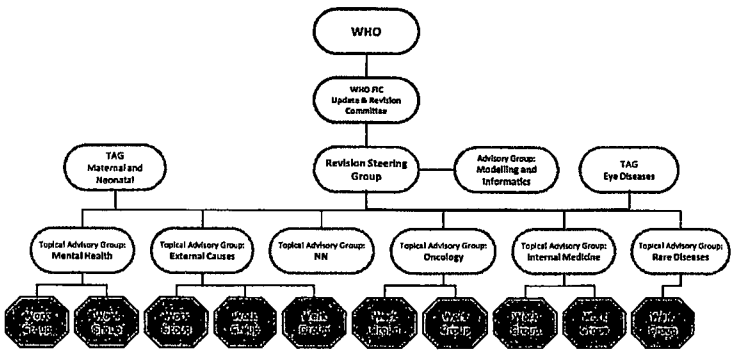
1 Introduction

This manual includes elements of the overall project plan that are of prime relevance to Topic Advisory Groups and Working Groups. Terms, roles and processes for work of groups contributing to revision of ICD are explained. The document includes a description of the main tasks for groups, Terms of reference of Working Groups, and of the Revision Steering Group, a brief overview of the organization structure and a list of procedural steps that ensure coordination among different groups. Terms of Reference, a Declaration of Conflict of Interest, and Terms and Conditions for participation will allow constructing ICD-11 in a transparent process and preventing conflicts in intellectual property and copyright.

The work for specified topics is organized through topic advisory groups (TAG). A TAG coordinates working groups that carry out the work that is described in the "tasks". The TAGs are coordinated by the Revision Steering Group, and chairs of TAGs are ex officio members of the RSG. All TAGs, Workgroups, and additional contributing specialists agree to comply with rules, regulations and workflows that are specified in the most recent version of the Revision project plan and Manual for TAG and working groups.

ICD-10 Revision Organization Structure



12 The tasks

Topic Advisory Groups will serve as the planning and coordinating advisory body for specific issues which are key topics in the update and revision process, namely Oncology, Mental Health, External Causes of Injury, Communicable Diseases, Non-communicable Diseases, Rare Diseases and others to be established.

The primary charge of each group will be to advise WHO in all steps leading to the revision of topic sections of ICD in line with the overall revision process. In particular:

- Advise on particular ***topic revision steps and establish workgroups and partners to involve*** - The TAGs will advise WHO on constitution of working groups to undertake generation of necessary evidence, to develop proposals for changes and to focus on specific issues as needed. Each TAG will (a) determine the number and content areas of the workgroups, (b) identify the members and chairs of the workgroups, (c) present an initial mandate to each workgroup, (d) establish procedures for the activities of the workgroups, and (e) facilitate cross-fertilization of ideas and reducing redundant efforts by making workgroups aware of one another's activities.
- Advise in ***developing various drafts of topic segments in line with the overall production timeline*** of ICD-11 TAGs will review initial recommendations of the workgroups and consolidate those to achieve consistency in proposals across groups and areas.
- Advise in ***developing protocols for and in implementing field trials*** - TAGs will also assist WHO in identifying appropriate representatives of various stakeholders and in establishing effective collaboration/consultative mechanisms.

Topic Advisory Groups (TAG) will lead the work in different fields of expertise. Such fields can be vertical, as cancers (oncology) or horizontal, as rare diseases that can be found in every chapter. The TAG will organize **workgroups** to deal with relevant subtopics, as necessary.

