BASG / AGES
Institute Surveillance
Traisengasse 5, 1200 Vienna, Austria

Guidance for submission and conduct of a clinical investigation with medical devices or performance study with in vitro diagnostics in accordance with §40 of the Austrian Medical Devices Act

NOTE: The English translations of Austrian legal documents are not authorized and therefore not legally binding. The original, legally binding, German text passages are included in the text for your reference.

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Glossary

BASG	Federal Office for Safety in Health Care, Bundesamt für Sicherheit im Gesundheitswesen
CI	clinical investigation
IVD	in vitro diagnostic
MD	Medical device
MPG	Austrian Medical Devices Act, Medizinproduktegesetz
PS	performance study
PE	performance evaluation
AIMD	active implantable medical device
AMG	Austrian Medicines Act, Arzneimittelgesetz

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1. REMIT OF THE FEDERAL OFFICE FOR SAFETY IN HEALTH CARE (BUNDESAMT FÜR SICHERHEIT IM GESUNDHEITSWESEN, BASG)

According to the Austrian Medical Devices Act (Medizinproduktegesetz, MPG), the oversight of clinical investigations (CI) of medical devices (MDs) and the performance study (PS) of in vitro diagnostics (IVDs) is in the remit of the BASG.

The currently valid MPG (in German) is publicly available at https://www.ris.bka.gv.at/Bundesrecht. In addition, the most pertinent paragraphs and definitions of the legislation are cited in this document in annex I.

1.1. Differentiating classification of the device versus that of the study

The responsibility for the classification of the investigational device lies mainly with the sponsor of the study. Reference can be made to the classification of the manufacturer, if that entity is not the sponsor of the study. The following paragraphs are intended to help the sponsor in that assessment.

The MPG legal definitions of medical device, in vitro diagnostic, clinical investigation and performance study do not differentiate whether commercialization of the investigated product is intended, or whether there is a clinical consequence for study participants.

At the time of study submission the investigated device should already be classified. The relevant legislations can be accessed via the overview webpage for the medical devices sector on the website of the European commission.

Questions on classification of MDs and IVDs are not in the remit of the Clinical Trials Division. In case of classification issues, a manufacturer or legal representative located in Austria may submit a request for classification based on §5a MPG to the Medical Devices Vigilance Division.

Questions on the classification of study proposals (e.g. whether they fall under the scope of the MPG and which reporting requirement might be applicable) may be addressed to clinicaltrials@basg.gv.at.

1.2. Clinical investigations with medical devices according to §3 (2) MPG

1.2.1. When does a project classify as clinical investigation of a medical device?

The project classifies as CI, when a medical device according to §2 (1) MPG is systematically investigated on study participants regarding one or more of the goals cited in §3 (2) MPG.

Example: A stent that is CE marked for use proximal to the knee is being investigated for distal use (deviation from the intended use and novel clinical use) with the endpoints including perfusion, duration of hospitalization (performance and clinical benefit) and rate of occlusion (side effect).

A research project further qualifies as CI, if the medical device does not have a CE mark or has one but is used outside the certified intended purpose. This is the case because an introduction to the market or a putting into service according to §15 MPG for research on man is otherwise not legally possible.

Example: A 7-Tesla-MRI without CE mark is used for imaging of cerebral structures and function (investigation of anatomical structure and physiological processes) for basic research in multiple sclerosis

Both situations also apply to existing products that (so far) have not been allocated a medical purpose, but fulfill the definition of a medical device in the context of the study proposal.

Example: An instrument to measure pulse and blood pressure designated as sports equipment is being used for monitoring patients with high blood pressure.

Example: A "home built" device to improve manual flexibility (relief for injuries or disabilities) is investigated for clinical use in patients after stroke.

1.2.2. When does a Clinical Investigation require reporting to the Agency?

All CIs with medical devices according to 1.2.1. require approval by the BASG or notification to it. For further information on procedures, see chapter 2.
The only studies exempt from the reporting obligation (§40 (5) MPG) according to Directive 93/42/EEC are those where

- the medical device carries a CE mark according to §15 MPG **and**
- the medical device is used exclusively according to its conditions of use in the study (reference declaration of conformity /instructions for use) **and**
- the CI does not foresee additional diagnostic or therapeutic measures

Caution!
Active implantable medical devices (AIMD) according to Directive 90/385/EEC are exempted from §40 (5) MPG and can only be investigated in a CI according to §40 (2) MPG, which requires Agency approval.

Note on "systematic investigation":
A project is considered as systematic investigation, if data from more than one investigated participant are aggregated and analysed. Case reports are not considered systematic investigations.

Note on "intended purpose":
The indented use is reflected in the conditions for use, in information/advertising leaflets, in product specific internet information and the technical documentation for the device. Special reference needs to be made to the certified mechanism of action and claim by the manufacturer.
Potential deviations from the intended purpose (for definition see annex I) as per conformity assessment can be additional indications, patient populations, disease severities or phase, or combination with other medical devices; further, if applied as part of other or changed medical procedures, if handled by a different user group (e.g. lay people), in different environmental settings or other changes compared to the intended use.
Note on "additional measures": Every measure that goes beyond the routine applicable in the respective hospital in Austria on the respective patient in his/her individual situation is seen as additional measure (e.g. additional sample taking or higher sample volume, additional examinations or visits). Whether a measure goes beyond the routine is usually reflected in section 6.1 of the ethics application and evaluated by the responsible ethics committee. The structure and documentation of a routine visit by a short questionnaire is not considered as additional measure by the BASG and ethics committees.

1.3. Performance study of an in vitro diagnostic

1.3.1. When is a project considered a performance study of an IVD?

A project is considered a PS, when an IVD according to §2 (5) MPG is systematically investigated on samples, including blood- and tissue-samples of study participants, to achieve one or more of the goals mentioned in §3 (2) MPG.

Example: Immunoassay for the quantitative in vitro detection of antibodies against the SARS-CoV-19 Virus in human serum and plasma. The test is intended to confirm an earlier infection or detect the antibody-titer after vaccination.

A study is further considered as PS, if a test is being used, that fulfills the definition of an IVD, without CE mark or outside its certified intended purpose as tool.

Example: An IVD intended for use with blood samples is used for the measurement of the analyte in urine, which is not reflected in the instructions for use.

Using an IVD in medical research *per se* is not a sufficient argumentation for "research use", as this exemption only applies if no medical purpose is being followed (Dir 98/79/EC und MEDDEV. 2.14/2). Whether or not that test is intended for commercialization, is not a relevant criterion.

1.3.2. When does a performance study require notification to the Agency?

All PSs according to 1.3.1 require notification to the BASG. For further information, see chapter 2. Agency jurisdiction is contingent on the location of sample taking, e.g. sampling in Austria.

Caution!
PSs conducted on **residual samples** according to §65a (2) MPG also need to be notified to the BASG and the concerned ethics committee (see 2.3).

The exemption according to §40 (5) MPG of PSs with IVDs according to Dir 98/79/EC only applies

- to IVDs according to §15 MPG that are CE marked **and**
- if the investigational scope of the PS does not go beyond the intended purpose as defined in the instructions for use

The notes on systematic investigation and intended purpose in section 1.2.2 are equally applicable to this section.

Additional measures are not common in a PS, in contrast to a CI on a medical device, as the PS is not conducted on study participants directly but on samples taken from them. The sampling itself is not considered as additional study-specific measure but is part of the indication to conduct the test. However, in situations where the design would foresee further measures, e.g. an additional blood- or tissue-sample in addition to the routine, §40 (5) MPG could not be applicable.

2. PROCEDURES FOR APPROVAL OR NOTIFICATION

The MPG, as amended, provides for the following procedures for the evaluation of clinical studies by the BASG according to §40 MPG (see also figure in annex II):

2.1. Investigations according to §40 (2) MPG

§40 (2) MPG applies to studies with high risk medical devices, in particular

- Active implantable medical devices
- Class III medical devices
- Class IIa or IIb implantable medical devices
- Class IIa or IIb long-term invasive medical devices

§40 (2) MPG *Mit der klinischen Prüfung von aktiven implantierbaren Medizinprodukten gemäß Richtlinie 90/385/EWG sowie von Medizinprodukten der Klasse III oder implantierbaren oder zur langzeitigen Anwendung bestimmten invasiven Medizinprodukten der Klassen IIa oder IIb gemäß Richtlinie 93/42/EWG kann nach*

befürwortender Stellungnahme durch die zuständige Ethikkommission und Erstattung einer ordnungsgemäßen Meldung an das Bundesamt für Sicherheit im Gesundheitswesen begonnen werden, sofern das Bundesamt für Sicherheit im Gesundheitswesen nicht innerhalb einer Frist von 60 Tagen nach ordnungsgemäßer Meldung der klinischen Prüfung die klinische Prüfung zum Schutz der Prüfungsteilnehmer, der öffentlichen Gesundheit oder wegen sonstigen Nichtvorliegens der Voraussetzungen des §41 Abs. 4 untersagt oder vor Ablauf dieser Frist die Durchführung der klinischen Prüfung genehmigt hat.

