

# MEDICAL ETHICAL GUIDELINES

Distinguishing between  
standard treatment  
and experimental treatment  
in individual cases



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Medical-ethical guidelines

# Distinguishing between standard treatment and experimental treatment in individual cases

Approved by the Senate of the SAMS on 20 May 2014;  
the guidelines were adapted with a decision taken on 19 May 2015.  
The German text is the authentic version.



These guidelines are an integral part of the Code of the Swiss Medical Association (FMH).

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## I. PREAMBLE

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Medicine is subject to a process of continuous development. Quality assurance and research efforts yield new knowledge and promote advances. Treatments which are now recognised as standard may soon be outdated. Because it takes time to carry out expert reviews and prepare practice recommendations, a given treatment may not initially be considered to be standard, even though this would be supported by the latest scientific findings. At the same time, older treatments may still be regarded as standard while recent data and experience makes them appear obsolete.

Novel treatments and methods are generally evaluated scientifically in research projects. However, a novel treatment may also be employed – independently of the conduct of a research project – on the basis of a *treatment decision in an individual patient*; this is known as “experimental treatment in individual cases”.<sup>1</sup>

While the benefits and risks of a standard treatment are generally well known, they cannot be so readily assessed for an experimental treatment. Whether the treatment used in a particular case is standard or experimental is therefore a matter of central importance both for the patient and for the attending physician. Physicians must have comprehensible reasons for using an experimental treatment, and only patients themselves can decide whether they wish to undergo a treatment involving risks which are not clearly defined. This requires that they should be appropriately informed. Although it may appear self-evident that any medical intervention requires the patient’s informed consent, practice shows that adequate information concerning the experimental nature of a treatment is not always provided.

1 Experimental treatments in individual cases are also sometimes known as “treatment attempts” (Heilversuche), “unproven/non-established treatments”, etc. By contrast, the terms “therapeutic research” or “human experiment”, which are also employed, refer to acts of research. The term “experimental treatment in individual cases” is used throughout the present guidelines.

For this reason, the Swiss Patient Organisation (SPO) called for so-called treatment attempts (Heilversuche) to be regulated under the Federal Act on Research involving Human Beings.<sup>2</sup> Though Parliament rejected this proposal, it acknowledged the need for further clarification of the various concepts. In a parliamentary motion, the Federal Council was requested to indicate the regulations applicable to treatment attempts in Switzerland, to identify any legal grey areas, to determine whether action is required and, if necessary, to present proposals for appropriately supplementing the existing regulations.<sup>3</sup> The present guidelines<sup>4</sup> define the terms “standard treatment” and “experimental treatment in individual cases” and explain the rights and duties of physicians and patients which need to be taken into account when experimental treatments are used in individual cases, outside of research projects.

2 Cf. the arguments in favour of supplementary provisions in the Human Research Act, published by an SPO expert group on 22 April 2010. The aim of regulating treatment attempts would be to establish legal certainty for patients and physicians.

3 Cf. the motion on treatment attempts, 12 January 2011 (11.3001).

4 SAMS guidelines are addressed to healthcare professionals (physicians, nurses and therapists). On being incorporated into the Code of the Swiss Medical Association (FMH), SAMS guidelines become binding for all members of the FMH.



## II. GUIDELINES

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### 1. Scope

The guidelines are applicable to the entire range of medical<sup>5</sup> treatments employed in individual cases on the basis of a treatment decision. This encompasses preventive, diagnostic, therapeutic, palliative and rehabilitative measures, particularly in the areas of pharmacotherapy, interventions and methods involving medical technologies, and surgical procedures.

The guidelines do not cover medical treatments undertaken within research projects.