Ten rules will ensure consistent quality of work across all groups:

I.	**Definition of the diagnostic entity as a medical disease or disorder.**
II.	**Clustering of signs, symptoms, and operational characteristics.**
III.	**Link to underlying pathophysiology and genetic markers.**
IV.	**Clinical utility of the classification entity.**
V.	**Reliability of the use of the classification entity. .**
VI.	**Validity of the classification entity.**
VII.	**Separation of disease and disability elements**
VIII.	**Cultural elements that need to be attended.**
IX.	**Threshold considerations.**
X.	**Other nosological issues relevant to this entity**

Work Groups will serve as the key functioning unit for the review of evidence and generation of main proposals at a specific topic in the classification. For example, the TAG in the Mental Health Area will be responsible for the whole of chapter V and its linkages, whereas it may generate 5-10 working groups to carry out the systematic reviews on special sections of the chapter such as schizophrenias and psychosis; mood and anxiety disorders or topics such as children and youth, common brain disorders, etc.

The workgroups are asked to consider core issues that they will seek to address for each diagnostic entity in their content domain, and to develop a preliminary position on each issue based on their pre-existing knowledge of this domain. The initial position statement will effectively set the agenda for the workgroup and will define the range and scope of questions that the workgroup will consider.

The broad range of activities can be described by a set of tasks:

- TASK 1. Develop a preliminary position statement on each core diagnostic issue. Blocks of ICD may be a suitable entity.
- TASK 2. Review the empirical evidence
- TASK 3 Generate summary proposals on the revision platform for comment by other groups, RSG and the global community.
- TASK 4. Revised reports
- TASK 5. Field trials
- TASK 6. Final revisions and recommendations

12.1 TASK 1 Develop a preliminary position statement on each core diagnostic issue

The initial set of core diagnostic issues to be considered by each workgroup are listed in box I - these may be taken as an example by each workgroup to expand further on the key classification issues on the topic of interest.

I. **Definition of the diagnostic entity as a medical disease or disorder.** Given the key taxonomic guidelines and definitions each group should draw a line around the entity of interest, identifying its critical properties. How does the workgroup fundamentally view the full spectrum of disorders/diseases in this chapter/field in terms of their classification? Identify key criteria and level of evidence.

II. **Clustering of signs, symptoms, and operational characteristics.** Identify the features that are necessary and sufficient to define the disease/disorder, based on the common disease model of ICD.

III. **Link to underlying pathophysiology and genetic markers.** Identify the intra-individual markers that are associated with the disease/disorder, considering their biological plausibility, their measurement properties (e.g., specificity, predictive power), and their role in treatment response.

IV. **Clinical utility of the classification entity.** Consider the usefulness of the classification entity in diagnosis, predicting treatment response, course, and outcome.

V. **Reliability of the use of the classification entity.** Consider the stability of the classification entity over time and its consistency of detection across assessors and measurement instruments.

VI. **Validity of the classification entity.** Consider the associations of theoretically relevant variables with measures of the disorder and the support they provide for the validity of the diagnostic construct.

VII. **Separation of disease and disability elements.** Identify the features that signal the presence of the disease/disorder, defining the disease/disorder without reference to the distress, impairment, or other consequences that it produces. Suggestions to link to WHO ICF and operationalize specifically the criteria on disability and distress related rubrics.

VIII. **Cultural elements that need to be attended.** Consider variability in the presentation of the disease/disorder across cultures. Identify ways to achieve cross-cultural comparability and utility of diagnostic criteria rather than listing separate culture-bound syndromes or formulations.

IX. **Threshold considerations.** Identify the number and nature of diagnostic criteria that should be required to qualify for the classification entity. Consider the nature of the boundary separating the disease/disorder from normality, including evidence for the categorical/continuous distinction. Consider the classification entity boundaries with other classes, including challenges of differential diagnosis.

X. **Other nosological issues relevant to this entity** Identify any other aspects of the classification entity that the workgroup believes to be in need of evaluation, including potentially controversial aspects of the disorder that will need to be addressed. This list of additional issues may change as the evidence related to this disorder is reviewed.

12.1.1 Points for consideration

- Which elements are included in current ICD-10 (e.g. review by Block)
- Do specialty adaptations or national clinical modifications identify needs for further subdivisions?
- What do the usage statistics/frequencies show?
- Are certain categories unused across all use cases and countries?
- Are unspecific categories used extensively in certain use cases and countries?
- Would it be possible to mark codes or blocks for "minimal care", primary care, reimbursement, public health or research to be able to recombine or regroup codes in broad or detailed categories?
- do internationally agreed definitions of categories exist that could be used to define the corresponding category of ICD?

