

**ICD-11 revision process for Rare Diseases**  
**Chapter III**  
**E80-E89**

Immunological diseases

*Draft structure n° 1*

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*Draft for ICD revision for rare diseases - Confidential*  
*Chapter III, codes D80-D89: Immunological diseases*

**Introduction and table of contents**

You are kindly invited to participate to the World Health Organisation's *International Classification of Diseases* (ICD) revision process. The following document will help you in making your comments. You will find:

1. The rationale and the general methodology of the ICD revision for rare diseases
2. The ICD-11 draft structure for *Immunological diseases*, which represents the proposal for a new ICD.

**You are invited to:**

1. Comment the ICD-11 draft structure indicating whether you agree or disagree with the new global structure and the way rare diseases are represented in it.

2. Send your feed-back to Orphanet.

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3. Disseminate this invitation to your colleagues who are experts in this field.

## **1. Rationale and general methodology**

WHO has established various Topic Advisory Groups to serve as planning and coordinating advisory bodies in the update and revision process for specific areas. A Revision Steering Group oversees the overall revision process. An internet-based workspace documents systematic reviews that obtain evidence from analysis of available data. WHO collaborates through this platform with all interested parties. Working groups organized by the Topic Advisory Groups (TAG) review the proposals. To learn more about the whole revision process:

<https://extranet.who.int/icdrevision/help/docs/ICDRevision.pdf>

A TAG for rare diseases was established in April 2007 as rare diseases should now be traceable in mortality and morbidity information systems. The production of the basic information to establish a first draft of the classification of rare diseases has been assigned to Orphanet and will contribute to the whole revision process, as rare diseases involve all areas of medicine.

The workplan is as follows:

1. Proposals from TAG for a new ICD structure are expected before the end of 2009.
2. A decision about it, after compilation of all proposals, should be taken in April 2010. This will define the category layers based on consensus hierarchies, called the Alpha version.
3. Work on the Beta version will then start at TAG level to populate the model and finalise the proposals. The Beta version will be due by the end of 2010. In 2011 field testing will start.

In order to prepare the ICD revision process, Orphanet has collected a series of rare diseases classifications mainly based on scientific grounds (aetiology and mechanism). To complement these classifications, Orphanet has developed a strictly clinical in-house classification to meet the needs of the clinicians. All the classifications can be viewed on the Orphanet website. They now serve as a basis to build the ICD-11 proposals. For an overview on the general methodology of Orphanet classification:

<http://www.orpha.net/data/patho/Pro/en/OrphanetClassificationRareDiseases.pdf>

Orphanet is a comprehensive peer-reviewed database of information on rare diseases. Over 5,800 are inventoried, and the database of diseases is updated monthly according to the evolution of knowledge. Each Orphanet entry is indexed with MeSH terms, Orphanet thesaurus of clinical signs and symptoms, ICD-10 codes, and linked to the OMIM database, to an in-house genes database and to PubMed as well as to other websites of interest. For each Orphanet entry there is an identity card with epidemiological data (prevalence rank, mode of inheritance, age of onset) and a set of synonyms. Orphanet produces a peer-reviewed encyclopaedia covering more than 2,600 entries and updated continuously.



## **2. Rationale for immunological diseases revision**

The current ICD10 classification of immunological diseases is currently mostly made of the block of codes [D80-D89](#) *Certain disorders involving the immune mechanism*. Other relevant diseases are included in the block [D70-D77](#) *Other diseases of blood and blood-forming organs*. However, these two blocks do not include every disease of immune origin, as the current classification is mostly organised by body systems. Many diseases of immune origin are clinically specific of one particular system and are thus coded in the corresponding chapter.

Notably, antoimmune and autoiflammatory diseases are not included in these block of codes, and are not dealt with in this document.

Orphanet will propose that ICD11 should contain a specific chapter for multisystemic diseases, that are difficult to place in the current ICD10 organized mainly according to anatomical systems. If such a chapter is ultimately created, it would conceivably include quite a number of immune disorders.

