

ESID Registry – Working Definitions for Clinical Diagnosis of PID



These criteria are only for patients with **no genetic diagnosis**.

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Disease	Contributors	Clinical criteria for a probable diagnosis (= clinical diagnosis)	Suggestions for alternative diagnosis (i.e. if these criteria are not completely fulfilled)
Agammaglobulinaemia	Annarosa Soresina, Nizar Mahlaoui, Hans Ochs, Isabella Quinti	Fewer than 2% circulating B cells (CD19 and CD20), preferably in two separate determinations and a normal number of T cells (CD3, CD4 and CD8) AND serum IgG levels below: -200 mg/dl in infants aged < 12 months -500 mg/dl in children aged > 12 months OR normal IgG levels with IgA and IgM below 2SD AND onset of recurrent infections before 5 years of age OR positive maternal family history of agammaglobulinaemia	For patients with normal B cells and agammaglobulinaemia, please consider “ Unclassified antibody deficiency ”.
Asplenia syndrome (Ivemark syndrome)	Nizar Mahlaoui David Edgar Stephan Ehl, Capucine Picard, Jean-Laurent Casanova	Asplenia or hyposplenia AND Documentation of Howell-Jolly bodies on blood smears AND radiological findings evidencing asplenia (US, CT scan, scintigraphy) AND heterotaxia defects (dextrocardia, situs inversus, other...) or other heart and great vessel defects	
Ataxia telangiectasia (ATM)	Nizar Mahlaoui David Edgar Stephan Ehl, Richard Gatti, Dominique Stoppa-Lyonnet	Ataxia AND at least two of the following : <ul style="list-style-type: none"> • Oculocutaneous telangiectasia • Elevated alphafetoprotein (tenfold the upper limit of normal) • Lymphocyte A-T caryotype (translocation 7;14) • Cerebellum hypoplasia on MRI 	
Autoimmune lymphoproliferative syndrome (ALPS)	David Edgar, Stephan Ehl, Frederic Rieux-Laucat and Benedicte Neven	At least one of the following: <ul style="list-style-type: none"> • splenomegaly • lymphadenopathy (>3 nodes, >3 months, non-infectious, non-malignant) • autoimmune cytopenia (>= 2 lineages) • history of lymphoma • affected family member AND at least one of the following: <ul style="list-style-type: none"> • TCRab+CD3+CD4-CD8- of CD3+ T cells>6% • elevated biomarkers (at least 2 of the following): <ul style="list-style-type: none"> • sFASL > 200pg/ml • Vitamin B12 > 1500ng/L • IL-10 > 20pg/ml • impaired FAS mediated apoptosis 	For patients with lymphoproliferation and/or autoimmunity who do not fulfil these criteria, please consider the following diagnoses: <ul style="list-style-type: none"> • CVID • Unclassified combined immunodeficiencies • Unclassified disorders of immune dysregulation

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CSR defects and HIGM syndromes	Stephan Ehl, Anne Durandy, Teresa Espanol	<p>At least one of the following:</p> <ul style="list-style-type: none"> • increased susceptibility to infections (recurrent and/or opportunistic, including cryptosporidium) • immune dysregulation (autoimmunity, lymphoproliferation, sclerosing cholangitis) • cytopenia (neutropenia or autoimmune) • malignancy (lymphoma) • affected family member <p>AND marked decrease of IgG (measured at least twice) AND normal or elevated IgM (measured at least twice) AND defined causes of hypogammaglobulinemia have been excluded AND no evidence of profound T-cell deficiency, defined as 2/3 of the following (mo=month, y=year of life):</p> <ul style="list-style-type: none"> • CD4 numbers/microliter: 0-6mo <1000, 6mo-1y <800, 1-2y <500, 2-6y <300, 6-12y <250, >12y <200 • % naive CD4: 0-2y <30%, 2-6y <25%, 6-16y <20%, >16y 10% • T cell proliferation absent <p>AND no evidence of Ataxia telangiectasia (cafe-au lait spots, ataxia, telangiectasia, raised AFP)</p>	
Chediak Higashi syndrome (CHS)	Nizar Mahlaoui, David Edgar, Stephan Ehl, Genevieve de Saint Basile, Despina Moshous	<p>At least one of:</p> <ul style="list-style-type: none"> • recurrent bacterial infections • episode of hemophagocytic lymphohistiocytosis (HLH) • Neutropenia • reduced lymphocyte degranulation/cytotoxicity • affected family member <p>AND one of:</p> <ul style="list-style-type: none"> • Typical hair shaft abnormalities • Presence of intracytoplasmic typical giant granules on blood or bone marrow smears 	Immunodeficiency with partial albinism

