is imperative. It is generally recommended to follow **JKU guideline 8213** "Guideline for Research Data Management Policy" to document data used for laboratory projects. Among other things, the guideline recommends applying the ALCOA principle of Good Clinical Practice. ALCOA is an acronym and describes the five most important aspects when working with clinical research data:

- **A**ttributable (assignability of the data)
- **L**egible (legibility, traceability and reproducibility)
- **C**ontemporaneous (prompt collection of data)
- **O**riginal (collection of original data)
- **A**ccurate (data is stored truthfully, completely and reliably).

Measurement methods

Adequate equipment and measurement methods must be used to guarantee the ALCOA principle, even with experimental data. The best possible and state-of-the-art measurement methods should always be used to minimize measurement errors. Correctly interpreting data requires comprehensive understanding of the equipment and methods used.

Data acquisition

Similar to clinical studies in which recorded data requires a case report form (CRF), any data recorded in the laboratory must also be properly documented by implementing a test record based on continuous and chronological documentation in a paginated or page-defined laboratory log. The test record documents each individual experiment. Ideally, the test record not only contains the instruction sheet for the respective experiment, but also the collected data (e.g.: the counting slip, the printed picture of a microscopic image, the printout of a recorded current, the printed documentation of an immunoblot, etc.). In accordance with Good Documentation Practice (GDocP), all entries, additions, alterations or corrections must be signed with an abbreviation and date. Removing pages from this type of laboratory log is forbidden. Full documentation protects against falsifying data and any unjustified accusation of falsifying data. Storing documentation complies with "Scientific Misconduct" (starting on page 40).

HANDLING DATA.

General Information

Progress in medical science depends on properly collecting, processing, and archiving research. Although collecting clinical study data is particularly important for medical research, new EU General Data Protection Regulations (GDPR), effective as of May 25, 2018, mean that in addition to outlined national laws (e.g.: AMG or MPG), researchers, sponsors and authorized persons must adhere to all applicable EU standards. This applies to health data which, according to Art. 9 of the GDPR, is part of the special categories pertaining to personal data and must be classified as subject to particular protection. This applies particularly if data is to be transferred to other EU countries.

Legal Basis to Collect Data

- For medicine and medical device studies in accordance with AMG and MPG, the signed patient explanatory document and declaration of consent (informed consent) are the main legal bases to collect patient data as part of a clinical study (§§ 38 f AMG, §§ 49 f MPG). The same applies to non-interventional studies according to the NIS regulation (NIS-VO).
- In regard to planned research projects (e.g., retrospective data collection, registry studies) that do not fall under AMG, MPG or NIS-VO, consent according to Art. 7 GDPR is a possible legal basis for data collection. In accordance with Art. 9 (2) lit. j GDPR in combination with the Research Organization Law, however, the processing of (sensitive) personal data for archival purposes in the public interest, for scientific or historical research purposes or for statistical purposes in the context of Art. 89 (1) GDPR, is permitted even without consent within the context of Art. 9 (2) lit. a GDPRA legal review is always required in order to determine whether or not consent can be replaced by other applicable legal bases in accordance with Art 6 & 9 GDPR.
- Furthermore, the criteria to determine the data and the recording tools (e.g., case report forms, electronic databases, etc.) must be specified in the study protocol and submitted to the ethics committee for review.

Processing and transferring data

- The responsibilities of the sponsor and investigator with regard to processing and/or transferring data as part of a clinical trial and as defined by AMG or MPG must - by law - be precisely recorded as part of a corresponding data protection clause included in a study contract.
- According to § 32 (4) AMG and § 63 (6) MPG, a Principal Investigator can also delegate processing and/or transferring of certain data (e.g., reporting a study to the authorities and ethics committee, statistical evaluation, etc.) to an external scientific institution (e.g., KKS Linz), provided that that institution is also the sponsor of the study.
- In regard to other research projects (e.g., registry studies, survey investigations, etc.) that do not fall under AMG or MPG provisions, clarification as to who is responsible for data processing in accordance with Art. 4 item 7 GDPR must be provided. The designated individual must ensure that all data protection principles are observed in accordance with Art. 5 GDPR along with the data subject rights as outlined in Chapter III of the GDPR. In accordance with Art. 28 GDPR, the responsible person can also delegate certain data processing tasks to a designated data processor. This, however, requires an order processing contract (AVV).