### 2. Dimensions of standardisation of treatment

No clear and unequivocal definition of “standard treatment” exists. In legal practice and the literature, standard treatment is generally defined as “the method based on the current state of scientific knowledge”. However, whether this term is used in everyday practice will depend, in part, on the dimension under consideration. In different contexts, a treatment may be recognised as standard on the basis of the strength of evidence of efficacy, the availability of practice recommendations, the existence of health authority regulations, the reimbursement of costs under mandatory health insurance, or the availability of quality standards for its use. To avoid misunderstanding, it is essential to specify the dimension under consideration.

#### 2.1. Medical evidence

Under the rules of evidence-based medicine (EBM), the available evidence of efficacy for medical interventions is classified into “levels of evidence”. There are numerous systems<sup>6</sup> according to which, in various ways, the quality of evidence is graded – from the highest level (systematic reviews of randomised controlled trials) down to case series with historical controls and pathophysiological considerations. For the assessment of evidence with a view to developing guidelines, it is recommended to use an approach adapted to the particular situation (e.g. GRADE<sup>7</sup>) rather than a simple list.

5 In what follows, the term “medical” is used in a broad sense, covering the activities of physicians, nurses and therapists.

6 Cf. the Oxford Centre for Evidence-Based Medicine ([www.cebm.net](http://www.cebm.net)) or the German Cochrane Centre ([www.cochrane.de](http://www.cochrane.de)).

7 [www.gradeworkinggroup.org](http://www.gradeworkinggroup.org)

To produce treatment recommendations, the best-possible available evidence needs to be critically evaluated. This calls for high levels of expertise, clinical experience and professional judgement. Experts may differ in their evaluation of the same evidence. It should be borne in mind that many treatments which have become established over time are based exclusively on case series and pathophysiological considerations and have never been systematically studied in controlled trials.

## 2.2. Practice recommendations

Treatment recommendations may take the form of official guidelines issued by national or international professional associations, the results of an expert consensus process, or the opinions of individual experts. The relevance of such recommendations will depend on the extent to which the evidence considered is current and comprehensive, the expertise of the specialists involved (as indicated by their research and teaching performance in the field), and the authority of the official bodies concerned (e.g. national or international professional associations). One instrument used for the assessment of guidelines is, for example, AGREE.<sup>8</sup> If guidelines recognised by national or international professional associations are available, they will specify a standard treatment approach. Practitioners then need to assess the applicability of the recommended approach to the specific clinical situation. If they choose a different treatment option, they must be able to provide a reasonable explanation for their choice.<sup>9</sup> In situations where no recognised guidelines are available, established medical practice – as reflected, for example, in internal hospital guidelines or the opinions of recognised experts – may also provide a basis for the definition of a standard treatment.

## 2.3. Regulatory approval

To obtain marketing authorisation for medicinal products or medical devices from the Swiss Agency for Therapeutic Products (Swissmedic), the supplier must demonstrate that the product concerned is safe and effective. However, the process of regulatory review differs significantly from the process of developing guidelines. Accordingly, it cannot be assumed either that an approach which is in accordance with the official product information automatically corresponds to applicable practice recommendations, or that the opposite is the case for off label or unlicensed use.<sup>10</sup> A registered drug may have become obsolete without having lost its authorisation. Many widely used therapeutic products – not only in complementary medicine – are indeed approved, but are not mentioned (or are

8 Cf. The AGREE Collaboration: Appraisal of Guidelines for Research & Evaluation (AGREE) Instrument, 2003, updated 2009.

9 Cf. the paper by the DDO department of the FMH on the identification of quality criteria for practice guidelines (SÄZ/BMS 2014;95(3):45–51) and the position of the FMH on the conditions for and application of guidelines (SÄZ/BMS 2014;95(3):52–53).

10 Cf. the Glossary in the Annex.

described as being of limited efficacy) in practice recommendations, so that authorisation in itself is not sufficient to define a standard treatment. Conversely, in various fields of medicine with a small market size (e.g. paediatrics, obstetrics, palliative and intensive care), many recommended treatments have to be undertaken off-label because the indication in question is not (yet) approved or because, for economic reasons, registration is not pursued.