Disease	Contributors	Clinical criteria for a probable diagnosis (= clinical diagnosis)	Suggestions for alternative diagnosis (i.e. if these criteria are not completely fulfilled)
Chronic granulomatous disease (CGD)	Maria Kanariou, Reinhard Seger	<p>At least one of the following:</p> <ul style="list-style-type: none"> • deep seated infection due to bacteria and/or fungi (abscesses, osteomyelitis, lymphadenitis) • recurrent pneumonia • lymphadenopathy and/or hepatomegaly and/or splenomegaly • obstructing/diffuse granulomata (gastrointestinal or urogenital tract) • chronic inflammatory manifestations (colitis, liver abscess and fistula formation) • failure to thrive • affected family member <p>AND absent/significantly decreased respiratory burst (NBT or DHR, measured at least twice)</p>	
Combined immunodeficiency (CID)	Stephan Ehl, Maria Kanariou, Alain Fischer	<p>At least one of:</p> <ul style="list-style-type: none"> • at least one severe infection (requiring hospitalization) • one manifestation of immune dysregulation (autoimmunity, IBD, severe eczema, lymphoproliferation, granuloma) • malignancy • affected family member <p>AND 2 of 4 T cell criteria fulfilled:</p> <ul style="list-style-type: none"> • reduced CD3 or CD4 or CD8 T cells (using age-related reference values) • reduced naive CD4 and/or CD8 T cells • elevated g/d T cells • reduced proliferation to mitogen or TCR stimulation <p>AND HIV excluded</p> <p>AND exclusion of clinical diagnosis associated with CID (e.g. defined syndromic diseases, DKC, AT, CHH)</p>	

Disease	Contributors	Clinical criteria for a probable diagnosis (= clinical diagnosis)	Suggestions for alternative diagnosis (i.e. if these criteria are not completely fulfilled)
Common variable immunodeficiency disorders (CVID)	Vojtech Thon, Natalia Martinez, Maria Kanariou, Klaus Warnatz, Isabella Quinti, Helen Chapel	<p>At least one of the following:</p> <ul style="list-style-type: none"> • increased susceptibility to infection • autoimmune manifestations • granulomatous disease • unexplained polyclonal lymphoproliferation • affected family member with antibody deficiency <p>AND marked decrease of IgG and marked decrease of IgA with or without low IgM levels (measured at least twice; <2SD of the normal levels for their age);</p> <p>AND at least one of the following:</p> <ul style="list-style-type: none"> • poor antibody response to vaccines (and/or absent isohaemagglutinins); i.e. absence of protective levels despite vaccination where defined • low switched memory B cells (<70% of age-related normal value) <p>AND secondary causes of hypogammaglobulinaemia have been excluded (see separate list)</p> <p>AND diagnosis is established after the 4th year of life (but symptoms may be present before)</p> <p>AND no evidence of profound T-cell deficiency, defined as 2 out of the following (y=year of life):</p> <ul style="list-style-type: none"> • CD4 numbers/microliter: 2-6y <300, 6-12y <250, >12y <200 • % naive CD4: 2-6y <25%, 6-16y <20%, >16y <10% • T cell proliferation absent 	<p>For patients <4 years old or patients with incomplete criteria please consider “Unclassified antibody deficiency”.</p> <p>For patients with evidence of profound T-cell deficiency, please consider Unclassified combined immunodeficiencies.</p>
Congenital neutropenia	Nizar Mahlaoui, Jean Donadieu	<p>Neutropenia below 0.5 g/L measured on at least 3 occasions</p> <p>OR Neutropenia below 1 g/L measured on at least 3 occasions with at least one of the following:</p> <ul style="list-style-type: none"> • deep seated infection due to bacteria and/or fungi • recurrent pneumonia • buccal and/or genital aphthous lesions or ulcerations • omphalitis • affected family member <p>AND exclusion of secondary causes of neutropenia</p>	<p>For other patients with chronic neutropenia, please consider Unclassified phagocytic disorders.</p>
Cyclic neutropenia	Nizar Mahlaoui, David Edgar, Stephan Ehl, Jean Donadieu	<p>Cyclic fluctuation of Neutrophil counts (every 16 to 28 days)</p> <p>During these neutropenic episodes, symptoms are at least one of the following:</p> <ul style="list-style-type: none"> • Increased susceptibility to infections • Oral apthae • Abdominal pain episodes 	