§40 (2) MPG CIs with AIMDs in accordance with Directive 90/385/EEC as well as medical devices falling within Class III or implantable and long-term invasive devices falling within Classes IIa or IIb in accordance with Directive 93/42/EEC may commence after the competent ethics committee has issued a favorable opinion and an adequate and complete notification has been submitted to the Federal Office for Safety in Health Care, provided that the BASG has not, within a period of 60 days after submission of an adequate and complete notification, prohibited the CI on considerations of the protection of the subjects enrolled in the investigation, public health, or no fulfilment of other prerequisites detailed in §41 (4) or has approved the CI within that 60-day period.

After the competent ethics committee(s) has/have issued a favourable opinion and the BASG has confirmed to have received a valid submission, the CI may commence either:

a. after the 60 day timeline, calculated from the date of written confirmation of valid submission, has expired (tacit approval = Nicht-Untersagungsverfahren) or
b. upon written notification of BASG approval of the CI within the 60-day assessment period (administrative decision = Bescheid)

To facilitate more rapid processing, the BASG will not issue an administrative decision in case of positive evaluation, but confirms within the 60-day-period that no deficiencies have been raised or that all open questions have been answered and that the study will be approved by tacitly. Tacit approvals are published on the BASG website (see 4.4.1) and are equivalent to administrative decisions.

2.2. Investigations according to §40(3) MPG

§40 (3) MPG applies to investigations with products of average risk and PSs with IVDs, in particular those that are not referred to in §40 (2) or (5) MPG:

- all classes of IVDs
- Class I medical devices
- Class IIa/IIb medical devices: use under 30 days and invasive
- Class IIa/IIb medical devices: non-invasive

***§40 (3) MPG** Mit der klinischen Prüfung von Medizinprodukten gemäß Richtlinie 93/42/EWG, die nicht in Abs. 2 und 5 genannt sind, und der Leistungsbewertungsprüfungen von In-vitro-Diagnostika gemäß Richtlinie 98/79/EG, die nicht in Abs. 5 genannt sind, kann nach befürwortender Stellungnahme durch die zuständige Ethikkommission und Erstattung einer ordnungsgemäßen Meldung an das Bundesamt für Sicherheit im Gesundheitswesen begonnen werden.*

§40 (3) MPG CIs with medical devices in accordance with Directive 93/42/EEC not referred to in paragraphs 2 and 5 and PSs with IVDs in accordance with Directive 98/79/EC not referred to in paragraph 5 may commence after the competent ethics committee has issued a favorable opinion and an adequate and complete submission has been submitted to the BASG.

The CI/PS may commence after the/all competent ethics committee(s) has/have issued a favourable opinion and the BASG has confirmed the validity of the submission via e-mail through the "Confirmation of formal completeness of a Clinical Investigation/Performance study according to §40 (3) Austrian Medical Devices Act (MPG)".

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2.3. Performance Studies according to §40 (3) MPG – Special type §65a (2) MPG

Paragraphs 47 to 54 MPG do not apply to performance studies of an IVD if the PS does **not** entail

- dedicated sampling in kind or amount from study participants **and**
- additional medical investigation or therapeutic measures **and**
- the in vitro investigations cannot have diagnostic or therapeutic consequences for the study participants

Paragraph 65a (2) MPG is limited to PSs with IVDs.

> ***§65a. (1) MPG*** *Die Regelungen der §§39, 40 Abs. 1, 3, 4, 5 und 7, 40a und 40b, 41 bis 44, 45 Abs. 2, 46 bis 64 gelten auch für Leistungsbewertungsprüfungen, sofern Abs. 2 nicht anders bestimmt.*
>
> *(2) Sofern im Rahmen einer Leistungsbewertungsprüfung eines In-vitro-Diagnostikums nicht eine nach Art oder Menge spezielle Probenahme von Prüfungsteilnehmern oder zusätzliche medizinische Untersuchungen oder Behandlungen vorgesehen sind oder die im Rahmen der Leistungsbewertungsprüfung durchgeführten In-vitro-Untersuchungen diagnostische oder therapeutische Konsequenzen für die Prüfungsteilnehmer haben können, gelten die §§47 bis 54 nicht für die Leistungsbewertungsprüfung von In-vitro-Diagnostika.*
>
> **§65a (1) MPG** Provisions of §§39, 40 (1, 3, 4, 5 and 7), 40a and 40b, 41 to 44 (2), and 46 to 64 also apply to all performance studies, unless determined otherwise in paragraph 2.
>
> (2) if the CI is not associated with a specific sampling in type or amount from study participants or with additional medical diagnostic or therapeutic measures or if there are no therapeutic consequences for the study participants. §§47 to 54 do not apply to PSs of an IVD.

Considering the prerequisite that no dedicated sampling in kind or amount from study participants must occur, and that diagnostic and therapeutic consequences are excluded, this implies, that this study type is essentially limited to evaluation of already existent and anonymized samples (biobank) and already concluded subject treatment. Prospective sampling in parallel to therapy and with knowledge of the patient therefore has to be separately justified in the context of §65a (2) MPG.

The procedure described for §40 (3) MPG above is applicable to a PS according to §65a (2) MPG. The requirements for insurance of study participants (§47 MPG) and the requirement for informed consent of study participants are waived for studies according to §65a (2) MPG.

This type of PS may also be conducted on samples from children (§51 MPG), pregnant women (§53 MPG), psychiatric patients (§52 MPG), persons performing military or non-military civil service (§49 MPG).

2.4. Studies according to §40 (5) MPG

Where §40 (5) MPG applies, the study can be initiated after the/all competent ethics committee(s) has/have issued a favorable opinion.

> ***§40 (5) MPG*** *Mit der klinischen Prüfung von Medizinprodukten gemäß der Richtlinie 93/42/EWG, die nach §15 die CE-Kennzeichnung tragen, kann - sofern die klinische Prüfung keine andere Zweckbestimmung des Medizinprodukts als die in der Konformitätsbewertung vorgesehene zum Gegenstand hat und die klinische Prüfung keine zusätzlichen diagnostischen oder therapeutischen Maßnahmen notwendig macht - nach befürwortender Stellungnahme durch die zuständige Ethikkommission begonnen werden. Mit der Leistungsbewertungsprüfung von In-vitro-Diagnostika gemäß der Richtlinie 98/79/EG, die nach §15 die CE-Kennzeichnung tragen, kann - sofern die Leistungsbewertungsprüfung keine andere Zweckbestimmung des In-vitro-Diagnostikums als die in der Konformitätsbewertung vorgesehene zum Gegenstand hat - nach befürwortender Stellungnahme durch die*

zuständige Ethikkommission begonnen werden. §47 gilt nicht. (siehe Erläuterungen zum MPG BGBl I Nr. 143/2009)

§40 (5) MPG CIs with medical devices in accordance with Directive 93/42/EEC that are authorized to bear the CE mark in accordance with §15 may commence after the competent ethics committee has issued a favourable opinion, provided that the clinical investigation does not use the device for a purpose other than that referred to in the relevant conformity assessment procedure and that the clinical investigation does not require any additional diagnostic or therapeutic measures to be taken. PSs with IVDs in accordance with Directive 98/79/EC that are authorized to bear the CE mark in accordance with §15 may commence after the competent ethics committee has issued a favorable opinion, provided that the performance study does not use the device for a purpose other than that referred to in the relevant conformity assessment procedure. §47 shall not apply (see explanatory notes on MPG Federal Gazette I No. 143/2009).

The legal requirements for vigilance and SAE reporting remain. SAEs therefore have to be reported to the BASG.

For studies according to §40 (5) MPG there is no insurance requirement for study participants according to §47 MPG. However, it is in the remit of the competent ethics committee to require insurance, if it is considered that the design of the study poses a risk to the participants.

2.5. Studies according to the Austrian Medicines Act (AMG) and the MPG (combined studies)

The study is considered as combined study, if a **non-integral** medical device/IVD is being investigated in the context of a clinical trial for a medicinal product, or a medical device/IVD is being used without CE mark or outside its intended purpose (see 1.2). If a device is investigated where the device and the medicinal product form a single integral product, which is intended exclusively for use in the given combination and which is not reusable, that product (and the clinical study) is governed by the medicines legislation. Nevertheless, the relevant essential requirements of Annex I apply as far as safety and performance-related device features are concerned.