#### **2.4. Reimbursement of costs under mandatory health insurance**

Decisions on reimbursement of costs under mandatory health insurance are the result of a further health authority procedure, based on regulatory information, practice recommendations and an assessment conducted by specially appointed experts. Thus, in the case of medicinal products, authorisation by Swissmedic is a prerequisite for inclusion in the List of Pharmaceutical Specialties (SL), which is maintained by the Federal Office of Public Health. Medicinal products included in the SL are covered by mandatory health insurance in all the indications approved by Swissmedic, provided that no restrictions are specified in the SL. Reimbursement of costs for a treatment involving unlicensed or off-label use in individual cases is possible under certain conditions (e.g. for orphan diseases).

#### **2.5. Quality of practice**

In recent years, there have been growing calls for standardisation of the treatments undertaken by medical service providers, in the interests of quality assurance and patient safety. Quality standards are developed and implemented mainly for widely used interventions. The notion of standard treatment has thus acquired the additional dimension of quality of practice. In recommendations for practice, medical interventions are primarily assessed independently of the specific circumstances in which they are used; at most, certain minimum requirements may be specified for the qualifications of the practitioner and the institution. The quality of practice in individual cases may, however, vary. While it may be relevant for the patient whether an intervention is performed by a service provider for the first time without supervision or as a routine measure subject to a quality standard, it is of no relevance for the general assessment of the intervention as such.

### 3. Definitions

#### 3.1. Standard treatment

Given the considerations discussed in Chapter 2, the dimension of practice recommendations is chosen for the definition of standard treatment in these guidelines, as this is best suited for the evaluation of the physician's duties of care. The crucial question is whether the treatment chosen by a physician falls within or outside currently recognised recommendations or established practice.

For present purposes, *standard treatment* covers all medical interventions which are based on currently applicable practice recommendations (cf. Section 2.2) or – in the absence of such recommendations – are in accordance with the established practice of recognised experts.

#### 3.2. Experimental treatment in individual cases

For present purposes, *experimental treatment in individual cases* refers to a treatment which differs from the standard treatment, or is employed in the absence of a standard treatment.

Gradual improvement of therapeutic or diagnostic methods as part of a quality-related project does not constitute experimental treatment in individual cases, so long as no (qualitatively) new steps of an experimental nature are added. The combination of two standard treatments may, however, be of an experimental nature.

#### 3.3. Treatment within a research project

Either standard or experimental treatment may be employed within a research project. Research does not represent an additional point on the therapeutic spectrum, but an additional *dimension* of treatment, namely the pursuit of scientific knowledge.<sup>11</sup>

<sup>11</sup> Cf. the diagram illustrating research in the Annex.

*Treatment within a research project* is treatment carried out in order to answer a scientific question and thus also designed to yield generalisable knowledge. In such cases, at least one of the following criteria will generally be met:<sup>12</sup>

- Data concerning several patients is prospectively collected and analysed.
- The type of treatment and mode of administration are determined not only by the needs of the patient but also by the requirements of the research project.
- Additional data, not required for treatment purposes, is collected, or additional (e.g. pharmacokinetic) investigations are carried out.

## **4. Procedure for use of experimental treatments**

### **4.1. Duties of care**

In the exercise of their therapeutic freedom, physicians may propose the use of an experimental treatment, provided that they can give good reasons for doing so.

According to Federal Supreme Court rulings,<sup>13</sup> the physician's duties of care depend on the circumstances of the individual case and are to be determined in accordance with the following criteria:

- the type of treatment;
- the associated risks and benefits;
- the physician's individual discretion;
- the resources and time available to the physician; and
- the physician's proficiency<sup>14</sup> and basic/specialist training and continuing education.