Disease	Contributors	Clinical criteria for a probable diagnosis (= clinical diagnosis)	Suggestions for alternative diagnosis (i.e. if these criteria are not completely fulfilled)
Deficiency of specific IgG (Specific antibody deficiency - SPAD)	Nizar Mahlaoui David Edgar, Stephan Ehl, Helen Chapel, Isabella Quinti, Esther de Vries	Infections (recurrent or severe bacterial) AND normal serum/plasma IgG, A and M and IgG subclass levels AND Profound alteration of the antibody responses to S. pneumonia pneumonia (or other polysaccharide vaccine) either after documented invasive infection or after test immunization. AND Exclusion of T cell defect	Unclassified antibody deficiencies
DiGeorge syndrome	Nizar Mahlaoui David Edgar Stephan Ehl	Documented microdeletion 22q11 AND signs of immunodeficiency (i.e. infections and/or immune dysregulation)	
Dyskeratosis congenita	Nizar Mahlaoui David Edgar Stephan Ehl, Inderjeet Dokal	At least two of the following: <ul style="list-style-type: none"> • Skin pigmentation abnormalities • Nail dystrophy • Mucosal leucoplakia • Bone marrow failure AND Very short telomeres	
Familial hemophagocytic lymphohistiocytosis syndromes (FHLH)	Stephan Ehl, Genevieve de Saint Basile, Gritta Janka	At least one of the following: <ul style="list-style-type: none"> • at least 1 episode of HLH (at least 5/8 criteria as defined by the Histiocyte Society) • affected family member AND at least one of the following: <ul style="list-style-type: none"> • recurrent disease (>4 weeks after initiating treatment for first episode) • persistent disease (no full remission can be achieved) • partial albinism • absent or significantly decreased Perforin expression in flow cytometry • at least one assay with absent degranulation (NK or CTL) or two assays with reduced degranulation • at least 2 assays with absent NK cell cytotoxicity 	For patients with incomplete criteria, please consider Unclassified disorders of immune dysregulation.

Disease	Contributors	Clinical criteria for a probable diagnosis (= clinical diagnosis)	Suggestions for alternative diagnosis (i.e. if these criteria are not completely fulfilled)
FOXP3 deficiency (IPEX)	Nizar Mahlaoui David Edgar Stephan Ehl, Hans Ochs, Benedicte Neven	At least one of <ul style="list-style-type: none"> • Severe and protracted enteropathy with villous atrophy in a male infant • Severe, often multiple endocrinopathies AND Exclusion of hypogammaglobulinaemia AND at least one of the following: <ul style="list-style-type: none"> • Low or absent Foxp3 expression by CD4+CD25+ on flow analysis • No overt T cell defect (proliferations are normal) • Elevated IgA and IgE levels • Normal CD25 expression 	Combined immunodeficiency
Glycogen storage disease type 1b (GS1b)	Nizar Mahlaoui David Edgar Stephan Ehl, Jean Donadieu	Recurrent infections AND Fasting intolerance AND Hypoglycaemic attacks AND Hyperlactacidemia AND Glycogen accumulation in the liver AND colitis mimicking Crohn's disease AND one of: <ul style="list-style-type: none"> • neutrophil function alterations • neutropenia 	
Griscelli syndrome type 2	Nizar Mahlaoui, David Edgar Stephan Ehl, Genevieve de Saint Basile, Despina Moshous	At least one of the following: <ul style="list-style-type: none"> • episode of hemophagocytic lymphohistiocytosis (HLH) • reduced lymphocyte degranulation/cytotoxicity • affected family member AND Typical hair shaft abnormalities AND Absence of giant granules on blood smear	Immunodeficiency with partial albinism