Requirements from both legislations need to be considered for combined studies. One application each needs to be submitted, e.g. one for a clinical trial according to AMG and one according to the MPG. It is recommended to submit the applications at the same time to facilitate aligning the procedures. Also, a reduced fee applies in this case (see chapter 8).

A combined submission needs to contain the required documents and application forms according to AMG (Eudra CT form) and MPG (BASG form). The cover letter should make reference to the combined application and respective relevant aspects.

The respective requirements of MPG and AMG need to be considered for substantial amendments and reporting of serious adverse events/serious adverse reactions. Reporting needs to occur separately.

See also the Guidelines for the submission of clinical trials according to AMG.

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Combination of a clinical trial according to AMG with a clinical investigation/ performance study according to §40 (5) MPG

Principally, §40 (5) MPG cannot apply where a clinical investigation demands study-specific measures including additional diagnostic or therapeutic measures (see 2.4).

However, where an applicant can provide sufficient justification that study specific measures are exclusive to the AMG part of the study, it is accepted to conduct the MPG part as §40 (5), provided that the criteria of CE mark and use within the intended purpose are fulfilled. The insurance required for the AMG part in this situation needs to cover all study specific measures.

3. SUBMISSION REQUIREMENTS

3.1. How to submit

Electronic submission is required for all CIs/PSs. The completed application form (see 3.2) as XML and PDF together with the other required documents (see 3.3) should be submitted per e-mail to clinicaltrials@basg.gv.at. The submission should be contained in one e-mail and not be split.

Where electronic submission is not feasible, the documents may also be submitted to the BASG on a data carrier per postal mail to the following address: *AGES Medizinmarktaufsicht, Abteilung Klinische Prüfung, Traisengasse 5, 1200 Wien*.

Only one means of submission may be chosen, and double submissions need to be avoided. Documents requiring a signature (e.g. the application form) preferentially should be signed electronically. Where this is not possible, a scan of the signed document may be submitted.

Folders on the data medium should be structured as follows (for details see Annex III and IV):

- ***„1_General information"***
  Cover letter and BASG submission form as xml and PDF
- ***„2_Protocol"***
  Current version of the clinical investigation plan with synopsis and signature pages
- ***„3_IB"***
  Investigator's Brochure
- ***„4_IFU"***
  Instructions for use and other product information
- ***„5_Certificates"***
  Declaration of conformity, certificates
- ***„6_Reports"***
  Other relevant documentation on the investigated devices
- ***„7_PatInfo"***
  Patient information
- ***„8_Additional information"***
  Insurance certificates and ethics committee opinions

The maximal file size is 50MB. Larger documents need to be split in the application. The internal structure of the document should be considered in this case.

3.2. Electronic notification form

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The electronic application form for CIs/PSs is applicable for all submissions according to §40 (2) and §40 (3) MPG. It can be accessed at the following link:

https://applicationform.basg.gv.at/mpgform/

In this system, the application form can be created, populated, stored locally and re-uploaded in case of amendments. The minimum technical requirement for storing a XML-form is the entry of a Clinical Investigation Identification Code (protocol number).
The protocol number serves to identify the clinical study and should be unique and distinct (e.g. it could contain a code for the sponsor, the product, the development program, etc.). A protocol number validated by the BASG is unchangeable for the duration of the study. Potentially variable components, such as version number or creation date should therefore not be part of the protocol number.

Completing the application form does not lead to automatic submission to the BASG. For study notification, the completed application form must be submitted to the BASG as XML and PDF (together with the other required documents, see 3.2. on a data medium.

The signature of the applicant or sponsor on the PDF application form guarantees the correctness of data. The XML is used for further processing and transmission to the EUDAMED database. Therefore, the signatory is responsible for ensuring that the information in the PDF and XML forms are identical.

In case of amendments the updated notification form (XML and PDF) needs to be submitted to the BASG.

3.3. Documents required for a valid submission

A valid submission according to §§40 (1) and (4) MPG needs to contain the documents listed in Annex III (CI) or annex IV (PS).

> ***§40 (1) MPG*** *Der Sponsor hat bei klinischen Prüfungen von Medizinprodukten das im Anhang 6 der Richtlinie 90/385/EWG, im Anhang VIII der Richtlinie 93/42/EWG, bei der Leistungsbewertungsprüfung von In-vitro-Diagnostika das im Anhang VIII der Richtlinie 98/79/EG angeführte Verfahren anzuwenden.*
>
> ***§40 (4) MPG*** *Die Meldung an das Bundesamt für Sicherheit im Gesundheitswesen hat unter Einschluss der in den in Abs. 1 angeführten Anhängen genannten Erklärung zu erfolgen. Die dort angeführte Dokumentation ist auf Anforderung unverzüglich zur Verfügung zu stellen.*
>
> **§40 (1) MPG** In the case of CIs with medical devices, the sponsor shall follow the procedure detailed in Annex 6 of Directive 90/385/EEC and in Annex VIII of Directive 93/42/EEC; in the case of PSs with IVDs, the sponsor shall follow the procedure detailed in Annex VIII of Directive 98/79/EC.
>
> **§40 (4) MPG** The notification submitted to the Federal Office for Safety in Health Care shall include the statement detailed in the Annexes referred to in paragraph 1. The sponsor shall undertake to make available, immediately upon request, the documentation referred to in these Annexes.

3.4. Opinion by the Ethics committee

The submission to the BASG should occur after the competent ethics committee(s) have issued a positive opinion. The date of submission to the ethics committee(s) should be referenced in the cover letter and application form.

In principle, the necessary application for an ethics opinion can be initiated before or simultaneously with the submission to the Agency. The submission date to the competent ethics committee(s) should be noted in the cover letter and in the electronic submission form. A CI/PS can only be declared as valid, when the positive vote(s) by the competent ethics committee(s) are provided

In cases of ethics votes with obligations, these need to be fulfilled in order for the submission to be considered as valid by the BASG. If available, a copy of the approval letter ('favorable opinion') by the ethics committee must accompany the submission documentation.

In case of a negative ethics opinion the study will be rejected by the BASG by official notification. Alternatively, the applicant has the possibility to withdraw the study.
In the case of multi-centre investigations, the competent ethics committee may decide to accept the opinion issued by another ethics committee involved in the same investigation. In this case, the ethics committee assessing the CI/PS must be provided with information regarding all additional investigators and with any documentation permitting assessment of the professional qualification and experience of the investigators, the available facilities, and the qualification of the supporting staff (§57 (2) MPG).

Multi-centre studies may be initiated after the first positive ethics vote has been submitted to the BASG, if the application form is reduced to the site the vote applies to. The residual study sites can then be added during the ongoing procedure or after, whenever the other sites become available. Of note, if study sites are to be added after the conclusion of the initial submission procedure, this is considered as substantial amendment with the respective associated fee (chapter 8).

It is possible for one competent ethics committee to accept that of another as sufficient in the context of a multi-centre study. In this case, the assessing ethics committee needs to have access to all participating investigators from the additional site that are required for the assessment of competence and experience of the investigator, available resources and personnel (§57 (2) MPG).

Further information on the application modalities to Austrian Ethics Committees can be found on the following website: www.ethikkommissionen.at

4. THE BASG PROCEDURE

4.1. Confirmation of receipt

Confirmations of receipt are sent to the contact person indicated in the BASG application form (applicant). The actuality of the information is sponsor/applicant responsibility. Each submission to a study will receive an automatically generated procedure number, which will be indicated in the confirmation of receipt. It is essential to quote this procedure number in any future correspondence pertaining to that procedure or in case of questions.

4.2. Confirmation of a valid and complete notification

The sponsor has to submit to the BASG an adequate and complete notification. Upon receipt, the BASG will assess the documentation for formal completeness as quickly as possible. The start date for the procedure is the next working day for those submissions that occur out of office hours.

If the notification of a CI/PS evaluation is found to be incomplete/incorrect, the BASG will request the applicant/sponsor to provide missing information and/or to correct deficiencies (improvement request, *Verbesserungsauftrag*). The notification submitted will not be considered valid until the deficiencies have been amended. Should the applicant/sponsor fail to submit the requested information, the BASG will reject the application.

Where an application is considered formally complete, this and the date of the valid submission are confirmed to the applicant as electronically signed BASG document. This will be issued per mail to the applicant listed in the application

form. An application that was submitted without deficiencies, is considered as valid from the date of submission. An application that required improvement is considered valid from the date of receipt of the additional/corrected documents.