In the case of experimental treatments, duties of care are increased in accordance with the expected risks. In cases where a treatment cannot be regarded as standard, given a lack of evidence of efficacy, but is deemed – on the basis of long-standing, widespread use – to involve only minimal risks, it must at least be considered whether the patient is not being denied an effective standard treatment as a result.

12 Cf. Art. 3 of the Federal Act of 30 September 2011 on Research Involving Human Beings and the Federal Council Dispatch of 21 October 2009 concerning the Federal Act on Research Involving Human Beings.

13 Cf., for example, the Federal Supreme Court decisions 134 IV 175, E. 3.2; 130 IV 7, E. 3.3; 120 II 248, E.2c; 113 II 429, E. 3a.

14 This refers to physicians' individual experience and knowledge (e.g. how often they have performed a procedure, which institutions and experts were responsible for their training, whether they were personally involved in the development of a new method or have only read about it, etc.). Depending on the extent of their experience and knowledge, a higher degree of care may be expected of certain physicians. Conversely, those who are less experienced may be required to delegate procedures to more experienced colleagues (or to seek assistance), as they (still) lack the necessary knowledge and experience.

Before an experimental treatment is proposed in an individual case, the physician must compare the standard and the experimental treatment, assessing and documenting the possible benefits and potential risks for the patient.

If no standard treatment is available, the experimental treatment must be weighed up against non-treatment. With experimental treatments, physicians must be particularly aware of the possibility of previously unknown risks and adverse effects. The risk/benefit assessment must be based on a comprehensible, rationally justified hypothesis, and the implications of available medical experience and scientific knowledge must be systematically considered. There must be a reasonable prospect of cure, improvement, alleviation or prevention.

If clinical expertise or technical skills are crucial to the success of treatment – e.g. in the case of an experimental surgical method<sup>15</sup> or a complex treatment strategy – the clinician must consider whether his/her skills are adequate or whether the patient should be referred to another centre with appropriate experience.

Before an experimental treatment is carried out in an individual case, the treatment option should be reviewed by a group of experts (e.g. tumour board, interdisciplinary case discussion) or at least a second opinion should be sought, unless the risks are considered to be minimal.<sup>16</sup> The question whether the available (preclinical and clinical) data offers an adequate basis for first use of a treatment can thus be assessed by experts with an interdisciplinary perspective. The results of the expert review must be documented.

The treatment must be discontinued if there are signs that it is ineffective or the risk/benefit ratio is unacceptable. For this reason, every precaution must be taken to ensure that the patient can be continuously monitored and any protective measures which may be required can be taken without delay. Since late effects may occur, appropriate arrangements must be made for follow-up.

15 A surgical method already used in certain centres but not yet established as standard (early adoption).

16 "Minimal" refers both to the likelihood of occurrence and to the severity of an event.

Since the experience gained with experimental treatment in individual cases may also be useful for other patients, provided that it is documented and published, it should be considered in advance whether the treatment could be carried out within an existing research project or whether a new project could be initiated.<sup>17</sup> If this is not feasible, the experience gained (including in particular adverse experiences) should if possible be published in a case report and/or recorded in a registry.

If experimental treatments are used systematically in multiple patients, then the regulations governing human research are applicable.<sup>18</sup>

#### 4.2. Providing information for the patient<sup>19</sup>

Information should be provided in an appropriate form and should include all the details required to enable the patient to make an informed decision.<sup>20</sup> If, in an emergency, comprehensive information cannot be provided for lack of time, this must be remedied as soon as possible. The individual need for information is determined by the patient directly concerned: in particular, all the information required to allow risks and benefits to be weighed up must be provided. When information is given on an experimental treatment, the patient must understand that it may be difficult to assess the possible risks and potential benefits. If a standard treatment would also be available in the specific circumstances, the physician must additionally explain why an experimental treatment is being proposed.