**The current ICD classification is monoaxial, meaning that every entity can figure only at one point in the classification; however, many diseases are associated with more than one medical specialty.** In the future ICD, every entity shall be assigned a unique identifying number, which will allow the classification to become *polyaxial*: diseases will be able to figure in all relevant places in the classification (for instance, “X-linked immunoneurologic disorder” will figure among both neurological and immunological diseases). This system will be fully operational in the electronic version of the future ICD. However, in the paper version, it will still be necessary for space reasons to keep the current monoaxial system: one medical specialty must then be given priority, and *exclusion notes* are put in the other relevant chapters to redirect users to the correct code. The priority specialty is related to the body system most severely affected by the disease and/or the specialist most likely to be relied on for the management of the disease. In a number of cases however, the choice is questionable and ultimately quite arbitrary.

**The Orphanet proposal for a new ICD classification favours a clinical approach.** Names of entities strive to include references to the clinical situation of patients in addition to a causal reference. Major groups of diseases are preferentially defined on the basis of shared clinical features. Aetiological causes are used secondarily for finer classification. For genetic diseases, references to mode of transmission are quite commonly used as it is commonly done in immunology.

**The ICD10 coding of rare tumours is not satisfactory**, because it cannot be made specific: the oncology chapter only allows to encode the localisation and severity of the tumour, and must be supplemented with an additional code to express morphology (vol. 1 p. 1145-1166). Moreover, the physiopathological consequences of tumours cannot accounted for: the ICD10 sometimes uses a double-coding system for similar issues (a first code with dagger is used for the primary disease, and a second code with asterisk for secondary manifestations), but the oncology chapter does not use this possibility. We advocate for generalised double coding in these cases.

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**A general problem is the coding of iatrogenic diseases.** In the current ICD10, iatrogenic disorders in every chapter are regularly included separately under a series of specific codes (labelled “post-procedural”). However, since the number of post-procedural codes is quite small, it is impossible to code many post-procedural entities with precision. How iatrogenic disorders will be represented in ICD11 is not settled, but the current system needs revision.

**ICD-11 draft structure  
for  
Immunological diseases**

**ICD-11 draft structure for immunological diseases**

NB: Main sections are highlighted in grey.

NB: Appropriate classification for excluded entries will be revised in the proper chapters; current ICD10 codes are indicated when existent.

NB: Synonyms are in italics.

<i>ICD11 table draft</i>	<i>Corresponding ICD10 code</i>	<i>Comments</i>
<b>Disorders involving the immune system</b>	<b>D80-D89</b>	
<i>Includes:</i> defects in the complement system		
<i>Includes:</i> immunodeficiency disorders, except human immunodeficiency virus [HIV] disease		
<i>Excludes:</i> autoimmune diseases		Two general exclusion notes; the diseases are to include in the chapters about the relevant system.
<i>Excludes:</i> autoinflammatory syndromes		
<i>Excludes:</i> human immunodeficiency virus [HIV] disease	<b>B20-B24</b>	Include with infectious diseases.
<b>Primary immunodeficiency with predominantly antibody defects</b>	<b>D80</b>	
<b>Hereditary hypogammaglobulinaemia or agammaglobulinaemia</b>	<b>D80.0</b>	
X-linked agammaglobulinaemia		
<i>Agammaglobulinaemia, Bruton type</i>		
Autosomal recessive agammaglobulinaemia		
<i>Agammaglobulinaemia, non-Bruton type</i>		
Nanism due to growth hormone isolated deficiency with X-linked hypogammaglobulinaemia		
Malignant myelodysplasia with hypogamaglobulinaemia		
ICF syndrome		
<i>Immunodeficiency - centromeric instability - facial anomalies</i>		
<b>Common variable immunodeficiency</b>	<b>D83</b>	
Common variable immunodeficiency associated with lymphoproliferative disease (due to TACI mutations)		
Hypogammaglobulinaemia due to CD19 or ICOS deficiency		
Hypogammaglobulinaemia due to CD19 deficiency		
Inducible co-stimulator protein deficiency		
<b>Recurrent infections associated with immunoglobulin isotypes deficiency</b>		
Selective deficiency of immunoglobulin A [IgA]	<b>D80.2</b>	
Selective deficiency of immunoglobulin G [IgG] subclasses	<b>D80.3</b>	
Selective deficiency of immunoglobulin M [IgM]	<b>D80.4</b>	
Immunoglobuline heavy-chain deficiency		
<i>Excludes:</i> X-linked immunoneurologic disorder		Include in neurology.
<b>Hyper-IgM syndrome without opportunistic infections</b>	<b>D80.5</b>	
<i>Immunodeficiency with increased immunoglobulin M [IgM]</i>		
Hyper-IgM syndrome type 2		