PSs/CIs according to §40 (3) MPG many be initiated after receipt of the "Confirmation of formal completeness of a Clinical Investigation/Performance study according to §40 (3) Austrian Medical Devices Act (MPG)" and the receipt of a positive ethics opinion.

In case of an application according to §40 (2) MPG, the effective date for the start of the 60-day assessment period will be indicated in the confirmation of completeness (see 4.3).

The BASG will issue a confirmation of completeness for all initial submissions and must be awaited. Initiating the study prior to its receipt or calculating the tacit-approval timeline based on the submission date is not legitimate.

4.3. Expert assessment and letters of deficiency

The expert assessment follows the confirmation of valid submission. The BASG experts will evaluate the technical safety profile, any available medical and scientific information, any remaining risk weighed against the expected benefit of the clinical investigation (risk analysis), and the plausibility of the documents submitted.

Deficiencies may be detected or additional questions may be raised during expert assessment, resulting in additional document/information requests. These will be compiled in a letter of deficiencies, which will be sent to the applicant listed in the BASG-application form by e-mail.

An adequate period of time will be granted to the applicant to remedy the deficiencies. Nevertheless, if this period were insufficient, a written request for extension of the timeline may me submitted with appropriate justification.
Responses to letters of deficiencies have to be submitted in writing together with any documents requested or changed.

Confirmation of resolved deficiencies will be issued by the BASG by e-mail to the applicant. Subsequent approval by the BASG follows the procedure outlined under 4.4.1.

If the deficiencies are not resolved within the given timeframe, the BASG will issue an official refusal as per 4.4.2.

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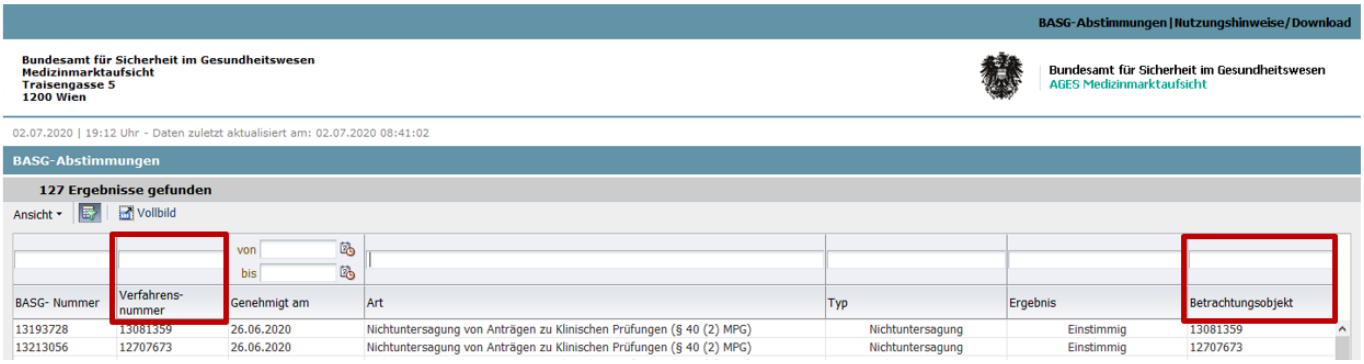
4.4. BASG decisions

4.4.1. Tacit approval/Non-interdiction

An application according to §40 (2) MPG is considered as approved, if a positive ethics opinion has been obtained **and** no deficiencies have been raised during the 60 day assessment timeline by the BASG. The 60-day period starts on the validation date for initial applications and on the submission date for amendments.

The list of decisions can be found on the following website: https://abstimmungen.basg.gv.at/abstimmung_→ "Abstimmungen". To search for a given procedure enter the procedure number ("Verfahrensnummer") of the application in the data fields "Verfahrensnummer" or "Betrachtungsobjekt".



Publication of the decision may occur prior to the expiry of the legal procedure timeframe and is considered sufficient for the documentation of approval of the initial application or amendment.

4.4.2. Official notification ("Bescheid")

Alternatively, an active approval by official notification earlier than the 60-day period is possible. Both paths to approval are equally valid.

Currently, the BASG will not issue positive notifications, but confirms within the 60-day assessment period that no deficiencies have been raised and tacit-approval is accepted. The decision will be published on the BASG website (see above).

4.4.3. Refusal/Interdiction

A study will be refused by official BASG notification, if objections to the conduct of the study, which were notified to the applicant by letter of deficiency have not been corrected satisfactorily or not within the allocated time. The notification will be issued on the basis of §41 (4) MPG.

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5. AMENDMENTS TO THE CLINICAL INVESTIGATION PLAN (§40a MPG)

Where required, the clinical investigation plan may be amended any time during the clinical study.

According to §40a the reporting obligation to the BASG and the competent ethics committee is limited to substantial amendments (i.e., amendments involving changes that may have an impact on the safety of the enrolled subjects and/or the scientific validity of the clinical study).

§40a (1) MPG *Nach dem Beginn der klinischen Prüfung kann der Sponsor den Prüfplan ändern. Wenn die Änderung bedeutsam ist und sich insbesondere auf die Sicherheit der Prüfungsteilnehmer auswirken oder die wissenschaftliche Aussagekraft der klinischen Prüfung beeinflussen kann, hat der Sponsor bei klinischen Prüfungen gemäß §40 Abs. 2 und 3 dem Bundesamt für Sicherheit im Gesundheitswesen und der zuständigen Ethikkommission den Inhalt der Änderung und sämtliche Gründe dafür zu melden. Bei klinischen Prüfungen nach §40 Abs. 5 hat der Sponsor der zuständigen Ethikkommission den Inhalt der Änderung und sämtliche Gründe dafür zu melden.*

§40a (1) MPG After commencement of the clinical study, the sponsor may make amendments to the clinical investigation plan. If, in the case of CIs in accordance with §40 (2) and (3), the amendment is substantial and likely to have an impact on the safety of the enrolled subjects or the scientific validity of the CI, the sponsor shall notify the BASG and the competent ethics committee of the content of, and the reasons for, this amendment. In the case of CI according to MPG §40 (5), the sponsor shall notify the competent ethics committee of the content of, and the reasons for, these amendments.

5.1. Submission

The classification of the amendment as substantial or non-substantial according to Annex V (Classification of amendments) is the sponsor's responsibility and needs to be indicated in the submission (amendment application form)

The amendment application form MPG (F_I200) and additional documentation should be submitted to the BASG by e-mail, or, if not feasible, on a data carrier (see 3.1).

The submitted information should include a summary and justification of changes together with the updated documents. The changes should be clearly identifiable for the assessor (e.g. by compiling a synopsis or summary of changes, by providing a track-changes version/highlighting the changes by colour).

Changes to the application form
Where the changes affect the information in the initial application form, the applicant needs update the latest XML version validated by the BASG. The amended application form as XML and PDF together with other required documents needs to be submitted to the BASG.

5.2. Substantial amendments

All substantial amendments are validated for formal completeness. The procedure followed is the same as for initial submissions as described in chapter 4.2.

As for initial applications, the BASG will issue a confirmation of completeness, which must be awaited. Implementing the changes prior to its receipt or calculating the tacit-approval timeline based on the submission date is not legitimate.

Amendments to CIs/PSs according to §40 (3) MPG may be implemented upon confirmation completeness by the BASG and a positive ethics opinion.

In case of a substantial amendment for a CI according to §40 (2) MPG, the effective start of the 35-day assessment period will be notified in the confirmation of completeness (see 4.3). These amendment procedures are concluded by tacit-approval or official notification.

The same options for decisions described in chapter 4.4 also apply to substantial amendments.

5.3. Non-substantial amendments

Non-substantial amendments should be documented and brought to the BASG's attention with the next substantial amendment and do not have to be immediately notified to the BASG with two exceptions:

- Non-substantial changes that impact on the information in the application form should be submitted to the BASG timely to ensure actuality of the database
- Changes to the protocol required by the ethics committee(s) that relate to the safety monitoring of the patients should be promptly submitted to the BASG

If a separate notification is desired, the amendment notification form F_I200 should be used.

5.4. Special types of amendments

5.4.1. Temporary Halt, Recruitment/Treatment Stop

A temporary interruption of recruitment or treatment with the goal to restart at a later date. If no restart is intended, the applicable procedure is that of an (early) termination (see chapter 7).

The temporary interruption of recruitment or treatment has to be notified to the BASG without delay by using the amendment notification form F_I200. Further details and justification should be provided in the cover letter.