- Special care is required if data is to be transferred outside of the EU/EEA as, for example, part of a collaboration effort with an American sponsor. This is to ensure GDPR protection standards even if personal data is being transferred to a non-EU country in accordance with Art. 44 GDPR. According to Art. 45 ff GDPR, transferring data to non-EU countries is permitted providing an adequacy decision has been issued by the EU Commission or standard data protection clauses, approved rules of practice, certifications (suitable guarantees), or binding internal data protection regulations. Art 49 GDPR allows for exceptions in certain cases so that data may still be transferred to non-EU countries without an adequacy decision, suitable guarantees or binding internal data protection regulations. The corresponding guarantees must be ensured in advance and documented in the study contract as well as in the patient explanation document and declaration of consent. The ethics committee will check both documents accordingly.

Pseudonymization of personal data

- According to Art. 4 item 5 GDPR, **pseudonymization** is the processing of personal data in such a way that the personal data can no longer be assigned to a specific data subject without the use of additional information (identification key), provided this additional information is stored separately and is subject to technical and organizational measures which ensure that the personal data cannot be assigned to an identified or identifiable natural person.

Note: In accordance with AMG or MPG, data originating from clinical research studies must always be pseudonymized data in order to identify any involved participant, guarantee patient safety, provide transparency and facilitate any inspection by the authorities. The principal investigator is responsible for pseudonymizing data. The same applies to non-interventional studies, meaning anonymizing data can only be applied to research projects that are not subject to AMG and MPG. GDPR does not apply in cases of complete anonymization.

Quality of the pseudonymization

GDPR does not inherently provide for any special degrees of pseudonymization. GDPR also does not explicitly provide for an obligation to pseudonymize. Personal references cannot be eliminated through pseudonymization, so the person concerned can be identified again via appropriate technical work (reidentification).

Ensure that the following data subject information is not included:

- Name details (including initials)
- Date of birth (unless the person concerned has expressly consented to this data point)
- Address details
- Contact details (e-mail, telephone number, etc.)
- Profession
- Identification numbers (e.g.: social insurance number, admission number, case number, etc.)
- Selective dates (e.g.: date of admission or discharge, date of examination, date of operation, etc.)
- Rare selective medical data
- Free text documents (e.g.: doctor's letters, findings texts, disease courses etc.)

The use of IDs is therefore recommended when pseudonymizing text-generated data.

Note: The fundamental right to data protection expires once the person concerned has passed away. The individual's legal successor is not entitled to the data. Data from those who have passed away can be processed without data protection requirements.

Cryptographic encryption

When transferring health data (special categories of data according to Art. 9 GDPR) electronically, corresponding technical measures must be taken to guarantee confidentiality. In these cases, cryptographic encryption is recommended. Select a secure cryptographic method for encryption, for example, the "Advanced Encryption Standard" containing a key length of a minimum of 256 bits (AES-256). This encryption is available in the 7-ZIP programs (www.7-zip.org) or Cryptomator (cryptomator.org).

Common encryption techniques are:

- Encryption using a private key
- Hash function (scatter function)
- Key-dependent cryptological hash functions
- Deterministic encryption or keyless cryptological hash function
- Tokenization

Additional criteria to support data protection is also available under Art 29 Data Protection Group pertaining to anonymization methods, WP 216 on page 24 ff.

Archiving data

According to § 2d (5) FOG in conjunction with Art. 5 (1) lit. e GDPR, personal data can be stored and processed for archival purposes in the public interest, for scientific or historical research purposes or for statistical purposes within the context of Art. 89 (1) GDPR. There is no obligation to determine a storage period/limit if no time limits are provided by law. **Minimum** storage periods stipulated by law do not conflict with § 2d (5) FOG, so longer processing of personal data is permitted in these cases. Only provisions that provide for a **maximum** storage period take precedence as special provisions over § 2d (5) FOG.