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<b>ICD11 table draft</b>	<b>Corresponding ICD10 code</b>	<b>Comments</b>
Hyper-IgM syndrome type 4 Hyper-IgM syndrome type 5 <b>Excludes:</b> Hyper-IgM syndrome with opportunistic infections		Reciprocal exclusions are made for clarity between hyper-IgM syndromes with and without opportunistic infections. For the forms without opportunistic infections, see below among combined immunodeficiencies.
<b>Specific antibody deficiency with normal immunoglobulin concentrations and normal number of B cells</b> <i>Antibody deficiency with near-normal immunoglobulins or with hyperimmunoglobulinaemia</i>	<b>D80.6</b>	
<b>Transient hypogammaglobulinaemia of infancy</b>	<b>D80.7</b>	
<b>Other immunodeficiencies with predominantly antibody defects</b>	<b>D80.8</b>	
Immunodeficiency due to selective anti-polysaccharide antibody deficiency Osteopetrosis - hypogammaglobulinaemia <b>Excludes:</b> X-linked lymphoproliferative disease <b>Excludes:</b> Say-Barber-Miller syndrome	<b>D82.3</b>	See below among immune dysregulation syndromes. Include among multiple congenital abnormalities.
<b>Other specified immunodeficiency with predominantly antibody defects</b>	<b>D80.8</b>	
<b>Combined immunodeficiencies</b>	<b>D81</b>	
<b>Excludes:</b> Deletion 22q11		Include among developmental abnormalities.
<b>Excludes:</b> Hoyerdal-Hreidarsson syndrome		Include among developmental abnormalities.
<b>Severe combined immunodeficiency [SCID]</b>	<b>D81.1</b>	
<b>Severe combined immunodeficiency [SCID] with reticular dysgenesis</b>	<b>D81.0</b>	
<b>Severe combined immunodeficiency [SCID] due to adenosine deaminase [ADA] deficiency</b>	<b>D81.3</b>	
<b>Immunodeficiency due to absence of thymus</b> <i>Nezelof's syndrome</i>	<b>D81.4</b>	
<b>Immunodeficiency due to purine nucleoside phosphorylase [PNP] deficiency</b>	<b>D81.5</b>	
<b>Major histocompatibility complex deficiency</b>	<b>none</b>	
<i>Bare lymphocyte syndrome</i>		
Major histocompatibility complex class I deficiency	<b>D81.6</b>	
Major histocompatibility complex class II deficiency	<b>D81.7</b>	
<b>Hyper IgM syndrome with opportunistic infections</b>	<b>none</b>	
Hyper-IgM syndrome type 1 Hyper-IgM syndrome type 2 Hyper-IgM syndrome type 3 <b>Excludes:</b> <b>Hyper IgM syndrome without opportunistic infections</b>		Reciprocal exclusions are made for clarity between hyper-IgM syndromes with and without opportunistic infections. For the forms without opportunistic infections, see below among combined immunodeficiencies.