17 Cf. the Helsinki Declaration § 37: "In the treatment of an individual patient, where proven interventions do not exist or other known interventions have been ineffective, the physician, after seeking expert advice, with informed consent from the patient or a legally authorised representative, may use an unproven intervention if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering. This intervention should subsequently be made the object of research, designed to evaluate its safety and efficacy. In all cases, new information must be recorded and, where appropriate, made publicly available."

18 Cf. the Federal Act of 30 September 2011 on Research involving Human Beings.

19 With regard to medical interventions, the following persons, in the following order, are entitled to act as representatives for the person lacking capacity: (1) persons appointed in an advance directive or power of attorney; (2) a duly authorised deputy; (3) a spouse or registered partner who shares the same household or regularly provides personal support for the person lacking capacity; (4) the person who shares the same household as and regularly provides personal support for the person lacking capacity; (5) the offspring, (6) the parents or (7) the siblings, if they regularly provide personal support for the person lacking capacity (Art. 378 Civil Code). For patients receiving medical treatment in connection with an involuntary committal, Art. 434 Civil Code is applicable.

20 It should be noted that, in certain areas, the content of the information to be provided and the formal procedure are prescribed by law.

When the proposed experimental treatment is discussed with the patient, the following points are also to be addressed in a comprehensible manner:

- the patient's current state of health and the likely course of the disease;
- the proposed treatment;
- possible risks and burdens associated with the treatment, with the information on risks covering not only the frequency and severity of possible adverse events but also, in particular, the significance of the risk and the likelihood of occurrence for the individual patient (irrespective of the absolute frequency);
- in the case of off-label use: all relevant information not included in the package leaflet;
- the nature, extent, schedule, duration, effects and urgency of the proposed treatment;
- possible alternatives;
- the right to an appropriate period for reflection prior to granting consent;
- the right to revoke consent without giving reasons;
- the right to obtain a second opinion (possibly, referral to another hospital or physician);
- the possible financial costs involved (e.g. copayment for pharmacotherapy or surgical procedures); and
- the fact that another centre has greater experience with the intervention.

The explanatory discussions must be documented in the medical records, and the relevant information given to the patient in writing. Decision aids (e.g. drawings, tables, diagrams, etc.) can facilitate understanding. The patient should be invited to ask questions, to bring along trusted individuals and to express any uncertainties. The discussions should permit a genuine understanding of the implications of the proposed treatment.



### 4.3. Obtaining informed consent<sup>21</sup>

Informed consent depends on the following conditions being met:

- The patient has capacity.
- The patient has been adequately informed.
- The patient is capable of understanding the information provided and the significance of granting consent.
- The patient can make and express a decision without being subjected to coercion or manipulation.

The patient's consent must be given in writing, unless the experimental treatment involves no more than minimal risks. The physician responsible for the treatment is also responsible for ensuring that the patient is duly informed and consent obtained.

<sup>21</sup> In the case of patients who lack capacity, the decision is to be taken by the legal representatives (cf. footnote 20), for whom information is to be provided in a similar manner.

## Glossary

### Compassionate use<sup>22</sup>

Use in patients, outside a clinical trial, of medicinal products which are not (yet) authorised. Compassionate use is always to be classified as experimental treatment and, legally, as unlicensed use.

### Experimental treatment in individual cases

Treatment which differs from the standard treatment, or is employed in the absence of a standard treatment.

### Off-label use

Use of ready-to-use medicinal products authorised in Switzerland in a way which does not comply with the approved prescribing information published in the Swiss Drug Compendium (e.g. use in a non-registered indication or age group, or administration in a dose/formulation or for a period which has not been approved).

### Standard treatment

Medical intervention which is based on currently applicable practice recommendations or – in the absence of such recommendations – is in accordance with the established practice of recognised experts.

### Treatment within a research project

Treatment carried out in order to answer a scientific question and thus also designed to yield generalisable knowledge. In such cases, at least one of the following criteria will generally be met:<sup>23</sup>

- Data concerning several patients is prospectively collected and analysed.
- The type of treatment and mode of administration are determined not only by the needs of the patient but also by the requirements of the research project.
- Additional data, not required for treatment purposes, is collected, or additional (e.g. pharmacokinetic) investigations are carried out.

