

Guideline for Creating Medical Terms

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Table of Contents

1	Purpose and Motivation	3
1.1	Lexical Foundation	3
1.2	Semantic Foundation	3
2	Definitions	4
3	Guidelines	4
3.1	Lexical Guidelines	4
3.2	Guidelines for Definitions of Concepts	9
3.3	Guidelines for Relations	12
3.4	Guidelines for Rules	13
3.5	Guidelines for Related Terms	14
3.6	Guidelines for Abbreviations	14
4	Assignment of Terms to Contexts	15
4.1	Measuring Procedure / Laboratory / Measurable or Quantitative Parameters	15
4.2	Medications / Materials / Medical Products / Substances	16
4.3	Treatments / Events / Processes / Actions	16
4.4	Organisms	16
4.5	Diagnoses / Diseases / Symptoms	16
4.6	Anatomy / Structures and Regions of the Body	17
4.7	Classification	17
4.8	Statistics / Biometrics / Epidemiology	17
4.9	Institutions / Persons / Roles / Functions	17
4.10	Administration / Management / Documentation	17
4.11	Meta-terms / Relational Nouns	17
4.12	Other	18
4.13	Realm of Validity of Terms	18
4.14	Temporal Validity	18
4.15	Geographical Validity	19
5	Sources	19
	References	20
	Appendix A: Sources	21

1 Purpose and Motivation

The purpose of the *Data Dictionary for Clinical Trials* is to facilitate the reusability of terms and descriptions in clinical trials, e.g. for definitions in new clinical trials, the harmonization of clinical trial databases, quality assurance in clinical trial processes, comparability of clinical trial results and a unified concept base for all clinical trial software applications.

The *Data Dictionary for Clinical Trials* provides clear and unambiguous definitions for terms in a clinical trial context. The construction of a data dictionary requires a uniform procedure for recording terms and relations. The present *Guideline for Creating Medical Terms* represents a first step in the direction of a lexically and semantically founded concept lexicon with high-quality content.

In the following section, an approach to lexical and semantic foundation will be elaborated in greater detail.

1.1 Lexical Foundation

The basis for the construction of a semantically founded *Data Dictionary for Clinical Trials* is terminology. Since the terminological determinations (obligatory conventions for concepts, their association with terms and the consequences of these associations) in the area of clinical trials are widely lacking at present, the *Onto-Builder* is in the first phase a definitional dictionary in the lexicographic sense, and supports terminology work in the area of clinical trials. It will therefore be necessary to find solutions to lexical problems, e.g. multiple-word compounds and their differentiation into terminological and non-terminological multiple-word compounds, synonymy, the treatment of abbreviations and polysemy. For these issues, solutions have been developed and arrangements made in order to optimize uniformity of operation. The present *Guideline* contains the defined lexical rules for the recording of concepts and relations and thus forms the basis for ensuring the lexical quality of the *Data Dictionary*.

1.2 Semantic Foundation

The semantic foundation of the *Data Dictionary* is understood as the clear illustration of the variance in term meanings, the consideration of context-dependent relations between concepts (static knowledge), and the definition of rules (dynamic knowledge). In order to achieve these goals, the *Guideline* contains rules for creating descriptions for certain concept groups, e.g. for *the measurement categories of clinical chemistry* and relation groups, e.g. for *causal relations*. In the second phase, the *Data Dictionary* will be expanded to include broader definitional provisions dependent on concept groups, i.e. special input windows for specific topic areas. Furthermore special input windows for relation groups and relations are planned. Ambiguities in concepts which arise in the clinical trial context will be made visible through the inclusion of context information. The available contexts in the *Onto-Builder* are described in the present document and supported with examples. Relations, e.g. *is a*, *connected to*, will be invoked in order to represent connections between concepts. Dynamic knowledge about procedures in the clinical trial context will be captured in rules.

2 Definitions

The following definitions are essential for working with the *Guideline*.

Concept A unit of thought formed by abstracting the common properties from the multitude of entities of the world [DIN, 10/1992].

Term A designation consisting of one or more words [DIN, 10/1992].
NOTE: Concepts are represented linguistically through terms and definitions.

Definition A linguistic designation of a concept [DIN, 10/1992].

In the following text, the expression “concept” will be used for concepts as well as for relations, since from a conceptual perspective both are treated as “concepts” in the future course of our work.

