

## The Adverse Reaction Terminology

Terminology for coding clinical information in relation to drug therapy

### Features:

Four-level hierarchical structure

Open-ended - new terms added as necessary

WHO-ART is updated with MedDRA terms  
appearing on WHO adverse reaction reports

Computer suitable record number system

Adverse reactions in English, French, German,  
Spanish, Portuguese and Italian

Used by drug regulatory agencies and  
pharmaceutical manufacturers in many countries

### Structure:

- 32 System-organ classes  
body organ groups
- 180 High level terms  
for grouping preferred terms
- 1930 Preferred terms  
principal terms for describing adverse reactions
- 2758 Included terms  
synonyms to preferred terms

## **The Adverse Reaction Terminology**

This terminology has been developed over more than 30 years to serve as a basis for rational coding of adverse reaction terms.

Because new drugs and new indications produce new terms to be incorporated, the structure of the terminology is flexible enough to allow new developments to be incorporated whilst maintaining the structure of the terminology and without losing previous relationships.

The basic logic allowing such flexibility is a hierarchical structure starting with body system/organ level, within which there are grouping (general or high level) terms which are useful for the broadest view of drug problems. Within these broad categories the specific, frequently used 'preferred terms' provide for precise identification of drug problems.

Preferred terms allow for precision, but everyday experience shows that adverse reaction reports contain colloquial terms. In this case the WHO 'included terms' help by pointing to the closest preferred term, but still allowing the actual reported term to remain unaltered.

Many users simply make up their own included term list based upon their own experience. Users are encouraged to let the Uppsala Monitoring Centre know about any useful included terms so that they can be incorporated in the official WHO-ART with appropriate relationship to preferred terms.

Also, if a frequently used, clearly defined term is considered by users as a possible preferred term, this can be requested. A final decision on incorporation is made after consultation with experts in the field.

There is also a glossary list of terms which are synonyms for preferred terms.

WHO-ART is available in six languages: English, French, Spanish, German, Italian and Portuguese.

The WHO-ART is the most widely used terminology by both regulatory agencies and pharmaceutical manufacturers.

## **Development**

Not only is the WHO-ART flexible, its maintenance is dynamic. Whilst the overall robustness of the terminology is demonstrated by almost 30 years of service, there is still room for improvement.

An important development with the terminology is the definition by international experts of preferred terms. When complete this will add a further level of precision to the terms.

A section for terms which can be used for events not likely to be a direct effect of a drug has been added - System Organ class 2000 - Secondary terms - events, as well as a section 2100 - Poison specific terms. Also a section for effects on clinical test results by drugs (false positives or negatives) has been requested.

Change in the terminology is driven by the needs of users, and our aim is to meet those needs as fast and completely as possible.

During 2001, a total of 32 Preferred terms and 96 Included terms were added to the terminology.

## Definitions and uses

### Preferred terms:

These are the principal terms used for describing drug adverse reactions. They are the main terms used at the input side, but may also be used for output purposes.

### High level terms:

These are group terms of related or similar conditions, which are used for easy retrieval of information. E.g. thrombophlebitis leg and thrombophlebitis arm represent two different preferred terms but are both grouped under thrombophlebitis as a high level term. All preferred terms may not have been assigned a high level term.

### System-organ classes:

These are groups of adverse reaction preferred terms pertaining to the same system-organ, and are for some purposes used at the output side. A preferred term can be allocated to a maximum of three different system-organ classes, e.g. respiratory depression is coded both under Respiratory disorders and Central nervous system disorders. The allocation of a preferred term to system-organ classes is fixed and does not change with specific reports. The first System Organ class listed for each preferred term is considered the most important one. A complete list of the classes and their codes is given at the end of this introduction (page 3).

### Included terms:

These are terms closely related to preferred terms. They are used to assist in finding the corresponding preferred term for proper coding of the adverse reaction reported.

(The layout of the Adverse Reaction Terminology and the relationship between the different types of terms are shown in an example below.)

### Record number system:

Each preferred term is designated a record number, in consecutive order as they are introduced. Preferred terms are always assigned the sequence number 001. Included terms get the same record number as their corresponding preferred terms, but with a higher sequence number. Where high level terms exist, a high level term link is assigned from all relevant preferred terms. A high level term is always in itself also a preferred term. A high level term link is a pointer to the record number of the preferred term that is also the high level term (see example below).