Disease	Contributors	Clinical criteria for a probable diagnosis (= clinical diagnosis)	Suggestions for alternative diagnosis (i.e. if these criteria are not completely fulfilled)
HLA class II deficiency (MHC2)	Nizar Mahlaoui, David Edgar Stephan Ehl, Capucine Picard, Amos Etzioni	<p>One of the following:</p> <ul style="list-style-type: none"> • Recurrent and/or opportunistic infections • Autoimmunity <p>AND one of the following:</p> <ul style="list-style-type: none"> • Hypogammaglobulinaemia • Lymphopenia • Low T-CD4 count • absence of Ab production in response to antigens or absence of T cell proliferations in response to antigens <p>AND Reduced or absent HLA DR expression at the surface of B cells and/or monocytes</p>	Combined immunodeficiency
Hoyeraal-Hreidarsson syndrome	Nizar Mahlaoui David Edgar Stephan Ehl, Inderjeet Dokal	<p>At least four of the following criteria:</p> <ul style="list-style-type: none"> • Microcephaly and/or neurocognitive impairment • Cerebellar hypoplasia • Bone marrow failure • Immune deficiency including B cell lymphopenia • Severe enteropathy • Severe failure to thrive <p>This can be substantiated by undertaking telomere length analysis (usually very short)</p>	
Hyper IgE syndrome (HIES)	Beata Wolska, David Edgar, Bodo Grimbacher, Steven Holland	<p>IgE > 10 times the norm for age</p> <p>AND pathologic susceptibility to infectious diseases</p> <p>AND no evidence of T-cell deficiency (low T cell numbers, low naive T cells, reduced proliferation)</p> <p>AND no evidence of B cell deficiency (low B cell numbers, hypogammaglobulinaemia)</p>	<ul style="list-style-type: none"> • For patients with evidence of T-cell deficiency, please consider: Unclassified combined immunodeficiencies. • For patients with evidence of B-cell deficiency, please consider Unclassified antibody deficiency. • For other patients, please consider Unclassified immunodeficiencies.

Disease	Contributors	Clinical criteria for a probable diagnosis (= clinical diagnosis)	Suggestions for alternative diagnosis (i.e. if these criteria are not completely fulfilled)
IgA with IgG subclass deficiency	Nizar Mahlaoui David Edgar, Stephan Ehl, Helen Chapel, Isabella Quinti, Esther de Vries	Infections (recurrent or severe bacterial) AND Undetectable serum/plasma IgA level (with normal/lowish IgG and IgM levels) AND Low levels in one or more IgG subclass (documented twice)	Unclassified antibody deficiencies
IPEX-like disease	Nizar Mahlaoui David Edgar Stephan Ehl, Hans Ochs, Benedicte Neven	At least one of <ul style="list-style-type: none"> • Severe and protracted enteropathy with villous atrophy in a male infant • Severe, often multiple endocrinopathies AND Exclusion of hypogammaglobulinaemia AND at least one of the following: <ul style="list-style-type: none"> • Normal Foxp3 expression by CD4+CD25+ on flow analysis • No overt T cell defect (proliferations are normal) • Elevated IgA and IgE levels 	Combined immunodeficiency
Isolated IgG subclass deficiency	Nizar Mahlaoui David Edgar, Stephan Ehl, Helen Chapel, Isabella Quinti, Esther de Vries	Infections (recurrent or severe bacterial) AND normal IgG, A and M serum/plasma levels AND Low levels in one or more IgG subclass (documented twice) AND Exclusion of T cell defect	Unclassified antibody deficiencies
Isolated congenital asplenia	Nizar Mahlaoui David Edgar Stephan Ehl, Capucine Picard, Jean-Laurent Casanova	Asplenia or hyposplenia AND Documentation of Howell-Jolly bodies on blood smears AND radiological findings evidencing asplenia (US, CT scan, scintigraphy) AND exclusion of any over developmental defect such as heterotaxia (dextrocardia, situs inversus, other...) or other heart and great vessel defects	

Disease	Contributors	Clinical criteria for a probable diagnosis (= clinical diagnosis)	Suggestions for alternative diagnosis (i.e. if these criteria are not completely fulfilled)
Selective IgM deficiency	Nizar Mahlaoui David Edgar, Stephan Ehl, Helen Chapel, Isabella Quinti, Esther de Vries	Infections (either invasive or recurrent, usually bacterial) AND Low IgM serum/plasma level (with normal IgG and IgG subclasses and IgA plasma level)	Unclassified antibody deficiencies
Omenn syndrome	Nizar Mahlaoui, Annarosa Soresina, Anna Villa, Alain Fischer	Desquamating Erythroderma in the first year of life AND one of the following: <ul style="list-style-type: none"> • lymphoproliferation • failure to thrive • chronic diarrhoea • recurrent pneumonia AND eosinophilia or elevated IgE AND T-cell deficiency (low naïve cells, reduced proliferation, oligoclonality) AND maternal engraftment excluded AND HIV excluded	For other patients with severe erythroderma, please consider: <ul style="list-style-type: none"> • SCID • IPEX • Unclassified disorders of immune dysregulation • Unclassified defects in innate immunity.
Schimke disease	Nizar Mahlaoui David Edgar Stephan Ehl	Predominantly T cell defects (low T cell counts, low T cell proliferations) AND osseous dysplasia (metaphyseal usually) AND kidney dysfunction	