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<i>ICD11 table draft</i>	<i>Corresponding ICD10 code</i>	<i>Comments</i>
<b>Wiskott-Aldrich syndrome</b>	<b>D82.0</b>	
<b>Other specified combined immunodeficiencies</b>	<b>D81.8</b>	
<ul style="list-style-type: none"> <li>Combined immunodeficiency due to CD3gamma deficiency</li> <li>Susceptibility to respiratory infections associated with CD8alpha chain mutation</li> <li>Severe combined immunodeficiency due to ZAP70 deficiency</li> <li>Severe combined immunodeficiency due to CRAC channel anomaly</li> <li>Winged helix deficiency</li> <li>Autosomal recessive hyper IgE syndrome</li> <li>Primary immunodeficiency with skin granulomas</li> <li>Omenn syndrome</li> <li>Immunodeficiency due to CD25 deficiency</li> <li>Biotin-dependent carboxylase deficiency</li> </ul>		
<b>Excludes:</b> Corpus callosum, agenesis – cataract – immunodeficiency		Include with corpus callosum agenesis.
<b>Other specified combined immunodeficiency</b>	<b>D81.8</b>	
<b>Immunodeficiency associated with other complex syndromes</b>	<b>D82</b>	
<b>Autosomal dominant hyperimmunoglobulin E [IgE] syndrome</b>	<b>D82.4</b>	
<b>Excludes :</b> Autosomal recessive hyper IgE syndrome		
<b>Immune dysregulation diseases</b>		
<b>X-linked lymphoproliferative disease</b>	<b>D82.3</b>	
<i>Immunodeficiency following hereditary defective response to Epstein-Barr virus</i>		
<b>Haemophagocytic lymphohistiocytosis</b>	<b>none</b>	
<ul style="list-style-type: none"> <li>Chediak-Higashi syndrome</li> <li>Griscelli syndrome, type 2</li> <li>Hermansky-Pudlak syndrome</li> <li>Familial hemophagocytic lymphohistiocytosis</li> </ul>		
<b>Excludes:</b> Hermansky-Pudlak syndrome type 2		See below in constitutional neutropenias.
<b>Immunodeficiency syndrome with autoimmunity</b>	<b>none</b>	
Autoimmune lymphoproliferative syndrome		
<b>Excludes :</b> Type 1 autoimmune polyendocrinopathy		Include in endocrinology.
<b>Excludes:</b> Immune dysregulation – polyendocrinopathy – enteropathy, X-linked		Include in gastroenterology.
<b>Immunodeficiency associated with other specified complex syndromes</b>	<b>D82.8</b>	
<ul style="list-style-type: none"> <li>Chronic mucocutaneous candidiasis</li> <li>Lichstenstein syndrome</li> <li>OLEDAID syndrome</li> </ul>		
<b>Excludes:</b> Dyskeratosis congenita		Include in dermatology.
<b>Excludes:</b> Wiskott-Aldrich syndrome		See above in combined immunodeficiencies.

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<b>Excludes :</b> Deletion 22q11		Include among developmental abnormalities.
<b>Excludes:</b> Hypohidrotic ectodermal dysplasia with immunodeficiency		Include in dermatology.
<b>Excludes :</b> Lutz-Lewandowsky epidermodysplasia verruciformis		Include in dermatology.
<b>Excludes:</b> Schimke immuno-osseous dysplasia		Include among skeletal abnormalities.
<b>Excludes:</b> Cartilage-hair hypoplasia		Include among skeletal abnormalities.
<b>Excludes:</b> Hepatic veno-occlusive disease - immunodeficiency		Include in hepatology.
<b>Excludes:</b> Spondylometaphyseal dysplasia with combined immunodeficiency		Include among skeletal abnormalities.
<b>Excludes:</b> DNA repair defect with immunodeficiency		
Ataxia telangiectasia	<b>G11.3</b>	Include in neurology.
<i>Louis-Bar syndrome</i>		
Nijmegen breakage syndrome		Include among developmental abnormalities.
Bloom syndrome		Include among developmental abnormalities.
<b>Other specified immunodeficiency associated with complex syndromes</b>	<b>D82.8</b>	
<b>Primary immunodeficiencies due to disorders of innate immunity</b>	<b>D70</b>	
<b>Congenital neutropenia</b>	<b>none</b>	
Autosomal dominant severe congenital neutropenia		
Kostmann syndrome		
X-linked severe congenital neutropenia		
Neutropenia cyclic		
<b>Other constitutional neutropenias</b>		
WHIM syndrome		
Hermansky-Pudlak syndrome type 2		
<b>Excludes:</b> Chediak-Higashi syndrome		See above in haemophagocytic lymphohistiocytoses.
<b>Excludes:</b> Griscelli syndrome, type 2		See above in haemophagocytic lymphohistiocytoses.
<b>Excludes:</b> Cohen syndrome		Include among developmental abnormalities.
<b>Excludes:</b> Shwachman-Diamond syndrome		Include in haematology.
<b>Excludes:</b> Glycogen storage disease type 1B		Include among metabolic diseases.
<b>Excludes:</b> Barth syndrome		Include among metabolic diseases (mitochondrial).
<b>Excludes:</b> Cartilage-hair hypoplasia		Include among skeletal abnormalities.
<b>Excludes:</b> Pearson syndrome		Include among metabolic diseases (mitochondrial).
<b>Excludes:</b> Onycho-tricho-dysplasia - neutropenia		Include in dermatology.
<b>Severe recurrent infections with present neutrophils</b>	<b>D71</b>	
Neutrophil immunodeficiency syndrome		
<i>Rac 2 deficiency</i>		