Example showing the structure of the Adverse Reaction Terminology and the relationship between the different types of terms;

<b>ARECNO</b>	<b>INCLUDED TERMS</b>	<b>ARECNO</b>	<b>PREFERRED TERMS</b>	<b>HL LINK</b>	<b>HIGH LEVEL TERMS</b>
0363 005	Acidos metabolic	0363 001	Acidosis	0363	Acidosis
0363 004	Bicarbonate reserve decrease				
0364 003	Lactate blood increase	0364 001	Acidosis lactic	0363	
0393 003	Ketoacidosis	0393 001	Ketosis	0363	
0393 004	Acetonuria				
0393 005	Aceton breath				
0393 006	Acetonaemia				

## Translations

The Adverse Reaction Terminology is developed in English. Translations exist into French, German, Spanish, Italian and Portuguese. As the WHO Centre relies on external sources for the translations, there may be a delay in updating the terminology with translations into other languages. Translations missing are seen as blanks on diskette files.

Some Included terms may not be translatable into other languages and will always show up as blanks.

Printed versions of the terminology exist in all six languages separately.

Computer files of the terminology contain all six current languages.

## The complete list of system-organ classes and codes:

<i>Skin and appendages disorders</i>	0100
<i>Musculo-skeletal system disorders</i>	0200
<i>Collagen disorders</i>	0300
<i>Central &amp; peripheral nervous system disorders</i>	0410
<i>Autonomic nervous system disorders</i>	0420
<i>Vision disorders</i>	0431
<i>Hearing and vestibular disorders</i>	0432
<i>Special senses other, disorders</i>	0433
<i>Psychiatric disorders</i>	0500
<i>Gastro-intestinal system disorders</i>	0600
<i>Liver and biliary system disorders</i>	0700
<i>Metabolic and nutritional disorders</i>	0800
<i>Endocrine disorders</i>	0900
<i>Cardiovascular disorders, general</i>	1010
<i>Myo-, endo-, pericardial &amp; valve disorders</i>	1020
<i>Heart rate and rhythm disorders</i>	1030
<i>Vascular (extracardiac) disorders</i>	1040
<i>Respiratory system disorders</i>	1100
<i>Red blood cell disorders</i>	1210
<i>White cell and RES* disorders</i>	1220
<i>Platelet, bleeding &amp; clotting disorders</i>	1230
<i>Urinary system disorders</i>	1300
<i>Reproductive disorders, male</i>	1410
<i>Reproductive disorders, female</i>	1420
<i>Foetal disorders</i>	1500
<i>Neonatal and infancy disorders</i>	1600
<i>Neoplasms</i>	1700
<i>Body as a whole - general disorders</i>	1810
<i>Application site disorders</i>	1820
<i>Resistance mechanism disorders</i>	1830
<i>Secondary terms - events</i>	2000
<i>Poison specific terms</i>	2100

\* RES - Reticuloendothelial system

## **Critical Terms**

From the third quarter of 1998, a new field has been added at the end of the WHOART file which indicates Critical Terms. Critical terms are a subset of adverse reaction terms referring to, or possibly being indicative of, serious disease states, which have been regarded as particularly important to follow up.

## **WHOART History, frozen databases**

There is now also a cumulative source to enable tracing of previously changed/deleted records, which could be used if there are problems updating data on a trial that was run in e.g. 1995. "WHOART History" is a listing showing all changes made, and provides an opportunity to "rescue" old database information, or to make databases generated using different versions of the WHOART compatible.

## Versions

The WHO-ART is available in paper print, or diskette as a copy of the data base. Files may also be distributed by file transfer.

The printed version presently in use contains all terms existing in the data base in December 2000. Printed versions of the terminology exist in all six languages separately. The computerized version always contains a copy of the full data base, in all six current languages, which is updated every three months.

### 1. Adverse Reaction Terminology - paper print

The Adverse Reaction Terminology is presented in two lists:

#### *1. Preferred terms - system-organ class version*

The system-organ part of the WHO-ART arranged in system organ code order.