An approval by the BASG of a temporary interruption of recruitment or treatment is not required. It can be implemented immediately. However, the restart after a temporary interruption constitutes a substantial amendment and requires approval.

5.4.2. Restart

The restart of a CI/PS after a temporary halt constitutes a substantial amendment and requires the submission of a substantial amendment to the BASG using the amendment notification form F_I200. Adequate documentation to justify the restart needs to be provided.

Where the sponsor changes intention and decides not to aim at a restart of recruitment or treatment, the BASG also should be notified without delay. Where this results in a termination of the study, a notification according to chapter 7.1 is also required.

5.4.3. Urgent Amendments

According to §40a (5) MPG, the sponsor and clinical investigator have to implement urgent safety measures to protect study participants/users in any situation concerning the course of the study or the development of the medical device(s), where the safety of the study participants/users might be at risk.

§40a (5) MPG *Unbeschadet der Abs. 1 bis 4 haben der Sponsor und der klinische Prüfer bei jeglichem neuen Umstand betreffend den Ablauf der Prüfung oder die Entwicklung des Medizinprodukts in klinischer Prüfung, der die Sicherheit der Prüfungsteilnehmer oder Anwender beeinträchtigen kann, die dringend gebotenen Sicherheitsmaßnahmen zu ergreifen, um die Prüfungsteilnehmer oder Anwender vor unmittelbarer Gefahr zu schützen. Sie haben bei klinischen Prüfungen nach §40 Abs. 2 und 3 unverzüglich das Bundesamt für Sicherheit im Gesundheitswesen und die zuständige Ethikkommission über diese neuen Umstände und die getroffenen Maßnahmen zu informieren. Bei klinischen Prüfungen nach §40 Abs. 5 haben sie unverzüglich die zuständige Ethikkommission über diese neuen Umstände und die getroffenen Maßnahmen zu informieren. Die Meldepflichten gemäß §70 bleiben unberührt.*

§40a (5) MPG Without prejudice to the provisions of paragraphs 1 through 4, the sponsor and the investigator shall, in case of any new event relating to the conduct of the CI or the development of the medical device that may compromise the safety of enrolled subjects or users, take any appropriate urgent safety measures to protect the subjects or users against any immediate hazard. In the case of CIs in accordance with §40 (2) and (3) they shall, without delay, inform both the BASG and the competent ethics committee of such new events and the measures taken. In the case of CIs in accordance with §40 (5), they shall inform the competent ethics committee of such new events and the measures taken. The notification requirements in accordance with §70 shall remain unaffected.

Reporting to the BASG should follow the usual procedure for amendments, using **the** amendment notification form F_I200. All impacted documents (e.g. protocol, investigator's brochure, instructions for use, patient information, etc.) need to be submitted.

6. NOTIFICATION REQUIREMENTS DURING A CLINICAL STUDY

6.1. Serious Adverse Events (SAE) reporting

6.1.1. Notification requirements for sponsors

§42 (8) MPG *Alle schwerwiegenden unerwünschten Ereignisse sind vom Sponsor vollständig zu registrieren und unverzüglich dem Bundesamt für Sicherheit im Gesundheitswesen und den zuständigen Behörden der anderen betroffenen Vertragsparteien des EWR, in denen die klinische Prüfung durchgeführt wird, zu melden.*

§42 (8) MPG The sponsor of a CI has to fully record all serious adverse events and notify them immediately to the BASG and to all other competent authorities in those member states of the EEA in which the CI is being conducted.

SAE criteria:

- the event is serious
- the event is undesired
- a causal context with the device under investigation is not required

The reporting obligation according to §42 (8) MPG applies to the sponsor irrespective of the legal procedure associated with the clinical study. There is no legal exemption for studies according to §40 (5) MPG.
Further, reporting obligations according to §70 MPG need to be considered (see 6.2.).

Examples:

a. Where a medical condition is already established prior to the initiation of a clinical study and surgery has been scheduled to amend it, the definition of an adverse effect according to MPG is not fulfilled and reporting to the BASG as SAE is not required. If the medical condition arises during the conduct of the clinical study, then SAE reporting to the BASG is required.
b. If a hospitalization preceded or was already planned prior to the initiation of a clinical investigation the definition of adverse effect according to MPG is not fulfilled, no reporting as SAE is required. However, if unplanned hospitalization occurs during the conduct of the clinical investigation, SAE reporting to the BASG is required - whether or not causality has been established with the investigational device(s).

6.1.2. Notification requirements for investigators

§61 MPG *Der klinische Prüfer hat die Ethikkommission unverzüglich über alle schwerwiegenden Nebenwirkungen im Rahmen der klinischen Prüfung zu informieren. Die Meldepflichten des §70 bleiben unberührt.*

The clinical investigator shall immediately report all serious adverse device effects occurring during a clinical study to the ethics committee. The notification requirements in accordance with §70 remain unaffected.

§64 (5) MPG *Der klinische Prüfer hat den Sponsor über alle Medizinproduktenebenwirkungen und alle schwerwiegenden unerwünschten Ereignisse im Rahmen der klinischen Prüfung zu informieren.*

The clinical investigator shall inform the sponsor of any adverse device effects and serious adverse events occurring during a clinical study.

Reporting obligations according to §70 MPG need to be considered (see 6.2.)

6.1.3. SAE forms for clinical studies

Reporting of SAEs occurring inside or outside Austria in the context of clinical studies submitted in Austria has to occur with the European SAE reporting forms (line listing). This form and the associated MEDDEV Guideline 2.7/3 "Clinical Investigation: serious adverse effect reporting" were published by the European Commission in may 2015.

Form F_I209 for Austrian SAEs may be requested by the BASG to obtain additional information.

Occurrence of new SAEs, changes or additions to already reported SAEs have to be notified to the BASG and competent authorities in the other participating member states, unless those member states have exempted sponsors from this requirement.

Each SAE in the line listing needs to be associated with a status, i.e.

"a" = added, new event, not reported so far
"m" = modified, new information on an already reported event
"u" = unchanged, no new information for this event since last reporting

Note:
Reporting obligations for SAEs in clinical studies according to MPG differ from those for clinical trials with medicinal products: According to the medicinal products act, (§41d AMG) all SAEs have to be reported by the investigator to the sponsor; however, there is no reporting obligation for SAEs to the BASG. SUSARs on the other hand, need to be reported and usually will be entered by the sponsor into the EudraVigilance (EV) database.

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6.1.4. Reporting timelines

Serious adverse effects that result in immediate risk of death, serious injury or illness, need to be reported without delay, at the latest within 2 calendar days to the BASG; all other events within 7 calendar days. See also: http://ec.europa.eu/DocsRoom/documents/10330/attachments/1/translations/en/renditions/native

6.2. General vigilance requirements according to §70 MPG

§70 (1) MPG *Angehörige eines gesetzlich geregelten Gesundheitsberufes, Gewerbeberechtigte, die berufsmäßig zum Betreiben oder zur Anwendung eines Medizinprodukts befugt sind, Leiter von einschlägigen Prüf-, Inspektions- und Zertifizierungsstellen und technische Sicherheitsbeauftragte von Krankenanstalten haben Informationen über Medizinprodukte im Hinblick auf Zwischenfälle, insbesondere*

1. *jede Fehlfunktion oder jede Änderung der Merkmale oder der Leistung eines Medizinprodukts sowie jeden Mangel in Bezug auf die Kennzeichnung oder die Gebrauchsanweisung, die geeignet sind, zum Tod oder zu einer schwerwiegenden Verschlechterung des Gesundheitszustandes eines Patienten, eines Anwenders oder eines Dritten zu führen oder die dazu geführt hat, oder*
2. *bisher unbekannte schwerwiegende Nebenwirkungen oder das vermehrte Auftreten bekannter schwerwiegender Nebenwirkungen, oder*
3. *bisher unbekannte wechselseitige Beeinflussungen, oder*
4. *schwerwiegende Qualitätsmängel, die ihnen auf Grund ihrer beruflichen Tätigkeit bekanntgeworden sind, unverzüglich dem Bundesamt für Sicherheit im Gesundheitswesen zu melden sowie alle Beobachtungen und Daten mitzuteilen, die für die Medizinproduktesicherheit von Bedeutung sein können.*

(2) *Meldungen gemäß Abs. 1 haben bei Krankenanstalten, außer bei sonstiger Gefahr im Verzug, einheitlich im Wege des ärztlichen Leiters zu erfolgen.*

(3) *Alle natürlichen oder juristischen Personen, die Medizinprodukte im EWR erstmalig in Verkehr bringen und jene Betriebe, Einrichtungen oder Personen, die Medizinprodukte in Verkehr bringen, haben dem Bundesamt für Sicherheit im Gesundheitswesen unverzüglich Zwischenfälle gemäß Abs. 1 und darüber hinaus korrektive Maßnahmen, wie etwa*

1. *jeden mit einem Medizinprodukt verbundenen technischen oder medizinischen Grund, der zum systematischen Rückruf von Medizinprodukten desselben Typs vom Markt durch den Hersteller geführt hat,*
2. *die Ausstellung einer Maßnahmenempfehlung,*
3. *die zusätzliche Überwachung oder Modifikation von Produkten,*
4. *Modifikationen des Produktdesigns von Komponenten oder des Herstellungsprozesses, und*
5. *Modifikationen der Kennzeichnung oder der Gebrauchsanweisung*

mitzuteilen.