Preliminary remark:

In the *Guideline for Creating Medical Terms* examples and bibliography are highlighted as follows:

- Examples for concepts and relations in the *Onto-Builder* are given in `Courier` font.
- Examples for comments and descriptions are given in guillemets, e.g. »comment«, »description«
- Examples for strings in source documents are given in quotation marks, e.g. “/”.
- Bibliographic references to standard works are given in *italics*.

3 Guidelines

3.1 Lexical Guidelines

3.1.1 Word type

Normally, terms will be entered as nouns. If verbs or adjectives are present for which the noun can be used, only the noun will be recorded as a term.

Examples: Randomization instead of “randomize“
 radiation therapy instead of “radiate“

Formal relations (relationships between concepts) form an exception; these will be entered as verbs (see Relations in section 3.3).

3.1.2 Case¹

Nouns will normally be recorded in the nominative case. When word combinations with genitive, dative, or accusative case occur, two orthographic variants are possible:

- (a) Combine the terms into a single compound word:

Example: Studienabbruch instead of “Abbruch der Studie”

- (b) Connect the terms with a hyphen:

Example: Bauch-Sonographie instead of “Sonographie des Bauches“

The hyphenated variant can be used in the following cases (Duden)

- (a) To emphasize individual parts of the compound:

Example: Emissions-Computertomographie

- (b) Opaque compounds:

Example: High-CHOEP-Regime

- (c) Compounds with abbreviations:

Example: HIV-Antikörpertest

3.1.3 Number

Nouns are to be recorded in the singular. If nouns are frequently used in the plural, this should be noted in the comments.

Examples: inclusion criterion (Comment: »frequently used in the plural«),
Hodgkin's cell (Comment: »frequently used in the plural«)

3.1.4 Language

German and English terms will be recorded. The language of the description should correspond to that of the source(s).

Example: The definition for *adverse event* will be recorded from the original document Guideline for Good Clinical Practice (GCP) as well as from the German translation.

3.1.5 Proper Names

Proper names will be recorded unchanged. If a German compound term contains a proper name, it should be set off with a hyphen; English compound terms containing a proper name are to be recorded without a hyphen.

¹ Only applies to entries in German

Examples for German: Karnovsky-Index, Likelihood-Schätzer

Examples for English: Karnovsky's index, Likelihood estimator

3.1.6 Concept Linkage

We can distinguish the following types of concept linkage (multiple-word concepts) [DIN, 12/1993]:

(a) Determinative Concept Linkage

A second concept occurs additionally, as a feature in the content of the original concept, whereby the latter is restricted. The resulting concept is a sub-concept.

Examples: randomized study, single blindness, primary endpoint

(b) Disjunctive Concept Linkage

The new concept encompasses the scope of both constituent concepts.

Example: consensus study

(c) Integrating Concept Linkage

Objects associated to concepts are combined into the next-higher whole.

Example: sponsor-investigator

(d) Conjunctive Concept Linkage

The new concept merges the contents of both constituent concepts, and is their next common sub-concept.

Example: investigator study

The types of concept linkages elaborated above are terminological multiple-word compounds (concepts with an established meaning) in the sense of [Schaeder, 1994]. Non-terminological multiple-word compounds, so-called collocations or *ad hoc* compounds, contain a word which does not have any special meaning for the definition of the concept (e.g. independent ethics committee). These two types of multiple-word compounds can in many cases only be distinguished by individuals with specialized expertise in a relevant field [Schaeder, 1994]. For this reason, relevant multiple-word compounds should generally be recorded.

Multiple-word terms or complex single-word terms can be created to represent concept linkages.

3.1.7 Single-word terms

A single-word term is a denomination consisting of one word.

NOTE: Compounds, including those joined with a hyphen or slash count as single-word terms as well [DIN, 12/1993].

In the following we present three spelling conventions for compound single-word terms: writing as a one-word expression, with hyphenation, and with a slash.

(a) One-word expressions

If the constituent parts of a compound are relevant individual terms, they should be defined separately in addition.

Examples: Histologiebefund (“histology finding”)

The meanings of the individual terms *Histologie* (“histology”) and *Befund* (“finding”) are relevant; the terms should also be defined separately.