For each system-organ class the listing starts with the high level terms (first column) in alphabetical order, each term being repeated for every preferred and included term belonging to it. This is followed by a listing, also in alphabetical order, of the preferred terms (second column) for which there is no high level term, with the corresponding included terms in the third column. The printed version does not contain the full adverse reaction record number, down to identifying each Included term.

If a preferred term is allocated to more than one system-organ class the term is listed in each class, and the other class(es) to which it belongs is indicated by the code number in the column headed "System-organ no. 2 and No. 3".

Example:

#### **ADVERSE REACTION TERMINOLOGY - SYSTEM ORGAN CLASS VERSION**

##### **System Organ Class: 0300 -Collagen Disorders**

High level terms	RECNO	Preferred Term	Included terms	System Organs NO2 NO3
ALVEOLITIS	1560	ALVEOLITIS		1100 1810
ALVEOLITIS	1019	ALVEOLITIS ALLERGIC	PNEUMONITIS HYPERSENSITIVITY	1100 1810
ALVEOLITIS	1017	ALVEOLITIS FIBROSING		1100 1810
VASCULITIS	0078	ARTERITIS	ENDARTERITIS	1040
VASCULITIS	0078	ARTERITIS	PANARTERITIS	1040
VASCULITIS	0078	ARTERITIS	CRANIAL ARTERITIS	1040
VASCULITIS	0085	VASCULITIS	VASCULITIS PULMONARY	1040
VASCULITIS	0085	VASCULITIS	RENAL VASCULITIS	1040
VASCULITIS	0085	VASCULITIS	SKIN VASCULITIS NOS	1040
VASCULITIS	0085	VASCULITIS	IDIOPATHIC CAPILLARITIS	1040
VASCULITIS	0085	VASCULITIS	VASCULITIS NODULAR	1040
VASCULITIS	0085	VASCULITIS	VASCULITIS NEUTROPHILIC	1040
VASCULITIS	0085	VASCULITIS	VASCULITIS CEREBRAL	1040
VASCULITIS	0085	VASCULITIS	VASCULITIS AGGRAVATED	1040

**II. All terms - alphabetical version**

The 'all terms' column contains, in alphabetical order, all included (I), preferred (P) and high level terms (H). Corresponding preferred terms are repeated in the next column, e.g. for ACHLORHYDRIA the corresponding preferred term HYPOCHLORHYDRIA is listed. For a preferred term e.g. ACIDOSIS LACTIC the same preferred term is listed in both columns.

By looking up an included term in the "ALL TERMS" column the relevant preferred term can be found.

A high level term may be repeated several times in the "ALL TERMS" column, once for each preferred term belonging to the same high level term. In this way all preferred terms having the same high level term are easily found. For example, ACIDOSIS appears three times in the "ALL TERMS" column designated as high level indicating that three preferred terms have this same high level term. Note that all high level terms are also in themselves preferred terms.

Under the heading HIGH LEVEL TERMS, the group terms for similar preferred terms are listed. There are, however, many preferred terms which have not been grouped under a high level term. In such cases the corresponding space in the high level term column is left blank.

**ADVERSE REACTION TERMINOLOGY - ALPHABETICAL VERSION**

Type	RECNO	All Terms	Preferred Term	High Level Term	System Organs
P	1152	<i>Achalasia cardiae</i>	<i>Achalasia cardiae</i>	<i>Diseases of oesophagus</i>	0600
I	0799	<i>Achlorhydria</i>	<i>Hypochlorhydria</i>		0600 0420
I	0799	<i>Achylia gastrica</i>	<i>Hypochlorhydria</i>		0600 0420
I	0279	<i>Acid indigestion</i>	<i>Dyspepsia</i>		0600
I	0992	<i>Acid phosphatase serum</i>	<i>Phosphatase acid increased</i>	<i>Enzyme abnormality</i>	0800
H	0364	<i>Acidosis</i>	<i>Acidosis lactic</i>	<i>Acidosis</i>	0800
H	0363	<i>Acidosis</i>	<i>Acidosis</i>	<i>Acidosis</i>	0800
P	0363	<i>Acidosis</i>	<i>Acidosis</i>	<i>Acidosis</i>	0800
H	0393	<i>Acidosis</i>	<i>Ketosis</i>	<i>Acidosis</i>	0800
P	0364	<i>Acidosis lactic</i>	<i>Acidosis lactic</i>	<i>Acidosis</i>	0800
I	0363	<i>Acidosis metabolic</i>	<i>Acidosis</i>	<i>Acidosis</i>	0800
P	0001	<i>Acne</i>	<i>Acne</i>	<i>Dermatitis</i>	0100
I	0005	<i>Acne bromata</i>	<i>Bromoderma</i>		0100
I	0001	<i>Acneiform dermatitis</i>	<i>Acne</i>	<i>Dermatitis</i>	0100
I	0114	<i>Activity motor exaggerated</i>	<i>Hyperkinesia</i>	<i>Dyskinesia</i>	0410