§70 (1) MPG Members of a legally regulated health care profession, trade certificate holders licensed to operate or use a medical device, heads of pertinent test-, inspection-, and certification-centres as well as technical safety officers of hospitals shall immediately notify the BASG of any information regarding incidents in relation to medical devices that have come to their knowledge as a result of their professional activity, especially

1. any malfunction or change in the characteristics or performance of a medical device as well as any inadequacy in the labelling or the instructions for use which might lead to or has lead to the death or to a serious deterioration in the state of health of a patient, user, or third party or
2. any hitherto unknown serious adverse device effects or an increase in the occurrence of known serious adverse events or
3. any hitherto unknown interactions or
4. serious quality deficiencies

and to report any observations or data that may be of relevance for the safety of medical devices.

(2) For hospitals, notifications in accordance with paragraph 1 are to be submitted, without exception, through the medical director, unless there is danger in delay.

(3) All natural or legal persons first placing medical devices on the market within the EEA as well as companies, institutions, or persons placing medical devices on the market shall immediately report to the BASG any incidents in accordance with paragraph 1, including any corrective measures taken, such as

1. any systematic recall of medical devices of the same type by the manufacturer, including the technical or medical reasons for the recall,
2. the issuance of recommendations on measures to be taken,
3. any additional surveillance measures or product modifications,
4. changes in the design of product components or in the manufacturing process, and
5. changes to the labelling or the instructions for use.

For more information and downloadable notification forms, see:
https://www.basg.gv.at/en/medical-devices/manufacturer

7. NOTIFICATION REQUIREMENTS TO THE BASG AFTER TERMINATION OF THE CLINICAL STUDY (§44 MPG)

7.1. Planned or premature end of study

The sponsor is obliged to report the end of study to the BASG within 15 days. The (National) end of study usually coincides with the last visit of the last patient (in Austria) unless defined differently in the protocol.

Two options are available for multi-national studies:

1. Sole reporting of the global end of study without reporting the National end - In this case all reporting obligations remain until the global end of study
2. Informal reporting of the National end of study in addition to the subsequent reporting of the global end of study - In this case reporting obligations to the BASG will end with the National end of study with the exception of the provisions for the final study report. The National end of study is usually defined as the last visit of the last patient in Austria.

The end of a CI/PS should be notified and the final report submitted to the BASG using form F_I207.
With the notification of the global end of the trial all open non-substantial amendments should be submitted and a final update to the notification form should be provided, where applicable.

In case of a premature end of study a justification needs to be provided in addition to the notification according to §40 (6) MPG. Where the premature end of study is decided for safety reasons, this notification also needs to be sent to all other affected competent authorities.

7.2. Final study report

The final report must contain a critical evaluation of the scientifically relevant data obtained during the clinical study (§46 (2) MPG).

The final report is to be submitted electronically to the BASG within 12 months of the end of study.

§46 (1) MPG *Für jede klinische Prüfung ist ein schriftlicher Abschlussbericht zu erstellen, der von allen an der Prüfung beteiligten klinischen Prüfern zu unterzeichnen ist.*

§46 (1) MPG For every clinical study (CI/PS), a written final report has to be prepared and signed by all investigators having participated.

§40 (6) MPG *Der Sponsor hat dem Bundesamt für Sicherheit im Gesundheitswesen und den zuständigen Behörden anderer betroffener Vertragsparteien des EWR den Abschluss der klinischen Prüfung, im Falle einer vorzeitigen Beendigung mit einer entsprechenden Begründung, zu melden. Diese Meldung hat auch an die zuständigen Behörden aller anderen Vertragsparteien des EWR und die Europäische Kommission zu erfolgen, wenn die vorzeitige Beendigung aus Sicherheitsgründen erfolgt. Der Abschlussbericht gemäß Anhang 7 Abschnitt 2.3.7 der Richtlinie 90/385/EWG bzw. Anhang X Abschnitt 2.3.7 der Richtlinie 93/42/EWG ist für das Bundesamt für Sicherheit im Gesundheitswesen und die zuständigen Behörden der anderen betroffenen Vertragsparteien des EWR bereitzuhalten.*

§40 (6) MPG The sponsor shall notify the BASG and the competent authorities of the other contracting parties to the EEA involved in the clinical study (CI/PS) of the end or early termination thereof, providing justification in case of early termination. In the case of early termination of the clinical study on safety grounds, the declaration of the end of the study shall be notified to all contracting parties to the EEA and to the European Commission. The final report referred to in Annex 7 Section 2.3.7 of Directive 90/385/EEC and Annex X Section 2.3.7 of Directive 93/42/EEC shall be kept at the disposal of the BASG and the competent authorities of the other contracting parties to the EEA participating in the clinical study.

8. FEES

In accordance with the Fees Regulation issued by the Federal Office for Safety in Health Care pursuant to the Austrian Health and Food Safety Act (*Gesundheits- und Ernährungssicherheitsgesetz*, GESG) applications for a CI/PS are associated with a fee (see fee schedule in German at www.basg.gv.at/en/about-us/fees/).

Should the billing address differ from that of the applicant, this needs to be clearly indicated in the cover letter.

Where an application is withdrawn or rejected prior to validation, 10% of the applicable fee will be leveraged. Withdrawal after validation (e.g. during assessment) requires payment of the full fee.

Combination studies: If the dossiers according to MPG and AMG are simultaneously submitted to the BASG the cost will be the fee for the MPG study plus 35% of the fee for the AMG clinical trial. Combined trials need to be indicated as such in the cover letter.

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9. CONTACT

Should you have further questions on clinical studies with medical devices please check our homepage (www.basg.gv.at) or address them to: clinicaltrials@ages.at

10. REFERENCES

Federal Office for Safety in Health Care (Bundesamt für Sicherheit im Gesundheitswesen, BASG)
www.basg.gv.at/medizinprodukte/klinische-pruefung-von-medizinprodukten/

Austrian Agency for Health and Food Safety (Agentur für Gesundheit und Ernährungssicherheit, AGES)
www.ages.at

Federal Ministery of Health (Bundesministerium für Gesundheit, BMG)
www.bmg.gv.at

European Commission – Legal framework
ec.europa.eu/growth/sectors/medical-devices/regulatory-framework/index_en.htm

European Commission – Legal framework – MEDDEVs
http://ec.europa.eu/growth/sectors/medical-devices/guidance/index_en.htm

European Commission – List of harmonized standards
http://ec.europa.eu/growth/single-market/european-standards/

Forum of the Austrian Ethics Committees
www.ethikkommissionen.at/

International Conference on Harmonisation (ICH)
www.ich.org/home.html

Legal Information System of the Republic of Austria (RIS), operated by the Austrian Federal Chancellery
www.ris.bka.gv.at/

Austrian Standards – Harmonized standards
http://austrianstandardsinstitute.com/

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11. ANNEXES

11.1. Annex I: Selected definitions according to MPG *(legally non-binding translation)*

§2 (1) "medical device" means any single instrument, apparatus, appliance, software, material or other article or combination thereof, including software intended by its manufacturer to be used specifically for diagnostic and/or therapeutic purposes and necessary for its proper application, intended by the manufacturer to be used for human beings for the purpose of:

- diagnosis, prevention, monitoring, treatment or alleviation of disease,
- diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap,
- investigation, replacement or modification of the anatomy or of a physiological process,
- control of conception,

and which does not achieve its principal mechanism of action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means.
A fully refurbished medical device is equivalent to a new one.

Note: Classification of MDs and IVDs is not in the remit of the Clinical Trials Division. It is the manufacturer's or sponsor's (where not identical) responsibility to decide, whether a product fulfills the definition of a medical device according to MPG. A fee-based formal request for qualification based on §5a MPG may be submitted to the Division Medical Devices Vigilance (medizinprodukte@ages.at).