The following statutory storage requirements/periods must be observed:

- Medical documentation: In accordance with § 10 (1) item 3 of the Hospital and Sanatorium Law (KAKuG) and § 21 (5) of the Upper Austrian Hospital and Sanatorium Law, medical histories must generally be stored for a minimum of **30 years.**
- Medicine study: **15 years** (in accordance with § 46 (2 & 3) AMG). Once EU Regulation No. 536/2014 comes into effect (expected 2022), data must be stored for **25 years.**
- Medical device study: There are **no** requirements in the Medical Devices Law (MPG), but once EU Regulation No. 745/2017 comes into effect (May 26, 2021), the storage period will be **10 years** and **15 years** for implantable products according to Annex XV, Chapter 3 (3).
- Performance studies for in vitro diagnostics: While MPG does not stipulate any guidelines in this regard, EU Regulation No. 746/2017 (effective May 26, 2022) states in Annex XIV, Chapter 2 (3) that once the clinical performance study ends, data must be stored for a minimum of **10 years.**
- Non-interventional studies: According to § 12 of the NIS regulation, those responsible for the study must store all documents and data for a period of **15 years** once the non-interventional study ends..
- Research projects at scientific institutions: In the case of research projects at scientific institutions in accordance with § 2b item 12 FOG, the storage period from the activity results publication date for data processed as the basis for activities for scientific research purposes is at least **10 years** to prove compliance with Good Scientific Practice and up to **30 years** for establishment, exercise and defense of legal claims (§ 2f (3) FOG).

Rights to data disposition

- The rights of use for works protected by copyright that have been created by university faculty members during their university activities are based on the relevant contractual provisions of JKU. In addition, the provisions of § 106 of the University Act and Copyright Law apply in their currently applicable version. According to § 106 (1) item 1 of the University Act, scientific staff of the university faculty are entitled to publish their own scientific research work and results. This also applies to doctors in specialist training and to scientific personnel in the context of third-party funded projects (project personnel). In addition, scientific staff of the university faculty who have made their own academic contribution to a research project have the right to be named as co-authors. Scientific personnel who independently create works that are protected by copyright therefore have the right to be named as the sole author.
- Service inventions in accordance with § 7 (3) PatG must be brought to the attention of the Rectorate. According to § 106 (3) of the University Act, JKU has claiming rights. The researcher is entitled to appropriate special remuneration for the transfer of an invention made by them to their employer and for the granting of a right of use with regard to such an invention. The inventor is entitled to be named as the inventor. In the case of service inventions by employees of JKU or Kepler University Hospital GmbH (KUK) and JKU, both KUK and JKU will ensure that they can directly or indirectly claim the inventions made by their employees within the scope of their work for the clinical area of the medical faculty, and, depending on the costs, that these can be used for the benefit of KUK or JKU.
- In the case of interactions and collaborations with industry partners, it must be determined to what extent the primary data usage right is contractually due (e.g., in the case of research contracts) to a legal entity other than JKU or KUK. It must therefore be contractually ensured that JKU or KUK is granted those rights of disposition over the data that are necessary to fulfill their storage obligations. Furthermore, it must be ensured that JKU or KUK is in any case entitled to use the results developed within the framework of the contract (also free from competition), whereby these can be used for teaching and research at a minimum.

AUTHORSHIP AND PUBLICATION.

Publication and use of JKU affiliation according to JKU SOP 8212

The purpose of science is twofold: first, to broaden humanity's knowledge base and secondly, to present this information for peer-review thereby giving rise to additional discoveries. To this end, scientific publications are the foundational tools that researchers can use to share their results. Through such publications, authors announce a research finding, identify themselves with that assertion and take responsibility for the accuracy of the published material. The content of a scientific publication is to state the paper's aim, the methodology used, the results of the research project as well as a critical discussion through the lens of the concurrent scientific developments. A publication must be structured in such a way that the reader is able to independently reproduce the experiment and achieve identical results. All results must be described in a comprehensible manner, both the author's and external preparatory work must be duly cited. Previously published results must be properly cited and only referenced insofar as it is necessary for a clearer understanding of the current investigation.

