



Innovative Medicines Initiative

# IMI indicative Call topic

## Developing an aetiological based taxonomy of human disease

**All information regarding future IMI Call topics is indicative and subject to change. Final information about the IMI's future Calls will be communicated after approval by the IMI Governing Board.**

### Background

Current classification of disease is built upon a hierarchical structure with subdivisions of morbid entities assigned based on consensus criteria. The classification is grouped into:

- epidemic diseases;
- constitutional or general diseases;
- local diseases arranged by anatomical site;
- developmental diseases;
- injuries.

The origin of the current classification of diseases dates back to William Farr's work in 1855. A major part of the criteria are based on anatomical foci of the disease, symptomatological and epidemic patterns of the disease and very little, if any, is based on molecular mechanisms which are likely to more closely reflect the effects of medicines.

Major issues with the current taxonomy are that the criteria are based on effects of the disease process rather than aetiological mechanism. As a result of this, several disease entities overlap, the identification of specific and objective diagnostic criteria is hampered, and consequently, the development of more molecularly directed and thereby more effective medicines is delayed. The lack of a clear relationship between molecular pathogenesis and disease classification means some patients are receiving therapies with little chance of receiving benefit and other patients are being denied access to potentially beneficial therapies.

A taxonomy based on aetiological mechanisms defined by molecular evidence will in general reduce the complexity and cost of drug development and increase success rates of drug development (make the drug discovery and development process more efficient to bring better medicines faster to patients).

### Need for public-private collaborative research

The magnitude of this issue of reclassifying disorders is so large that it can only be addressed by a major public-private-partnership involving many partners that are primarily involved in understanding molecular mechanisms of disease, and biopharmaceutical companies which endorse the approach and have a complementing research. The desired areas of expertise include -omics technologies, genetics, informatics, epidemiology, and modelling.

### Overall objectives

To evaluate the scientific status for, and initiate a new taxonomical approach to classification of human diseases which is based on objective, aetiologicaly relevant molecular evidence related to a syndrome (a disease), rather than based on anatomical foci, and/or symptomatological and epidemic patterns.

- The first step will be to select a few disorders (SLE - Systemic Lupus Erythematosus) and related connective tissue diseases; RA (Rheumatoid Arthritis); neurodegeneration with a focus on dementias and Parkinson's disease (PD); and respiratory disease with a focus on COPD (Chronic Obstructive Pulmonary Disease), which all are heterogeneous according to ICD-10 diagnostic criteria, and evaluate the use of molecular criteria to stratify associated syndromes/diseases into more homogenous segments based on underlying aetiological mechanism.
- The next step will be to widen the scope to include related immunological and neuroscience disorders. A reassessment may be needed to evaluate if this is feasible within the current project structure and plan.
- Thereafter, other disorders will be included.

A novel taxonomy of disease may require a multi-axial approach for example using mutations and polymorphisms within a genetic axis, gene expression data on a genomics axis, protein modifications and protein expression patterns on a proteome axis, protein interactions on a biological system axis and so forth. The approach will be driven by research as well as existing data review and analysis.

### **Expected key deliverables**

It is planned, within the five-year lifetime of the project, to propose a new aetiological based taxonomy of common immunological (and/or neurological) disorders or a subset thereof. This will provide the foundation for the taxonomy of other disorders. Considered disease areas are the following:

- SLE and related disorders;
- RA;
- dementia and PD,
- respiratory disease with a focus on COPD.

Other deliverables include a rationale for more specific diagnostic tools, and a basis for a more efficient and improved drug development process.