Disease	Contributors	Clinical criteria for a probable diagnosis (= clinical diagnosis)	Suggestions for alternative diagnosis (i.e. if these criteria are not completely fulfilled)
Selective IgA deficiency	Vojtech Thon, Natalia Martinez, Maria Kanariou, Klaus Warnatz, Isabella Quinti	<p>At least one of the following:</p> <ul style="list-style-type: none"> • increased susceptibility to infection • autoimmune manifestations • affected family member <p>AND diagnosis after 4th year of life AND undetectable serum IgA (when measured with nephelometry less than 0.07 g/L) but normal serum IgG and IgM (measured at least twice) AND secondary causes of hypogammaglobulinaemia have been excluded. AND normal IgG antibody response to vaccination</p>	<ul style="list-style-type: none"> • For patients with abnormal vaccine responses, please consider Deficiency of specific IgG (SPAD). • For other patients, please consider Unclassified antibody deficiency.
Severe combined immunodeficiency (SCID)	Stephan Ehl, Alain Fischer	<p>At least one of the following:</p> <ul style="list-style-type: none"> • invasive bacterial, viral or fungal/opportunistic infection • persistent diarrhoea and failure to thrive • affected family member <p>AND manifestation in the first year of life AND HIV excluded AND 2 of 4 T cell criteria fulfilled :</p> <ul style="list-style-type: none"> • low or absent CD3 or CD4 or CD8 T cells • reduced naive CD4 and/or CD8 T cells • elevated g/d T cells • reduced or absent proliferation to mitogen or TCR stimulation 	For other (e.g. older) patients with T-cell deficiency, consider Unclassified combined IDs .
Thymoma with immunodeficiency	David Edgar, Helen Chapel	Presence of thymoma AND reduced serum IgG (< 2SD below the mean reference for age)	
Transient hypogammaglobulinaemia of infancy	David Edgar, Maria Kanariou, Esther de Vries	IgG below age-related normal value detected in the first three years of life (measured at least twice) AND defined causes of hypogammaglobulinaemia have been excluded AND spontaneous resolution approx. after the 4th birthday NB: Patients will initially be registered as Unclassified antibody deficiency , in the registry and moved to THI , if there is spontaneous resolution before age 4.	

Disease	Contributors	Clinical criteria for a probable diagnosis (= clinical diagnosis)	Suggestions for alternative diagnosis (i.e. if these criteria are not completely fulfilled)
Wiskott-Aldrich syndrome (XLT/WAS)	Annarosa Soresina, Natalia Martinez, Michael Albert, Adrian Thrasher	<p>At least one of the following:</p> <ul style="list-style-type: none"> • eczema • recurrent bacterial or viral infections • autoimmune diseases (incl. vasculitis) • malignancy • reduced WASP expression in a fresh blood sample • abnormal antibody response to polysaccharide antigens and/or low isohaemagglutinins • positive maternal family history of XLT/WAS <p>AND male patient with thrombocytopenia (less than 100,000 platelets/mm³) (measured at least twice)</p> <p>AND small platelets (platelet volume < 7,5 fl)</p>	
Unclassified antibody deficiency	Esther de Vries, Nizar Mahlaoui, David Edgar, Isabella Quinti, Helen Chapel	<p>At least 1 of the following 4:</p> <ul style="list-style-type: none"> • Recurrent or severe bacterial infections • Autoimmune phenomena (especially cytopenias) • Polyclonal lymphoproliferation • Affected family member <p>AND at least one of the following:</p> <ul style="list-style-type: none"> • marked decrease of at least one of total IgG, IgG1, IgG2, IgG3, IgA or IgM levels • failure of IgG antibody response(s) to vaccines <p>AND secondary causes of hypogammaglobulinaemia have been excluded (infection, protein loss, medication, malignancy)</p> <p>AND no clinical signs of T-cell related disease</p> <p>AND does not fit any of the other working definitions (excluding 'unclassified immunodeficiencies')</p>	
Unclassified phagocytic disorders	Nizar Mahlaoui, Capucine Picard, Jacinta Bustamante	<p>At least one of the following:</p> <ul style="list-style-type: none"> • deep seated infection due to bacteria and/or fungi • recurrent severe pneumonia • buccal and/or genital aphthous lesions or ulcerations • omphalitis • chronic inflammatory manifestations (e.g. colitis, fistula formation) • affected family member • BCGitis or BCGosis <p>AND normal to subnormal respiratory burst (NBT or DHR, assessed at least twice)</p>	