12.2 TASK 2. Review the empirical evidence

Workgroups will survey the available evidence for each diagnostic entity to address the ten diagnostic issues described above. Evidence will be reviewed using a three-tiered, iterative process that maximizes input from sources that are most readily accessible.

Review the published literature. A standardized system should be chosen to guide the compilation and coding of published results. This system will be selected by the Revision Steering Group and provided to co-chairs early in the update and revision process. Participants will also receive guidelines concerning the parameters to be used in the literature reviews (e.g., inclusion criteria, exclusion criteria, review, and reporting style). Workgroup coordinators will then carry out these reviews at collaborating sites throughout the world. Study managers based at WHO Headquarters will remain in constant contact with the workgroup coordinators and the workgroup co-chairs throughout the review process.

Targeted secondary analysis of existing data. If no published studies are available to answer a particular question identified by a workgroup, workgroup members will search for existing data that would address this question but that have not yet been analyzed or published. Workgroup co-chairs will seek appropriate data by (a) directly contacting researchers in the field who may have relevant data and (b) putting out an open call for data relevant to the question at hand. When researchers with relevant data are identified, the co-chairs will, at their discretion, arrange with these researchers to share or analyze their data or to collaborate with workgroup members on analyses to address the knowledge gap. Results of these analyses will be evaluated using the same standardized rules used to evaluate published results in the literature reviews. Informative results may be published in the online Classifications Journal or in books or articles to be published by WHO on the ICD update and revision process.

Collection and analysis of new data. When no data sets are available to address unanswered questions of the workgroups, new data need to be collected. Because time and resources for new data collection are limited, such efforts will likely be restricted to questions that are relatively circumscribed and that can be fruitfully addressed through basic descriptive studies. Workgroups will generate proposals for data collection to address unanswered questions through rapid distribution of target measures to clinicians in the Global Health Practice Network that can be completed by the clinicians themselves or administered to their patients. These data will then be analyzed and their results systematically coded and integrated with evidence gathered in the first two tiers.

12.3 TASK 3 Generate summary proposals on the revision platform for comment by other groups, Revision Steering Group, and the global community.

Documenting the evidence on which recommendations are based. Using the results of their evidence-based reviews, the disorder workgroups will formulate suggestions for updating and revising the ICD-10 diagnostic categories, operational criteria, and/or overall coding structure.

Reporting interim and final results. Each disorder group will be asked to write and to post on the Revision platform an interim report of its progress every six months as well as a final report documenting its final results and recommendations. The Revision Coordinating Group, in consultation with the workgroup co-chairs, will establish explicit guidelines for the workgroups to use in preparing these reports, including separate templates for interim and final reports. The purpose of these guidelines will be to ensure completeness of desired information and consistency across documents submitted by different workgroups. As an incentive to engage in the report-writing process, workgroup members will have the opportunity to publish interim reports in special issues of the online Classifications Journal.

In addition to their review by the coordinating group, interim and final reports of the workgroups will be posted on the Revision Platform. This platform will serve as a public forum in which end-users can provide feedback to the workgroups throughout the development process, increasing the likely usefulness of the revised ICD for the wide range of constituents for whom it is being devised. To that end, comments on reports will be solicited from the scientific community and other ICD stakeholders. In addition to general comments, workgroups may request suggestions for future directions or call for information or data on a particular topic. Public comments will be continually collected and reviewed by postdoctoral fellows, who will screen them for content and relevance before forwarding them to the appropriate workgroups. These comments will be considered and weighed using the same criteria as those used in the review of empirical evidence.