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<b>ICD11 table draft</b>	<b>Corresponding ICD10 code</b>	<b>Comments</b>
Leukocyte adhesion deficiency Leukocyte adhesion deficiency, type I Leukocyte adhesion deficiency, type II Leukocyte adhesion deficiency, type III		
Myeloperoxidase deficiency <b>Excludes:</b> Papillon-Lefèvre syndrome <b>Excludes:</b> Glucose-6-phosphate-dehydrogenase deficiency [Favism]		Include in dermatology. Include in haematology.
<b>Granulomatous disease, chronic</b> Recurrent infection due to specific granule deficiency	<b>none</b>	
<b>Defects in the complement system</b> Immunodeficiency with a complement cascade protein anomaly Immunodeficiency with an early components of complements deficiency (C1, C4, C3 or C2) Immunodeficiency with a late components of complements deficiency (C5 to C9) Recurrent Neisseria infections due to factor D deficiency Immunodeficiency with factor I anomaly Immunodeficiency with factor H anomaly Immunodeficiency with properdin deficiency Immunodeficiency with CD59 deficiency <b>Excludes:</b> Atypical hemolytic uremic syndrome <b>Excludes:</b> Paroxysmal nocturnal hemoglobinuria <b>Excludes:</b> Hereditary angioedema [C1 esterase inhibitor [C1-INH] deficiency]	<b>D84.1</b>	
<b>Predisposition to invasive bacterial infections</b> Immunodeficiency due to interleukin-1 receptor-associated kinase-4 deficiency Pyogenic bacterial infections due to MyD88 deficiency.	<b>none</b>	Include in haematology. Include in haematology. Include among other hereditary angioedemas, the classification of which remains to be seen..
<b>Mendelian susceptibility to atypical mycobacteria</b>	<b>none</b>	
<b>Secondary agranulocytosis</b> Secondary agranulocytosis, toxic Secondary agranulocytosis, drug-induced	<b>D70</b>	
<b>Acquired neutropenia (immunologic neutropenia)</b> Felty syndrome Leukaemia, T-cell large granular lymphocyte Idiopathic neutropenia, adult form	<b>none</b>	
<b>Other specified disorder of innate immunity</b>	<b>none</b>	

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ICD11 table draft	Corresponding ICD10 code	Comments
<b>Diseases of thymus</b>	<b>E32</b>	
<i>Excludes:</i> aplasia or hypoplasia with immunodeficiency	D82.1	
<i>Excludes:</i> myasthenia gravis	G70.0	
<b>Persistent hyperplasia of thymus</b>	E32.0	
<b>Hypertrophy of thymus</b>		
<b>Abscess of thymus</b>	E32.1	
<b>Thymic tumor</b>	none	The whole group is also to be considered in oncology.
Thymic epithelial tumor		
Thymoma		
Thymic carcinoma		
Thymus malignant tumor		
Thymic endocrine tumor		
<b>Other diseases of thymus</b>	E32.8	
Good syndrome		
<b>Other specified disease of thymus</b>	E32.9	
<b>Other disorders involving the immune system, not elsewhere classified</b>	<b>D89</b>	
<i>Excludes:</i> monoclonal gammopathy	D47.2	Include in malignant haemopathies.
<i>Excludes:</i> transplant failure and rejection	T86.-	
Graft-versus-host disease		Include in complications of surgical and medical care.
Anti-HLA hyperimmunization		Include in complications of surgical and medical care.
<i>Excludes:</i> Twin to twin transfusion syndrome		Include among perinatal diseases.
<b>Benign hypergammaglobulinaemic purpura</b>	D89.0	
<b>Simple cryoglobulinaemia</b>	D89.1	
<i>Monoclonal cryoglobulinaemia</i>		
<i>Excludes:</i> Mixed cryoglobulinaemia		Include among vasculites.
<b>Hypergammaglobulinaemia, unspecified</b>	D89.2	
<b>Other specified disorders involving the immune mechanism, not elsewhere classified</b>	D89.8	