

Primary Immunodeficiencies [PID]

Driving Diagnosis for Optimal Care in Europe

Primary Immunodeficiencies are genetic defects in the immune system that cause increased susceptibility to a wide range of infections, affecting the skin, the ears, the lungs, the intestines and other parts of the body. These infections are often chronic, persistent, recurring, debilitating, and in some cases, fatal.



We invite you to endorse and sign the following **Primary Immunodeficiencies (PID) Call to Action**, which explains the steps that EU Member State governments should take to understand, appropriately diagnose and manage PID.

CALL to ACTION

The PID Community calls upon EU Member States to take heed of these devastating and under-diagnosed diseases by developing national rare disease plans that include PID and ensuring that both new and existing national rare disease plans cover PID and incorporate the following components:

1 Raising Awareness on Primary Immunodeficiencies

- Encourage and support EU Member States governments to implement targeted campaigns to increase recognition of PID among parents, school teachers, day care centre employees, physicians, researchers and nurses, with the objective of increasing understanding of the disease, knowledge of the '10 Warning Signs' and available testing methods and treatments.

2 Education of Health Professionals and Expertise Exchange

- Work together with medical specialists organisations (e.g. ESI, EFIS, INGID, UMES, etc) and academia to encourage and support EU Member States to:
 - > provide standards for basic and applied immunology training, with emphasis on PID, in the education programmes for general practitioners and nurses;
 - > integrate basic and applied immunology teaching, particularly alongside immunisation, into specialised programmes for training fellows in general paediatric internal medicine, rheumatology, respiratory medicine, and infectious diseases;
 - > develop cross country initiatives to allow the exchange of expert experience and education, including capacity to network and funding of visits of immunology centres representatives in other countries.

3 Early Diagnosis and Screening

- Encourage and support EU Member States to develop clinical protocols to reliably identify all forms of PID;
- Encourage and support EU Member States to promote the development and wide-spread use of simple diagnostic tests for PID at local level;
- Promote the creation of European guidance for recognition of symptomatic patients and ensure appropriate immunologic and genetic laboratory tests are available at national level via centres of excellence;
- Promote transnational research into the feasibility of screening programmes to ensure early detection.

4 Gathering Knowledge and Data

- Provide funding under the various European programmes to conduct epidemiological studies to assess: prevalence and incidence of PID in the population; impact of PID on public health; impact of PID on health care costs;
- Encourage the creation of and input into international registries which will enable future diagnostic processes by identifying: pattern of clinical presentation of these diseases; natural history of the various PID (morbidity, mortality, complications); relationships between clinical disease patterns and genetic backgrounds;
- Encourage every EU Member State to have a national PID patient registry;
- Encourage transnational cooperative research and remove the administrative obstacles to multinational clinical trials;
- Establish EU Centres of Reference to promote best practice in terms of disease classification, treatment outcome measures, assessment of cost of treatments for an integrated approach to PID recognition and treatment throughout Europe.

5 Comprehensive and Adequate Treatment

- Encourage EU Member States to ensure access to treatment for people with PID as it has been shown to prevent and improve chronic disease, improve social well-being and reduce the burden of the disease;
- Encourage EU Member States to ensure that safe immunoglobulin treatments are available to all patients who require antibody replacement;
- Encourage EU Member States to recognise the social needs of PID patients and their family and facilitate their access to adequate support services;
- Ensure the adequate and high quality supply of human plasma;
- Ensure the reimbursement of orphan drugs according to their medical efficacy for the patient and not according to the price of the product.

These Warning Signs were developed by the JMF Medical Advisory Board

10 Warning Signs of Primary Immunodeficiency

Primary Immunodeficiency (PI) causes children and adults to have infections that come back frequently or are unusually hard to cure. 1-500 persons are affected by one of the known Primary Immunodeficiencies. If you or someone you know is affected by two or more of the following Warning Signs, speak to a physician about the possible presence of an underlying Primary Immunodeficiency.

- 1 Two or more new ear infections within 1 year.
- 2 Two or more new sinus infections within 1 year, in the absence of allergy.
- 3 One pneumonia per year for more than 1 year.
- 4 Chronic diarrhea with weight loss.
- 5 Recurrent viral infections (colds, herpes, warts, condyloma).
- 6 Recurrent need for intravenous antibiotics to clear infections.
- 7 Recurrent, deep abscesses of the skin or internal organs.
- 8 Persistent thrush or fungal infection on skin or elsewhere.
- 9 Infection with normally harmless tuberculosis-like bacteria.
- 10 A family history of PI.

4 Stages of Testing for Primary Immunodeficiency

- 1 History and physical examination, height and weight
 - CBC and differential
 - Quantitative Immunoglobulin levels IgG, IgM, IgA (related to age)
- 2 Specific antibody responses (tetanus, diphtheria)
 - Response to pneumococcal vaccine (pre/post) (for ages 3 and up)
 - IgG subclass analysis
- 3 Candida and Tetanus skin tests
 - Lymphocyte surface markers CD3/CD4/CD8/CD19/CD16/CD56
 - Mononuclear lymphocyte proliferation studies (using mitogen and antigen stimulation)
 - Neutrophil oxidation burst (if indicated)
- 4 Complement screening CH50, C3, C4
 - Enzyme measurements (adenosine deaminase, purine nucleoside phosphorylase)
 - Phagocyte studies (surface glycoproteins, mobility, phagocytosis)
 - NK cytotoxicity studies
 - Further complement studies AH50
 - Neo antigen to test antibody production
 - Other surface/cytoplasmic molecules
 - Cytokine receptor studies
 - Family/genetic studies

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- 1 Four or more new ear infections within 1 year.
- 2 Two or more serious sinus infections within 1 year.
- 3 Two or more months on antibiotics with little effect.
- 4 Two or more pneumonias within 1 year.
- 5 Failure of an infant to gain weight or grow normally.
- 6 Recurrent, deep skin or organ abscesses.
- 7 Persistent thrush in mouth or fungal infection on skin.
- 8 Need for intravenous antibiotics to clear infections.
- 9 Two or more deep-seated infections including septicemia.
- 10 A family history of PI.