Disease	Contributors	Clinical criteria for a probable diagnosis (= clinical diagnosis)	Suggestions for alternative diagnosis (i.e. if these criteria are not completely fulfilled)
Unclassified disorders of immune dysregulation	Stephan Ehl, Maria Kanariou	<p>At least one of the following:</p> <ul style="list-style-type: none"> • autoimmune manifestations • lymphoproliferation • severe eczema • inflammatory bowel disease • granuloma • vasculitis • HLH-like disease <p>AND at least one numeric or functional abnormal finding upon immunological investigation</p> <p>AND no evidence of profound T-cell deficiency, defined as 2 out of the following (y=year of life):</p> <ul style="list-style-type: none"> • CD4 numbers/microliter: 0-6mo <1000, 6mo-1y <800, 1-2y <500, 2-6y <300, 6-12y <250, >12y <200 • % naive CD4: 0-2y <30%, 2-6y <25%, 6-16y <20%, >16y 10% • T cell proliferation absent <p>AND no evidence of B-cell deficiency (low B cell numbers, hypogammaglobulinaemia)</p>	<ul style="list-style-type: none"> • For patients with evidence of profound T-cell deficiency, please register these as Unclassified combined immunodeficiencies. • For patients with evidence of B-cell deficiency, please register as Unclassified antibody deficiency.
Unclassified defects in innate immunity	Nizar Mahlaoui, Maria Kanariou, Capucine Picard, Jacinta Bustamante	<p>At least one of the following:</p> <ul style="list-style-type: none"> • onset of disease before 5 y of age • pyogenic bacterial infections • unusual infections and/or atypical clinical course <p>AND the dominant abnormal immunological finding concerns the innate immune system (excluding defects in phagocyte number or function) i.e. NF-κB-dependent TLR and IL-1R immunity</p> <p>AND functional spleen (no Howell-Jolly bodies on blood smears)</p>	For patients with evidence of profound defect of phagocytes, please consider Unclassified phagocytic disorders .
Unclassified complement deficiencies	Annarosa Soresina	<p>At least one of the following:</p> <ul style="list-style-type: none"> • one episode of bacteraemia, meningitis or systemic Neisserial infection • recurrent respiratory infections <p>AND persistent defect of CH50 or AP50 (in three determinations in 6 months)</p> <p>AND no evidence of other conventional immunological defects</p>	

Disease	Contributors	Clinical criteria for a probable diagnosis (= clinical diagnosis)	Suggestions for alternative diagnosis (i.e. if these criteria are not completely fulfilled)
Unclassified autoinflammatory diseases	David Edgar, Beata Wolska, Helen Lachmann	<p>Recurrent fever (temperature >38 degrees Celsius) having occurred on at least 6 occasions.</p> <p>AND exclusion of other known infective / inflammatory autoimmune disorders</p> <p>AND documented evidence of increased inflammatory markers (ESR/CRP)</p> <p>AND age of onset under 40 years</p> <p>AND predominantly but not exclusively systemic symptoms</p>	
Unclassified syndromic immunodeficiencies	Stephan Ehl	<p>At least one of the following:</p> <ul style="list-style-type: none"> • dysmorphic features such as short stature, facial abnormalities, microcephaly, skeletal abnormalities • other organ manifestations such as albinism, hair or tooth abnormalities, heart or kidney defects, hearing abnormalities, primary neurodevelopmental delay, seizures <p>AND at least one numeric or functional abnormal finding upon immunological investigation</p> <p>AND exclusion of secondary causes for immunological abnormalities (infection, malignancy)</p>	
Unclassified immunodeficiencies	Stephan Ehl, Alain Fischer	<p>At least one of the following:</p> <ul style="list-style-type: none"> • at least one major infection • abnormal course or frequency of minor infections • at least one manifestation of immune dysregulation • failure to thrive • affected family member <p>AND at least one numeric or functional abnormal finding upon immunological investigation</p> <p>AND exclusion of secondary causes for immunological abnormalities (infection, protein loss, medication, malignancy)</p> <p>AND does not fit any of the other working definitions (including 'unclassified syndromic immunodeficiencies')</p>	<p>For patients with syndromic manifestations, consider Unclassified syndromic IDs.</p>