12.4 TASK 4. Revised reports

Workgroups are likely to complete multiple rounds of reports in an iterative process in which they report their findings, receive feedback from the Revision Steering Group and the world community for a health field, and revise their work in response to feedback. The Revision Steering Group will establish a set of criteria for evaluating workgroup reports and may bring in external consultants to assist in the evaluation process. Evaluations may be followed by requests for clarification of competed work or for additional work in particularly important, controversial, or understudied areas. In addition, workgroups will complete annual updates of their literature reviews to ensure that the information in their final report—and the evidence on which final recommendations are based—is as comprehensive and up-to-date as possible.

12.5 TASK 5. Field trials

The provisional revised diagnostic criteria recommended by the workgroups will be tested in one or more iterations of field trials. Field trials will be conducted in collaboration with existing global networks.

Proposing questions for the field trials. Given the key questions identified in the review process workgroups will be asked to develop feasible questionnaires that could be applied within the global Network.

Evaluation of the feedback from the field trials. Results of the field trials will be provided to the workgroups to serve in developing the final revisions and recommendations.

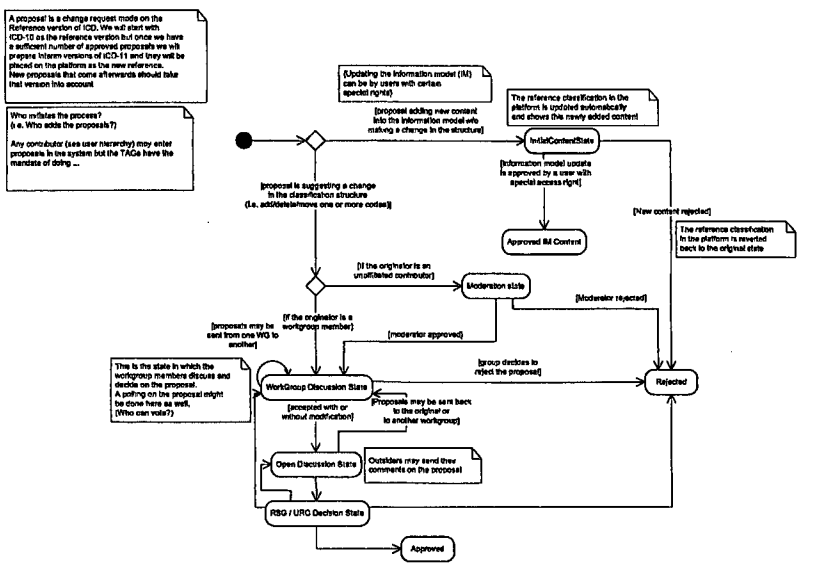
12.6 TASK 6. Final revisions and recommendations

Preparing a final report. Based on the results of field testing, the workgroups will finalize the ICD-11 diagnostic criteria/external causes and prepare a final report summarizing their results and recommendations. The report will be presented to the Revision Steering Group and posted on the Internet platform.

Setting an agenda for future work. While it is hoped that the comprehensive survey and synthesis of the literature will yield important advances in our understanding of disorders and their external causes, it is also expected that many questions will remain unresolved and that some new questions will become apparent as the update and revision process draws to a close. Having just reviewed and contributed to the available literature, the workgroups will be in an ideal position to identify remaining gaps in knowledge, chart the steps needed to fill these gaps, and set an agenda for the field for future research. The resulting proposals will be published in one or more of several possible forums, including the ICD text itself, the ICD web page, the knowledge portal, books published by WHO on the ICD update and revision process, or a companion workbook accompanying the newly-published ICD-11.