22 Cf. Art. 9 para. 4 of the Federal Act of 15 December 2000 on Medicinal Products and Medical Devices, and Art. 18 of the Ordinance of 22 June 2006 of the Swiss Agency for Therapeutic Products on the simplified authorisation of medicinal products and the authorisation of medicinal products with the notification procedure (VAZV).

23 Cf. Art. 3 of the Federal Act of 30 September 2011 on Research involving Human Beings and the Federal Council Dispatch of 21 October 2009 concerning the Federal Act on Research involving Human Beings.

## Unlicensed use

Use of a ready-to-use medicinal product which is not authorised in Switzerland. Hospitals, physicians and pharmacists are generally permitted to import such products without a licence if the product is authorised in a country recognised as having an equivalent regulatory system,<sup>24</sup> or if a tourist requires a medicinal product which is authorised in his or her home country.<sup>25</sup> In all other cases, a special authorisation from Swissmedic is required.<sup>26</sup> The healthcare professional responsible is required to keep records of such imports.<sup>27</sup>

## Explanatory diagram: Research



The diagram shows how various types of research are related to the different forms of treatment.

24 Cf. Art. 36 para. 3 of the Medicinal Products Authorisation Ordinance of 17 October 2001. The countries in question include the US, Japan, Australia and EU members (except for eastern accession countries).

25 Cf. Art. 36 para. 3 let. a and b of the Medicinal Products Authorisation Ordinance of 17 October 2001. It is also stipulated that no alternative medicinal product should be authorised in Switzerland – or that if such a product is authorised, it must not be available in this country – or that it must not be appropriate to change the patient’s medication (Art. 36 para. 3 let. d).

26 Cf. Art. 36 of the Medicinal Products Authorisation Ordinance of 17 October 2001. Authorisation is always required for vaccines, for medicinal products containing genetically modified organisms and for radiopharmaceuticals. Cf. also the Swissmedic information sheet on authorisation for the use and import of a product not authorised in Switzerland (special authorisation), [www.swissmedic.ch/bewilligungen](http://www.swissmedic.ch/bewilligungen)

27 Cf. Art. 36 para. 4 of the Medicinal Products Authorisation Ordinance of 17 October 2001.

## Information on the preparation of these guidelines

### Mandate

On 27 April 2011, the Central Ethics Committee (CEC) of the SAMS appointed a sub-committee to draw up guidelines on "non-established treatment of patients in individual cases".

### Responsible sub-committee

Professor Dieter Conen (Internal Medicine), Aarau (Chair)  
Professor Nicolas Demartines (Surgery), Lausanne  
Professor Richard Herrmann (Oncology), Riehen  
Professor Irene Hösli (Obstetrics), Basel  
Professor Christian Kern (Anaesthesiology), Lausanne  
Margrit Kessler, Swiss Patient Organisation, Zurich  
Professor Christian Kind (Paediatrics), St Gallen (CEC President)  
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Professor Brigitte Tag (Criminal and Medical Law), Zurich  
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### Experts consulted

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Professor Christian Brückner, Basel  
Professor Urs Haller, Appenzell  
Dipl. pharm. Annette Magnin, Swiss Clinical Trial Organisation, Basel  
Professor Felix Niggli, Isabelle Lamontagne, Swiss Paediatric Oncology Group, Bern

### Consultation procedure

On 28 November 2013, the Senate of the SAMS approved a draft version of these guidelines to be submitted for consultation to professional associations, organisations and other interested parties. The comments received have been taken into account in the final version.

### Approval

The final version of these guidelines was approved by the Senate of the SAMS on 20 May 2014; the guidelines were adapted with a decision taken on 19 May 2015.