**III. Supplements**

Supplements to the paper print version are printed every three months and can be obtained on request.

The supplement is cumulative over the year and lists all additions made to the WHO-ART.

## 2. WHO-ART - Computer file information

The WHO-ART files are available as a sequential copy of the data base, suitable for use in relational data bases. They can be obtained on diskette or as e-mail attachment files

Computerized versions are full copies of the Adverse Reaction Terminology, including all terms in all six existing languages, together with record number system, high level terms and system organ classes. The files contain the full Adverse reaction record number, which identifies each term uniquely.

Computer files are updated quarterly.

### File descriptions:

<b>ADVERSE REACTION DICTIONARY (WHOART)</b>	<b>Field</b>	<b>No of positions</b>	<b>Position in record</b>	<b>Comment</b>
Adverse reaction record number	1	4	1-4	
Sequence number	2	3	5-7	001 = preferred term, ≥002 = included term,
Check digit	3	1	8	
High-Level term link	4	4	9-12	
<b>System-Organ Class 1</b>	5	4	13-16	
<b>System-Organ Class 2</b>	6	4	17-20	
<b>System-Organ Class 3</b>	7	4	21-24	
Text in English	8	33	25-57	
Text in French	9	33	58-90	
Text in German	10	33	91-123	
Text in Spanish	11	33	124-156	
Text in Portuguese	12	33	157-189	
Text in Italian	13	33	190-222	
Year, quarter	14	3	223-225	
<b>Critical term</b>	15	1	226	Time of inclusion in the terminology, 85:4 given for records added before 86:1

### **SYSTEM ORGAN CLASS (SOC)**

<b>System Organ Class Code<sup>1</sup></b>	1	4	1-4
Text in English	2	100	5-104
Text in French	3	100	105-204
Text in German	4	100	205-304
Text in Spanish	5	100	305-404
Text in Portuguese	6	100	405-504
Text in Italian	7	100	505-604

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<sup>1</sup> Linkage field to System-Organ Class 1, 2 and 3 in WHOART file



## Proposed new entry in WHO-ART

Reporter \_\_\_\_\_

Company \_\_\_\_\_

Address \_\_\_\_\_

Country \_\_\_\_\_

Fax No. \_\_\_\_\_

**Please mark the desired alternative below:**

**Regular updates**

- Update in regular quarterly input
- No separate info on new entry
- No charge

**Expedited updates**

- Immediate update
- Info sent by fax or mail
- Charge 900 SEK/hour,  
min. 450 SEK

<b>Suggested term</b>							
<b>Description</b>							
<b>Suggested SOC</b>							
<b>Entered term</b>				<b>WHO record No</b>			
<b>Included to:</b>				<b>WHO record No</b>			
<b>HL term link</b>		<b>SOC 1</b>		<b>SOC 2</b>		<b>SOC3</b>	
<b>Suggested term</b>							
<b>Description</b>							
<b>Suggested SOC</b>							
<b>Entered term</b>				<b>WHO record No</b>			
<b>Included to:</b>				<b>WHO record No</b>			
<b>HL term link</b>		<b>SOC 1</b>		<b>SOC 2</b>		<b>SOC3</b>	
<b>Suggested term</b>							
<b>Description</b>							
<b>Suggested SOC</b>							
<b>Entered term</b>				<b>WHO record No</b>			
<b>Included to:</b>				<b>WHO record No</b>			
<b>HL term link</b>		<b>SOC 1</b>		<b>SOC 2</b>		<b>SOC3</b>	