Ethikkommission (“ethics committee”)

The meanings of the individual terms *Ethik* (“ethics”) and *Kommission* (“committee”) are not relevant to the clinical trial context; thus, the terms should not be defined individually.

(b) Hyphenated expressions¹

Some compounds should be written with hyphenation. This spelling convention gives an indication that the individual components in the present context are of textual relevance. The hyphen indicates that there is no more closely specified bond between the terms.

Examples: Salvage-Protokoll

Abdomen-Sonographie (Hyphenation indicates a substantiation)

Sponsor-Prüfer (Hyphenation means “and”)

(c) Expressions written with a slash

A slash “/” between two terms in the source document can have the following meanings.

- term A / term B – in the sense of “or” (concept A \vee concept B). The concepts should be defined as individual terms.

Example: Indication in the Text: “double input / second look”

Entry in the *Onto-Builder*: double input, second look

- term A / term B – in the sense of “and” (concept A \wedge concept B)

In German the terms should be connected with a hyphen and defined as a single term.

Example for German:

Indication in the Text: “Sponsor / Prüfer”

Entry in the *Onto-Builder*: Sponsor-Prüfer

¹ Only applies to entries in German

- term A / term B – in the sense of “and/or”, i.e. indeterminate. Please notify the Moderator team in this case, indicating the term and context (info@onto-builder.de). The decision whether a compound should be analyzed as terminological or non-terminological is often very difficult. Normally the slash will be retained in these cases.

Example: Indication in the Text: “investigator / institution”
Entry in the *Onto-Builder*: investigator / institution

3.1.8 Multiple-word terms

A multiple-word term is a denomination composed of at least two words separated by a space [DIN, 12/1993]. The words used in multiple-word terms can themselves be elementary (e.g. consensus study) or complex (e.g. High CHOEP-21 study). Multiple-word terms should be recorded with unchanged word order.

Example: Division of stages for non-Hodgkin’s Lymphoma

3.1.9 Concepts with intrinsic meaning

Concepts with intrinsic meaning should be recorded and defined; it should be indicated in the comments which meaning the term has in the present context, or which term would be more concrete.

Examples: Cigarette consumption covers in addition to quantity of cigarettes, also smoker behavior (e.g. “only evenings”, “spread throughout the day”). Compliance is a cognitive concept which includes the intrinsic attitude of a patient to the application of a therapy.

3.1.10 Concept Variants

In the clinical trial context, concept variants sometimes occur, i.e. concepts with a stable part and a variable part. Due to the potential for redundant concept descriptions, it is not always sensible to record all concept variants as individual terms. One must judge to what extent the variable part of the concept influences the definition of the term. Accordingly, the concept variants should be recorded as individual terms or as a single consolidated term.

- (a) For concept variants where the variable part exerts a high degree of influence, the concept variants should be recorded as individual terms and are to be described separately.

Example: leukocyte count in urine, leukocyte count in blood Both should be recorded as individual terms.

- (b) For concept variants where the variable part exerts little influence, the stable part should be recorded as a term, and the variants (variable parts) will be referred to in the description.

Example: CHOEP-14, CHOEP-21: only CHOEP should be recorded as a term.

3.2 Guidelines for Definitions of Concepts

3.2.1 General Guidelines for the Definition of Concepts

3.2.1.1 *The Use of Concepts and their associated Terms in Definitions*

In definitions, if the meaning of terms and/or the concepts themselves are not generally known, they must be defined [DIN, 12/1993].

3.2.1.2 *Definition of superordinate Concepts*

If concepts are defined for which a superordinate concept is known, the latter should be recorded and defined as well.

Example: peroral , subcutan

The superordinate concept for this example is application.

3.2.1.3 *Accuracy of Definitions*

A definition must record the contents of the concept in question with an adequate degree of precision, but without violating the maxim of succinctness [DIN, 12/1993].

3.2.1.4 *Succinctness of Definitions*

A definition should contain only those features which are necessary to describe the term in the given context, but without violating the maxim of accuracy [DIN, 12/1993].

Example: The description of the term `blood volume` should define only the term itself, and should not include a definition of `plasma volume` as well:

term: `blood volume`

description: »total quantity of circulating blood, composed of plasma volume and the volume of corpuscular blood components«

3.2.1.5 *Avoidance of Circularity in Definitions*

Two or more definitions should not be circular; i.e. it should never be the case that a term is described by one or more terms which are, conversely, defined on the basis of the original term [DIN, 12/1993].