The correct use of affiliation for publications, lectures and research projects is specified in **JKU SOP 8212** ("Guideline for Indicating Affiliation for Publications and Research Projects"). University employees are obliged to publish under the JKU affiliation, employees at university clinics or clinical institutes who have no employment relationship with the JKU are encouraged to use the JKU affiliation. Instructors who are published within the academic year of their lecturing activity are entitled to use the JKU affiliation. Because of their contracts, this also applies to KUK researchers at non-professorial institutions without an employment relationship with JKU.

Legal publication obligations

A clinical study report, per AMG or MPG respectively, is issued to the authorities and the appropriate ethics committees as a report for the benefit of trial participants. Once EU Regulation No. 536/2014 on clinical medicine trials comes into force (expected 2022), every clinical trial will be summarized in terms accessible to the non-specialist, this summary will also be added to an EU database. The lay summaries should be written using plain language and will act to inform the public regarding all salient aspects of the clinical trial. The information should be factual and not of a promotional nature. The lay summaries are intended to describe the main aims and reasons for conducting the clinical trial. The demographic data for the trial participants and the key results relating to efficacy and safety should be given particular emphasis.

Copyright

In research projects, intangible goods are created in the form of intellectual creations (i.e., scientific works protected by copyright) and inventions. Both are the subject of intellectual property rights (IPR), whereby copyright has a special position: no application, registration, examination, etc. of the work is required. Since the University Act came into effect on 1/1/2004, an important decision-making power of the federal government relating to the right to claim service inventions has passed to the universities. As a result, intellectual property rights (especially patents) are now of great importance to Austrian universities in addition to copyright.

All pertinent legal provisions must be respected in order to uphold copyright law and international scientific practice. This also applies to study protocols for submission to the appropriate authority and ethics committee, publishing or initiating an individual study protocol is the first step in documenting a work protected by copyright law. Should the research project involve numerous contributors, great care should be taken when defining the division of labor, particularly with regard to primary authorship and the attendant intellectual rights thereof. Additional information is available on the JKU homepage (help.jku.at/forschung/de/intellectual-property-rights-ipr-immaterialgueterrecht-erfindungen-patente-urheberrecht) or via the IPR management (patent@jku.at).

Authorship

Being named as an author in a scientific paper is associated with active intellectual and practical or procedural participation in a project. All authors are therefore responsible, either individually or jointly, for the correct content of a scientific publication. The order of the authors or at least the distribution of the main roles should be determined in advance.

The following three requirements must be met to be named as an author:

- Substantial contribution to the planning, organization and execution of the study, collecting, processing and interpreting of data (e.g.: statistics)
- Compose and/or perform critical review(s) of the manuscript
- Approval of the final version of the manuscript for publication

All persons who meet these three criteria may be named as authors. An “honorary authorship”, i.e., authorship without fulfilling the above points, is not valid and will not be recognized.

Order of authors

Typically, the researcher who has made the greatest procedural, intellectual and/or conceptual contribution to the research project will be named first on the list of authors. The main task of the first author is to write a preliminary manuscript. Sharing the first authorship is only permitted if the first and second authors have contributed to the creation of the data to the same extent. The authorship of the project manager can be documented by a second or last authorship, provided that this employee contributed intellectually and conceptually to the creation of the publication. In the case of cooperation between several institutions, the key members and roles of the list of authors should be clarified in advance.

SCIENTIFIC MISCONDUCT.

General Information

Researchers, by the very nature of their work, have a responsibility to society. This is made manifest through ethical behavior in their scientific endeavors. In order to maintain a high level of quality and to keep research at a high international level – which actively contributes toward supporting innovations in business, technology, medicine and society – implementing preventive and corrective measures to ensure ethical conduct in scientific work is imperative. More detailed information can be found in JKU guideline 8201 "Guideline for Ensuring Good Scientific Practice".