§2 (3) MPG "active medical device" means any medical device relying for its functioning on a source of electrical energy or any source of power other than that directly generated by the human body or gravity. A medical device, that serves to transfer energy, material or parameters between an active medical device and the patient is not considered as active medical device.

§2 (4) MPG "active implantable medical device" means any active medical device relying for its functioning on a source of electrical energy or any source of power other than that directly generated by the human body or gravity, which is intended to be totally or partially introduced, surgically or medically, into the human body or by medical intervention into a natural orifice, and which is intended to remain there after the procedure.

§2 (5) "in vitro diagnostic medical device" (IVD) means any medical device, which

1. on its own or in combination is used according to the manufacturer's intended use as
   a) reagent
   b) reagent product
   c) calibrator
   d) control material
   e) kit
   f) instrument
   g) apparatus, equipment or
   h) system for the in vitro examination of specimens, including blood and tissue donations, derived from the human body and
2. is solely or principally used for the purpose of
   a) providing information on the physiological or pathological state, or congenital abnormalities, or
   b) to determine the safety and compatibility with potential recipients, or
   c) to monitor therapeutic measures

Specimen receptacles are considered IVDs, whether vacuum-type or not, specifically intended by their manufacturers for the primary containment and preservation of specimens derived from the human body for the purpose of in vitro diagnostic examination.

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Products for general laboratory use are not in IVDs unless such products, in view of their characteristics, are specifically intended by their manufacturer to be used for in vitro diagnostic examination.

§2 (9) MPG intended purpose ("Zweckbestimmung") means the use for which the device is intended according to the data supplied by the manufacturer on the labelling, in the instructions and/or in promotional materials. The determination of the intended purpose according to §2 (9) MPG and the intended primary mechanism of action according to §2 (1) MPG are in the responsibility of the manufacturer.

Note: According to §9 (6) MPG medical devices can only be dispensed to users or consumers, if the relevant information has been provided in the local language, e.g. the German language for Austria (Dir 93/42/EEC Annex I (13))
No further instructions are provided on the translation requirements of instructions for use in the Austrian medical device legislation. The information has to be complete and has to be provided in an understandable form for the user/consumer. The safe and effective use of the medical device needs to be assured. Translation by a certified translator is recommended and reference is made to DIN EN 15038 Translation services - Service requirements. The "quality" of the translation can only be assured by peer review and therefore a translation service needs to encompass at minimum review by a person other than the translator.

§2 (17) MPG: An **adverse device effect** ("Nebenwirkung") is any undesirable clinical event occurring under and related to the normal conditions of use of a medical device, i.e., a device-related adverse event.

§3 (15) MPG: An **adverse event ("unerwünschtes Ereignis")** means any undesirable clinical event occurring with a study particpant, independently of whether there is a causal relationship with the investigated medical device or IVD:

§3 (16) MPG*:* A **serious adverse event/device effect** in accordance with §2 (17) MPG is where it is fatal or life-threatening, causes permanent damage, or requires or prolongs hospitalization. Any adverse event or adverse device effect causing fetal damage, fetal death, or a congenital anomaly as well as any occurrence of a malignant tumor shall, without exception, be classified as serious.

§3 (2) MPG: Clinical Investigation (CI, „Klinische Prüfung") means the systematic investigation of a medical device except IVDs on study participants with the goal of

1. evaluating the performance of a medical device or verifying if the performance of the medical device in normal conditions of use conforms with those stated by the manufacturer or other sponsor
2. investigating adverse events according to type, severity and frequency under normal conditions of use and if those can be considered as acceptable risks in the context of the stated performance.
3. identifying the mechanisms of action and the suitable clinical use of a medical device to determine its safety and efficacy

§3 (2) MPG a performance study (PS, „Leistungsbewertungsprüfung") means the systematic investigation of an IVD on samples of study participants, including blood and tissue samples in medical laboratories or other institutions with the goal of:

1. determining or verifying the performance of the in vitro diagnostic, or determining of the performance of the in vitro diagnostic conforms with the performance under normal conditions of use as stated by the manufacturer or other sponsor
2. investigating risks under normal conditions of use according to type, severity and frequency and if those can be considered as acceptable risks in the context of the stated performance or
3. determining the capacity and suitable clinical use of the in vitro diagnostic to determine the safety and performance of the in vitro diagnostic

§3 (5) MPG Sponsor means a natural or legal person who takes the responsibility for the planning, initiation, conduct and financing of a clinical study. The sponsor has to reside in a signatory party of the EEC.

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A clinical investigator additionally has sponsor responsibility if he/she conducts the study in his/her full responsibility independently of the manufacturer of the medical device(s).

Note: §3 (5) the MPG does not specifically provide a definition for the legal representative, nevertheless the legal interpretation is in analogy to that of the medicinal product legislation (AMG):
§2a (16) AMG A Sponsor is a natural or legal person who takes responsibility for the initiation, management and/or financing of a clinical trial; The sponsor or his legal representative have to reside in a signatory party of the EEC. The clinical investigator additionally has to take sponsor responsibility if he conducts the study in his full responsibility independently of the manufacturer of the medicinal product.

Further definitions according to Annex IX Dir 93/42/EEC as amended (Classification of medical devices):

Duration of use:

- Transient: Normally intended for continuous use for less than 60 minutes.
- Short term: Normally intended for continuous use for not more than 30 days.
- Long term: Normally intended for continuous use for more than 30 days.

Invasive device: A device which, in whole or in part, penetrates inside the body, either through a body orifice or through the surface of the body.

Body orifice: Any natural opening in the body, as well as the external surface of the eyeball, or any permanent artificial opening, such as a stoma

Implantable device: Any device which is intended:

- to be totally introduced into the human body or,
- to replace an epithelial surface or the surface of the eye, by surgical intervention which is intended to remain in place after the procedure.
  Any device intended to be partially introduced into the human body through surgical intervention and intended to remain in place after the procedure for at least 30 days is also considered an implantable device.

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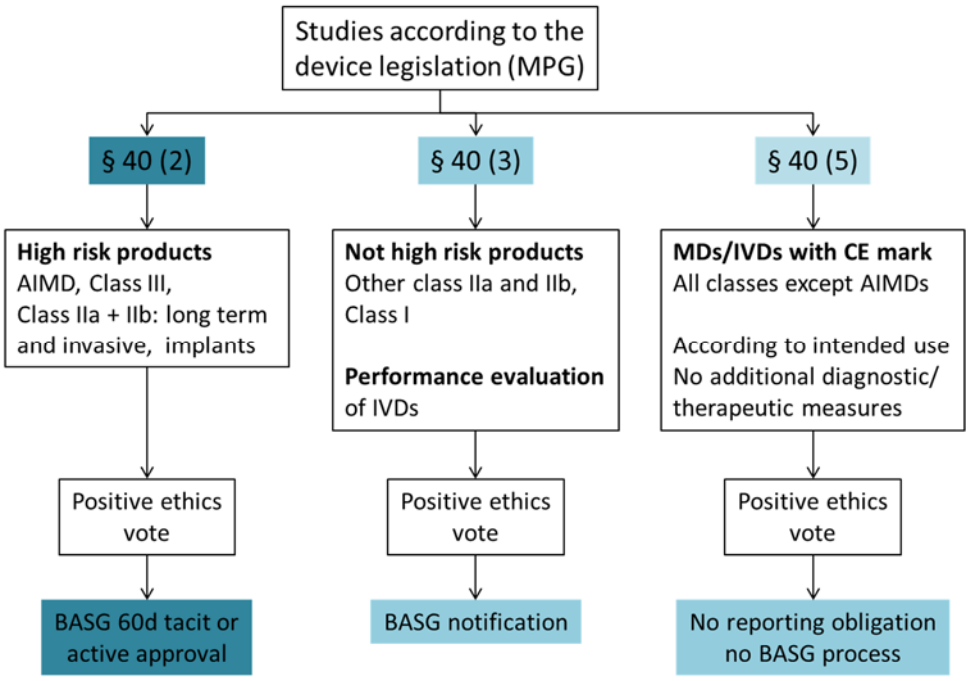
11.2.Annex II - Overview of notification requirements



Notification requirements are based on the medical device classification AIMD: Dir 90/385/EEC: Annex 6

- Medical devices according to risk classification: Dir 93/42/EEC: Annex VIII
- IVD: Dir 98/79/EC: Annex VIII

Notification according to §40 (2) MPG – applicable to:

- Dir 90/385/EEC: all AIMDs (no exceptions)
- Dir 93/42/EEC:
  - all class III medical devices
  - all implantable medical devices class IIa/IIb
  - class IIa/IIb medical devices:
    - for > 30 days continuous (long term) and invasive use (fully or partially implanted)

Notification according to §40 (3) MPG – applicable to:

- Dir 98/79/EC: all IVDs
- Dir 93/42/EEC: all medical devices not mentioned in §40 (2) or (5) MPG:
  - all class I medical devices
  - IIa/IIb medical devices used < 30 days and non invasive; < 30 days and invasive, or > 30 days and non invasive

Notification according to §40 (5) MPG – applicable to medical devices of Dir 93/42/EEC and IVDs of Dir 98/79/EC with the exception of AIMDs if

- the medical device/IVD carries a CE mark
- the medical device/IVD is used within its intended use (see conformity assessment)
- the study protocol does not necessitate additional diagnostic or therapeutic measures

no insurance requirement for study participants (§47 MPG)

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Medical device/IVD classification	Notification procedure
AIMD	§40 (2)
Implant	§40 (2)
Class III	§40 (2)
Class IIa/IIb > 30d + invasive	§40 (2)
Class IIa/IIb < 30d + invasive	§40 (3)
Class IIa/IIb non invasive	§40 (3)
Class I	§40 (3)
IVDs	§40 (3)

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11.3.Annex III: Documents required for Notification of a CI with a medical device

An adequate and complete notification (dossier) submitted to the BASG consists of the following documents:	
Document	**Notes**
Completed form "Notification of a Clinical Investigation with a medical device"	PDF (signed electronically or scanned signed original) and XML
Clinical Investigation Plan	With version number and date; compiled according to EN ISO 14155
Investigator's Brochure	Summary of the literature, including an evaluation thereof; general description of the device and its components; description of the mechanism of action of the device, along with supporting scientific literature; manufacturer's instructions for use and installation, including possible risks, contraindications, and warnings; description of the intended clinical performance; description of the materials used in the device; summary and evaluation of the in vitro and/or ex vivo data relevant to the device, including preclinical data; summary of relevant previous clinical experience with the device and with other devices with similar features; a list of international standards the device complies with in full or in part; results of the risk analysis.
For CE-marked medical devices, German-language instructions for use	General description of device and intended use, including description of software necessary for the proper application
Favourable opinion of the competent ethics committee(s)	"positive vote"
Patient Information and Informed Consent Form	In German, with version number and date
Confirmation of insurance coverage for the subjects enrolled in the clinical investigation	Personal injury insurance; see §47 of the Austrian Medical Devices Act (*Medizinproduktegesetz*, MPG) as amended The number of subjects to be enrolled in the CI must correspond to the number stated in the insurance contract. In addition to providing a personal injury insurance, the sponsor has to asssure that the investigator is covered by an adequate personal liability and legal costs insurance (see §48 MPG as amended).
Written confirmation that the medical device complies with the essential requirements of the applicable Directive in all aspects except those that will be assessed in the CI	Directive 93/42/EEC Annex I Directive 90/385/EEC Annex 1

The following documents shall be available and provided to the BASG immediately upon request or no later than 7 days thereafter.	
Document	**Notes**
Declaration of conformity of the manufacturer	
Certificate(s) of notified bodies	
Proof of qualification of the clinical investigator(s)	Currently dated and signed curriculum vitae
Written agreements between the sponsor, monitor, and clinical investigator establishing each party's responsibilities	In accordance with §44 MPG as amended
Case Report Forms (CRFs)	
Information on the construction and manufacture of the device, especially sterilisation	
Results of construction calculations, assessments, technical tests, etc.	e.g., results of biocompatibility tests in accordance with EN ISO 10993, results of the assessment of the electrical safety in accordance with the standards of the EN 60601 series
Results of the risk analysis	Risk analysis, risk minimisation measures See EN ISO 14971
List of standards applied in full or in part	
For products manufactured using tissues of animal origin, risk management measures aimed at reducing the risk of infection	See Directive 2003/32/EC, MEDDEV Guidelines of the European Commission
Data on tests performed to assess the safety, quality, and benefit of substances or derivatives from human blood	See Directive 2000/70/EC or Directive 2001/104/EC as well as Directive 2001/83/EC

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11.4. Annex IV: Documents required for Notification of a PS of an IVD

An adequate and complete notification (dossier) submitted to the BASG consists of the following documents:	
Document	**Notes**
Completed form "Notification of a Performance study with an In Vitro Diagnostic medical device"	PDF (signed electronically or scanned signed original) and XML
Evaluation Plan	With version number and date Compiled according to ÖNORM EN 13612 Statement of objectives; scientific, technical, or medical rationale; methods; required samples and analyses, the performance criteria and requirements to be assessed, type and scope of the evaluation, number of products involved
Information necessary to understand the function and application of the device	General description of device and intended use, including description of software necessary for the proper application of the medical device
German-language instructions for use for CE-marked IVD(s)	
Favourable opinion(s) of the competent ethics committee(s)	"positive vote"
Patient Information and Informed Consent Form for subjects	In German, with version number and date Except for PSs according to §65a (2) MPG
Confirmation of insurance coverage for the subjects enrolled	Personal injury insurance; see §47 MPG The number of subjects to be enrolled in the PS must correspond to the number stated in the insurance contract, except for PSs according to §65a (2) MPG In addition to providing a personal injury insurance, the sponsor has to assure that the investigator is covered by an adequate personal liability and legal costs insurance (see §48 MPG).
Written confirmation that the IVD complies with the essential requirements of Directive 98/79/EC in all aspects except those that will be assessed in the PS	See Directive 98/79/EC Annex I

The following documents shall be available and provided to the BASG immediately upon request or no later than 7 days thereafter:	
Document	**Notes**
Declaration of conformity of the manufacturer	
Certificate(s) of notified bodies	
Proof of qualification of the coordinator of the PS	Currently dated and signed curriculum vitae
Agreements between the sponsor, monitor and clinical investigator defining responsibilities	In accordance with §44 MPG as amended
Information on how the data obtained during the PS will be recorded	
Documentation on the construction and manufacture (manufacturing method, sterilisation, etc.)	
Results of assessments and technical tests	
Results of the risk analysis	Risk analysis, risk minimisation measures , see EN ISO 14971
List of standards applied in full or in part	
Documentation on the safety of components of animal or human origin	See Directive 2003/32/EC, MEDDEV Guidelines of the European Commission

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11.5. Annex V: Classification of Amendments

A change is considered substantial, if it relates to

- the safety or the physical or mental integrity of the study participants OR
- the change can impact on the scientific validity of the clinical study

The classification as substantial or non-substantial is the sponsor's responsibility and only substantial amendments need to be reported to the BASG.

Change	substantial	non-substantial
Title or short title of the investigation		**X**
Main objective	**X**	
Indication/main indication	**X**	
Study design: randomized, cross-over, parallel, blinded, double-blind, controlled	**X**	
Adding or modifying sub-studies	**X**	
Type of location: hospital, outpatient clinic, private practice	**X**	
Control groups: treatment/placebo groups; other medical devices, medicinal products, placebo, no treatment	**X**	
Study duration/ recruitment period		**X**
Study duration per study participant providing that treatment exposure, endpoints and safety monitoring remain unchanged		**X**
Number of study participants (cases for analysis)	**X**	
Number of study participants per site (unchanged total study participants)		**X**
Change of in-/exclusion criteria	**X**	
Stopping rules	**X**	
Reducing follow-up/control visits	**X**	
Investigator contacts		**X**
Applicant/Sponsor contacts		**X**
Contacts of the legal representative in Austria/EEA		**X**
Sponsor, legal representative, principal investigator	**X**	
Logistics (sample storage/transport)		**X**
Clinical research organization (CRO)/ Clinical research associate (CRA)		**X**
Addition of study site in Austria	**X**	
Termination of a study site in Austria		**X**
Adding/eliminating endpoints	**X**	
Withdrawal of independent data monitoring board (DSMB)	**X**	
Change of case report forms/administrative changes		**X**

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Development of the investigated device(s)	**X**	
Name of the investigated device(s)	**X**	
Classification of the investigated device(s)	**X**	
Replacement of investigated device(s)	**X**	
Adding a CE mark	**X**	
Relevant accessory/ies to investigated device(s)	**X**	
Software required for functioning of the investigated device(s)	**X**	
Medicinal products used in supportive function to the investigated device(s)	**X**	
Therapeutic/medical measures associated with the investigated device (type of therapy, medication), diagnostic tests, diagnostic measures	**X**	
Minor changes to the protocol		**X**
Correction of typos		**X**