Examples of circularity:

term 1: inclusion criterion

description 1: »criteria for the inclusion of a patient in a clinical trial«

term 2: patient inclusion

description 2: »inclusion of a patient in a clinical trial by means of inclusion criteria«

The circularity in this example arises in that `inclusion criterion` is defined in terms of `patient inclusion` (description 1), while `patient inclusion` is defined in terms of `inclusion criterion` (description 2).

Avoidance of circularity:

term 1: inclusion criterion

description 1: »If a patient fulfills all conditions for enrollment in the trial, as specified in the clinical trial protocol, then the patient may participate in the trial.«

term 2: patient inclusion

description 2: »enrollment of a patient in a clinical trial«

3.2.1.6 Avoidance of Tautological Definitions

It is completely impermissible to define a term in terms of itself [DIN, 12/1993].

Example of a tautology:

term: clinical trial planning

description: »process of planning a clinical trial«

3.2.1.7 Avoidance of Negative Definitions

It is completely impermissible to define a term negatively, i.e. in such a way that the definition consists only of features that the term lacks [DIN, 12/1993].

Example of a negative definition:

term: day

description: »period of time which is not night«

3.2.2 Specific Guidelines for the Definition of Concepts

3.2.2.1 Medications

The description of medications is based on the *Gelbe Liste* [Gelbe Liste, 2002]. The generic name of the drug taken from the *Gelbe Liste* should be recorded as a term. If necessary, the commercial name can be used in the description, accompanied with tags:

General Notation:

```
term:          generic name

description:   »<commercial_name> ...</ commercial_name >«
```

Example:

```
term:          Vincristin

description:   »<commercial_name> Vincristin Liquid, Lilly

               Injektionslösung</ commercial_name >«
```

In the second phase of the *Data Dictionary*, the internet version of the *Gelbe Liste* will be directly accessible from within the user-interface.

3.2.2.2 Measurement Categories (Clinical Chemistry)

For the description of measurement categories in the domain of clinical chemistry, the so-called laboratory parameters (see standard reference *Labor und Diagnose* in Appendix A: Sources) will be used. The following information should be recorded in the description.

General Notation:

```
term:          name of the laboratory parameter

description:   methodology

               material under examination

               reference area

               units
```

Example:

term: leukocyte count

methodology: cell count, haematology analyzer, strobe-light method

material: EDTA-blood (1 ml); cell count method, capillary blood (0,1 ml)

reference area:adults: 7,8 (4,4-11,3)

children

newborns: 18,1 (8,0-30,0)

12 h: 22,8 (13,0-38,0)

.....

units: conventional: $10^3/\mu\text{l}$

SI-unit: $10^9/\text{l}$ (numerical values are identical)«

3.3 Guidelines for Relations

Relations describe interactions between one or more terms (e.g. *»is influenced by«, »is part of«, »is a«, »is a consequence of«*). Relations are to be recorded in the *Onto-Builder* as follows:

General Notation:

term: <rel>name_of_the_relation</rel>

description: »<rel>relation_found</rel>«

source personal definition

Example:

term: <rel>is a</rel>

description: »<rel>single blind is a type of blindness</rel>«

source: personal definition

If it is necessary to specify, in addition to the context of the relation, contexts for the individual terms of the relation as well, the following format should be used.

General Notation:

term: <rel>name_of_the_relation</rel>

description: »<rel><context1>first word of the context designation for the first term</context1>first term relation<context2> first word of the context designation for the second term</context2>second term</rel>«

Example:

term: <rel>is a</rel>

description: »<rel><context1>biometrics</context1>
randomization procedure is <context2> biometrics </context2>
biometric procedure</rel>«

source: personal definition

Other relations which are found between terms of the same relation type should be entered as other descriptions of the relation. A description of a relation which defines the relation itself should not be enclosed with tags (<rel> </rel>).

Example:

term: <rel>is a</rel> (a previously-recorded term)

description: »<rel>hair loss is an undesirable but expected event</rel>«

source: personal definition

3.4 Guidelines for Rules

Rules consist of two parts: the premise (IF) and the logical consequence (THEN). Rules should be recorded in the *Onto-Builder* as descriptions of terms. The procedure is as follows:

- (a) Choose a denomination for the rule and enter it as a term.
- (b) Enter a description or definition for the term.
- (c) Enter the rule as a second description in the form <rule>text_of_the_rule</rule>.