Definition

Scientific misconduct includes all deliberate or grossly negligent false information, manipulative acts, violations of intellectual property rights and/or hindering other scientists' research. Misconduct can manifest itself as active participation in, knowledge of, or responsibility for scientific misconduct or malversation.

Types of scientific misconduct

False information
- Fact-twisting while collecting data
- Fabrication of data, meaning the use or publication of data that has been fabricated, i.e., baselessly invented, in connection with scientific experiments or scientific studies
- Falsification and/or manipulation of data, e.g.:
  - Selecting and/or rejecting undesired or insignificant results without disclosing them or by manipulating a representation or illustration
  - Data elimination, i.e., unfounded and non-transparent omission of data
  - Forging signatures to feign data authorship
  - Distorted interpretation or deliberate misinterpretation of results and unjustified conclusions

Intellectual property infringement
- Plagiarism and intellectual property theft
- Exploitation of research approaches and ideas, particularly as a reviewer
- Presumption or unfounded assumption of academic authorship or co-authorship
- Failure credit co-authors who have contributed significantly to the achievement of a scientific finding or publication
- Failure to note controversial opinions
- Elimination of primary data if this violates legal provisions or generally recognized principles of scientific work

Other
- **Sabotage** and/or removal of documents or data from other scientists
- **Covering up** and/or **concealing** scientific misconduct and inciting the same

Ombudsman's Office for Good Scientific Practice

In order to promote scientific integrity and as a point of contact in cases of suspected scientific misconduct, an Ombudsman's Office for Good Scientific Practice has been set up in accordance with **JKU guideline 8201 "Guideline for ensuring Good Scientific Practice".** The Ombudsman's Office consists of five members who have been elected for a three-year term. The members must carry out their duties independently and without interference. The Ombudsman's Office must investigate any suspicious facts or indications of scientific misconduct by researchers at JKU that are brought to its attention and take appropriate action.

Procedure

If the Ombudsman's Office becomes aware of a suspected case of scientific misconduct, it must start preliminary investigation immediately. If the suspected case cannot be refuted during the preliminary investigation, the Ombudsman's Office must set up a specialist committee. If necessary, this committee must obtain additional information relevant to its decision. During this process, the committee must obtain a written statement from the informant and from persons whose rights could be impaired by the suspected case or give them the opportunity to verbally present their viewpoints. Oral statements must always be recorded.

The employee concerned in the potential case must be personally informed of the allegations or suspicious facts. The employee concerned has the right to make a statement within 3 weeks of becoming aware of the accusations. The person concerned must also be given the opportunity to comment on the allegations verbally. All proceedings, including all incriminating and/or exonerating facts and evidence, must be documented in writing. The person concerned has the right to inspect all documents relating to their case.

After the deadline has expired, the committee meets privately to discuss and decide on whether there has been scientific misconduct. If necessary, the committee may call in experts as consultants or commission additional expert reports in order to make a decision. Finally, the chairperson of the specialist committee must inform the person concerned, the chairperson of the Ombudsman's Office and the Rectorate in writing of the result of the investigation and the committee's decision. The person concerned has the right to file an objection to the Rectorate regarding any deficiencies in the procedure or related to the decision, whereby a different decision could have been made based on objective observation. The Rectorate must review the objection and, if necessary, arrange for the procedure to be repeated. If the objection is not sustained, the person concerned must be informed in writing. There are no means available to appeal the second decision.

Consequences in the event of scientific misconduct

If the specialist committee decides that there has been scientific misconduct, the Rector must take appropriate legal action against the individual concerned.

If, on the other hand, the suspicion is not confirmed, the specialist committee must terminate the proceedings with a decision. This must be communicated in writing to the Rectorate, the Ombudsman's Office, the person concerned, and the persons involved in the procedure. If requested by the person concerned, the decision must be published by the Rector in the JKU newsletter.


Cryo-
Apron
TEMPSHIELD

COOPERATION WITH INDUSTRY.