Example:

term: early termination of a clinical trial

description 1: »The early termination of a clinical trial results when one or more criteria for the early termination of a clinical trial are fulfilled.«

context: other: clinical trial

comments: »The early termination of a clinical trial can refer to an individual patient, an investigation center, a clinical trial branch, or the entire trial.

description 2: »<rule>If

severe side-effects ensue, or there are cumulative occurrences of therapy-conditioned death, or the superiority of another therapy branch is confirmed, or new knowledge from other studies or publications becomes available, or the rate of recruitment is insufficient, or there is an accumulation of protocol violations in the therapy branch Hi-CHOEP-21

Then Notification of the protocol committee by the clinical trial management and decision on the early termination of the clinical trial by the protocol committee</rule>«

context: clinical trial, therapy branch

source: clinical trial protocol: DSHNHL 1999-2

3.5 Guidelines for Related Terms

Related terms belong to a family of terms or are textually connected with one another (e.g. `patient informed consent` and `patient information`). This information about terms should be recorded in the *Onto-Builder* as well — in the comments. Entering a related term is an alternative to entering a relation in cases where it is not yet possible to express the relationship between the two terms.

General Notation:

term:

description:

comments: »<vb>related_term</vb>«

Example:

term: patient informed consent

description:

comments: »<vb>patient information</vb>«

3.6 Guidelines for Abbreviations

All types of abbreviations should be treated as equivalents and recorded as abbreviations. Abbreviations used as jargon, e.g. “chemo” for “chemotherapy”, should not be recorded.

Example:

term: adverse event
abbreviation: AE

4 Assignment of Terms to Contexts

As an initial classification, terms should be assigned to contexts. This classification is intended as a pre-sorting for the assignment of terms to categories, the identification of processes, relations, rules, etc., and preparation for the construction of a formalized system of terms. In the first version of the *Onto-Builder*, the contexts are not hierarchically arranged and do not represent any disjoint categories. With respect to simple and intuitive classification, various dimensions and granularities should be taken into account.

The available contexts are described in more detail below.

4.1 Measuring Procedure / Laboratory / Measurable or Quantitative Parameters

This context includes measuring procedures, laboratory terms, and terms to which a quantitative value or interpretation can be assigned. This category includes among other things the physical weights and measures used in the context of clinical chemistry, i.e. the so-called *laboratory parameters*. In describing terms of this group, qualitative assessments (e.g. good, bad, low, high) and/or units (e.g. cm, kg, ml, day, month, year) should be recorded as well.

Examples: cell counting chamber procedure, weight, size, temperature,
 leukocyte count, compliance, Body Mass Index

Example:

term: weight

description: »units: ounce (oz.), pound (lb.), stone (st), short ton (US), long
 ton (UK), gram (g), kilogram (kg), ton (t) «

comments: For conversions, see: <http://dict.tu-chemnitz.de/calc.html>

source: <http://dict.tu-chemnitz.de/calc.html>

Special rules have been determined for the definitions of the *laboratory parameters* (see section 3.2.2.2).

4.2 Medications / Materials / Medical Products / Substances

This context includes all medications, materials, and medical products as defined by the *Medical Product Law*, [Medizinproduktegesetz., August 1994] functional categories and physical states of substances (e.g. liquid, solid, gas). The term substance includes all materials with a defined chemical composition.

Examples: Vincristin, carrier substance, banked blood, saline, object slide, pipette, whole blood

4.3 Treatments / Events / Processes / Actions

This context includes diagnostic / therapeutic procedures and laboratory procedures. In addition, this context includes generic and specific processes as well as biological and non-biological processes. This description is based on the hierarchy in GALEN – Entity: Generalised Process [Rogers, Rector, 1999].

Examples of diagnostic / therapeutic procedures:

radiation therapy, chemotherapy, electrophoresis

Examples of generic processes:

transport, open, close

Examples of biological processes:

peristalsis

Examples of non-biological processes:

radiation, histological coloring

4.4 Organisms

This context includes all organisms, microorganisms and infectious particles as well as fungi, plants and animals.

Examples: Streptococcus, Escherichia coli, Myxomycetes, mouse

4.5 Diagnoses / Diseases / Symptoms

This context contains all terms that can be interpreted as a diagnosis, illness, symptom, or diagnostic finding. For example, the term high blood pressure can occur as a diagnosis or illness, a symptom or a diagnostic finding, depending on the situation.

Examples: mantle cell lymphoma, adiposity, fever, hypertension

4.6 Anatomy / Structures and Regions of the Body

This context contains anatomical terms, abnormal body structures, and terms for regions of the body and body positions.

Examples: intravenous, subdural, spleen, bone marrow, bulk caudal, ventral

4.7 Classification

This context contains all medical classifications relevant to clinical trials for malignant lymphoma, nomenclatures and thesauri.

Examples: International Classification of Diseases, International Prognostic Index, Karnovsky's Index, Common Toxicity Criteria, REAL-Classification

4.8 Statistics / Biometrics / Epidemiology

This context contains all relevant biometric terms.

Examples: case, chi-squared-test, randomization

4.9 Institutions / Persons / Roles / Functions

This context includes all relevant terms for organizations, institutions and individuals, which play a role in the context of clinical trials.

Examples: patient, clinic, reference pathology, ethics committee

4.10 Administration / Management / Documentation

This context contains all terms which are connected with the management and documentation of clinical trials.

Example: case report form

4.11 Meta-terms / Relational Nouns

Relational nouns are nouns which have their own argument structure. These terms are marked by indistinct points of reference. In order to describe these terms exactly, meta-knowledge is required.

Examples: prognosis, efficacy, toxicity, side-effect, dose reduction

4.12 Other

This is a “free” context. Here you can enter suggestions for additional new contexts and specify them for terms you have entered.

4.13 Range of Validity of Terms

Concepts in the clinical trial context can have temporal and geographical ranges of validity. In such cases, the validity can extend over the term itself (term level), over certain properties of the term (attribute level), or over later instances of the term.

4.14 Temporal Validity

Capturing temporal validity in the *Data Dictionary* is especially meaningful for the use of terms in the standard operating procedures (SOPs).

(a) concept level

During the course of a trial, certain terms are often of interest only within a certain temporal period.

Example: The documentation concept is meaningful only during the trial planning and implementation phase.

(b) attribute level

Properties of terms can be of varied importance (meaningless, meaningful) over the course of time.

Example: Patient informed consent declaration
Requests for the document → is only important during the trial planning and implementation phase.

Procedure of agreement → is only important during the realization of the trial.

4.15 Geographical Validity

Concepts in the clinical trial context can have a geographical reference.

(a) concept level

To some extent, terms are used differently in different geographical areas. In this regard, international, European, and national regions should be taken into account.

Example: Studienkoordinator \leftrightarrow study coordinator: The term Studienkoordinator, used in German-speaking areas, should not be viewed as a translation of the English (American) term study coordinator. The terms differ from one another with respect to content.

(b) instance level

Instances of terms can have a geographically-restricted domain of application.

Example: ethics committee: Specific ethics committees have jurisdiction over specific geographical areas.

5 Sources

Term definitions can be gathered from a variety of sources. It is important to distinguish (a) public sources and (b) institutional / clinical trial sources. Drawing from both types of sources is pursuant to the goal of obtaining sound explanations for terms as well as the terminological and documentational harmonization of clinical trial documents.

- (a) Public sources are standard reference works (e.g. scientific literature), general guidelines (e.g. *Guideline for Good Clinical Practice (GCP)*) [ICH, May 1996] or legal texts. The collection of definitions from public sources leads to high-quality entries in the *Data Dictionary* and supplies a basic definition for the description of the usage of a term in clinical trial documents, e.g. in case report forms.
- (b) Clinical trial and institutional sources include standard operating procedures (SOPs), case report forms (CRFs), clinical study protocols, working instructions and guidelines drawn from clinical trials. Collecting term descriptions from clinical trial and institutional sources serves to identify the various usages of terms as well as documentational properties (e.g. laboratory numbers expressed as a percentages or absolute values). This method facilitates the harmonization of clinical trial documents (primarily case report forms) within the Competence Network Malignant Lymphoma.

Personal definitions — e.g. when no appropriate public definition can be found, or when one does not agree with a present definition — can be entered as well, of course.

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