General Information

Collaborations with external industry partners in the clinical trials phase often result in a mutually advantageous outcome. Patients benefit by receiving access to new treatment options at a significantly earlier stage. At the same time, JKU benefits by being an active agent in advancing the cause of science. JKU has enacted a variety of structural measures to cultivate and promote such collaborations and ensure an ongoing transfer of knowledge and expertise.
The execution of projects with industry, inter alia, is described in the **JKU guidelines 8204** "Guideline for Projects According to §27 of the University Act", **8203** "Guideline for Projects According to §26 of the University Act" and **8205** "Guideline for Reimbursement of Costs for Projects According to §26 and §27 of the University Act". When collaborating with industry partners and KUK researchers, KUK specifications must be considered.

Contract research or application research

Once initial contact has been made with the collaboration partner, it must be clarified whether the work is a contract or an application research project. According to § 27, the EU, the Austrian Research Promotion Agency (FFG), the Austrian Science Fund (FWF), the Christian Doppler Research Association (CDG) and regional authorities can act as major donors for research funding or application research projects. In the case of a contract research project, the contractor commits to provide a specific research service within a specific time and to surrender rights to the research results, while the client commits to pay a fee. Clients can be companies, private individuals or (regional) corporate bodies.

In the case of applied and contract research projects, the processes required in **JKU guideline 8203** "Guideline for Projects According to §26 of the University Act" and **8204** "Guideline for Projects According to §27 of the University Act" must be observed. The full cost coverage prescribed in accordance with §26 and §27 of the University Act must be guaranteed in accordance with the specifications in JKU guideline **8205** "Guideline for Reimbursement of Costs for Projects According to §26 and §27 of the University Act".

SUPERVISION OF JUNIOR RESEARCHERS.

Mentoring and supervising junior scientists is fundamental for the continuity of sound and effective scientific training, Supervision in the clinical environment must be singularly thorough. Due to the inherent complexity involved with measurement methods, interpretation of data, obligatory controls, and proper data analysis, it is vitally important that an experienced scientist lend their expertise to nurture the next generation of science professionals.
The extent of supervision also depends on the respective training stage of the junior scientist. For the supervision of Bachelor's theses at the medical faculty of JKU, a corresponding Guide in the currently valid version is available at the Center for Medical Teaching ("Guide for Bachelor's Theses for Tutors in the Human Medicine Bachelor's Program"). The guide "Master's Thesis for Students in the Human Medicine Master's Program" is available for students.

The following recommendations are intended to provide guidelines regarding junior researchers:

- Every junior researcher should be assigned a contact person (mentor) in a working group who is responsible for training and supervision
- The ratio of supervisor to supervised persons should allow for adequate individual attention
- The supervisor must provide guidance for the planning of experiments, data acquisition, their documentation and the interpretation of results
- Holding regular lab meetings and seminars (e.g., journal clubs) is recommended. These gathering contribute significantly to training and support, and constitute an important element of the informal peer review system

Each supervisor will take their ethical and moral responsibilities to heart. Each supervisor will ensure that intensive guidance and training in the principles of Good Scientific Practice and Good Clinical Practice is provided to students, graduate students and doctoral candidates alike. For the sake of holistic learning, theory and practice should be mutually supportive in the introduction, preparation and execution of scientific work and research projects. This includes ongoing reviews of and reflection on methodological and theoretical skills, including statistical procedures, and compliance with data protection. Supervisors will strive to foster an awareness and appreciation for patient safety and data integrity.

In addition to supervision, junior researchers should also receive guidance on the topics of statistics and legal frameworks. Comprehensive Good Clinical Practice (GCP) training is also required for scientists who wish to work as investigators in clinical medicine or medical device studies. Please refer to the consultation and training service of KKS Linz (see "Legal bases" on page 52).

COMPETENCE CENTER FOR CLINICAL STUDIES (KKS LINZ) AT THE MEDICAL FACULTY LINZ.

The KKS Linz at the Center for Clinical Research (ZKF) was founded in autumn 2019 by the faculty of medicine in the hope of providing advice and operational support to researchers for the proper planning, implementation and completion of clinical research projects. This is made possible by access to expert advice, providing effective services and support through training and continuing education, especially for clinical studies and clinical research projects. By establishing efficient, qualified and internationally competitive structures, KKS Linz strives for a sustainable increase in the quality of research projects. The defined goal of the KKS Linz is to create an environment wherein reproducible data – the foundation of evidence-based medicine and reputable academic publications – can be generated.

In addition, KKS Linz is an active member of the KKS Network Austria. The aim of the KKS Network is to continuously develop expertise in the field of clinical studies and to continually improve the quality of patient-focused clinical research. Investigators, researchers and members of various professional groups in hospitals, outpatient clinics and doctors' offices, as well as partners from industry are supported through all phases of clinical research projects. The cooperation between the coordination centers in Austria is underwritten in part by university structural funds from the Federal Ministry for Science and Research.

Tasks of KKS Linz

1. Provide advice and support for basic and clinical research projects, in academic or commercial settings including trials with medicinal products, non-interventional and registry studies, medical device studies and performance evaluation tests of in vitro diagnostics (IVDs) in accordance with the applicable laws and regulations
2. Ensure that the quality requirements of clinical research are met, e.g., quality control in the form of monitoring and internal audits in cooperation with investigators, study teams and authorities
3. Provide education and training programs for employees who work in the field of clinical research
4. Promote the interdisciplinary exchange of information and experience between the research institutions, study coordination centers and networks

Services of KKS Linz

Consultations and quality assurance
KKS Linz supports researchers with their planning, execution and statistical evaluation of clinical medicine or medical device studies as well as non-interventional studies. The services are billed according to a corresponding pricing model. The range of services includes:

- Presentation of the general course of clinical research projects/studies as well as the key challenges and problems
- Advice on financing options and eligibility for clinical research projects/studies
- Sharing helpful addresses, contacts and templates
- Compilation of the regulatory and normative requirements to be considered (e.g.: AMG, MPG, GCP, ISO 14155, etc.)
- Support with study planning, including submissions to the ethics committee, study design, sample size estimation, biometrics, etc.
- Support in the planning of data collection, recording and preparation for statistical analysis
- Implementation of data management including the coding of medical terms (MedDRA) and ATC classification
- Support with the statistical analysis of previously collected data
- Provision of statistical services (e.g.: data evaluations)
- Support in the creation of study protocols, explanatory documents and declarations of consent
- Assistance with the official approval, namely in generating an EudraCT form for AMG studies
- Advice and support in the preparation of submission documents for the ethics committee
- Quality assurance through clinical monitoring and support audits

Training
In addition, KKS Linz offers a corresponding training program. The training program includes the following courses and meets all TransCelerate criteria:

- **AMG/MPG/GCP Basic Training** for investigators, employees of the study team as well as researchers and employees of external institutions
- **AMG/MPG/GCP Refresher Training** for investigators, employees of the study team and external parties
- Organization of **external training** (e.g.: IATA-DGR training, Medical Dictionary for Regulatory Activities (MedDRA) terminology etc.)

Contact and registration

Contact details and information regarding the registration process and conditions are available on the KKS Linz homepage (jku.at/med/kks-linz/) and at its statistics department (jku.at/med/medstat).

CONTACT

Competence Center for Clinical Studies (KKS Linz)

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Legal bases.

- Austrian Medicines Law (AMG)
- Austrian Data Protection Law (DSG)
- Austrian Research Organization Law (FOG)
- Austrian Hospital and Sanatorium Law (KAKuG)
- Austrian Medical Devices Law (MPG)
- Austrian System Regulation 2002
- Austrian Release Ordinance (FrSV)
- Austrian Biological Agents Ordinance (ASchG)
- Upper Austrian Hospital Law (Oö. KAG 1997)
- EU General Data Protection Regulation (GDPR)
- EU Regulation No. 536/2014 – on Clinical Trials with Medicinal Products for Human Use
- EU Regulation No. 745/2017 – on Medical Devices
- EU Regulation No. 746/2017 – on in vitro Diagnostics
- EU Directive 93/42/EEC – on Medical Devices
- EU Directive 2001/20/EC – Application of Good Clinical Practice
- EU Directive 2001/83/EC – Creation of a Community Code
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