13 Workflow

Proposals for update of ICD can be generated by Workgroups, or everybody accessing the revision platform. The proposals can relate to modifications of the structure of ICD, to modification of definitional content of ICD or to both. Any structural changes will be decided before definitional content is formulated. In some cases definitions will exist from previous versions of ICD, IND, and other internationally agreed sources, thus guiding decisions that may lead to structural changes. The graphics below depicts the flow of a proposal:



14 Forming TAGs and Workgroups

Each workgroup will be led by preferably two co-chairs, one of whom will be a member of the relevant TAG. These individuals will be responsible for selecting the members of the workgroup and establishing the membership and focus of the subgroups. They will supervise the work of the workgroup, monitoring progress, and ensuring quality control. If necessary each workgroup may include subgroups corresponding to subclasses of disorders or other areas requiring focused attention within the workgroup domain. TAGs and Workgroups are expected to include approximately 10-12 members. Subgroups can include participants who are not members of the workgroup, but must be chaired by a member of the workgroup. An effort will be made to draw members of workgroups and subgroups from multiple disciplines and nations.

Members are proposed by the chairs of the Groups. All members and chairs are nominated by WHO following consultations with chairs, and relevant stakeholders, as necessary.

- Formation of a Group includes:
- Identification and nomination of chairs
- Identification and nomination of members

Previous to nomination, the members will sign the WHO Declaration of Conflict of Interest. The procedure will make sure, in particular, that

- all contributions will be owned by WHO and there are no conflicts of intellectual property
- no single financial groups interest prevail in the revision
- the members comply with all ToR, rules, guidelines and procedures that are and will be established by WHO for the revision of ICD.

Membership of a group should cover the following criteria:

1. Active input providers: They provide input themselves or organise with others to provide the input needed
2. Regional coverage: to make sure all regions are represented adequately (for WHO regions see also www.who.int/about/regions/)
3. Available for the next 10 years
4. Able to transfer their knowledge to the next ICD revision
5. Practical experience with previous versions of ICD
6. In summary the members of a TAG/workgroup should cover the range of stakeholders addressed by the outcome of the work of that individual group.

Additional points for consideration are:

- Are all relevant stakeholders involved in the overall revision process, or is there a specific need to include one or the other party in a working group?
  - International organizations, as OECD <=> WHO
  - NGOs
    - Vertically, as FIGO or Diabetes
    - Horizontal, as paediatric or geriatric, or rare diseases
  - vertical: FIGO, KDIGO, Diabetes, other
  - Medical, non medical, statistical and policy communities

15 Copyright

It is envisaged that ICD-11 becomes an international public good. Copyright of parts of ICD vested with bodies other than WHO would seriously compromise implementation and distribution. Any person contributing, reviewing, or otherwise participating to the revision of ICD, legal bodies and other entities and all other possible parties are required to make sure that WHO can own the exclusive licence of their contributions and grant to WHO for the full period of copyright including any renewals or extensions throughout the world and in all languages an exclusive licence to publish their contribution to the 11th revision of ICD, or permit others to do so in print editions and in digital formats including online and network editions of the ICD and in other derivative or collective works and to exploit subsidiary rights in the contributions, including database rights. They have to confirm they are the sole author of the contribution and that they are the sole owner of the copyright, or that they have explicitly been authorized to use the contribution in the context of ICD-11.

16 Chairing of TAGs and Workgroups

Co-chairs of all workgroups will have privileged access to the ICD Update and Revision Portal and will participate in a monthly telephone meeting with the TAG so that co-chairs of each workgroup can learn about the activities of other workgroups.

Chairs are liable to WHO that rules and regulations of the revision process are followed by their groups.

Chairing is a proactive undertaking, and the range of activities and responsibilities that a chairman must perform is huge. The chair of a TAG is accountable to WHO. The chair of a committee must realize that the success or failure of that committee rests squarely on his/her shoulders. The primary duty is to guide the group's discussions. He/she should encourage every member to participate in the work and keep track of the discussion focused on the matter at hand. The chair ensures there are agendas and structured reports.

In particular, the chair ensures revision procedures are applied by the TAG and its workgroups

- Creation of workgroups
- Workflows
    - Proposals
    - Comments
    - Conflict resolution
- Evidence based review guidelines
- Communication with RSG /WHO

The chair is also responsible for encouraging opportunities for interactions between the members. Group should be provided the opportunity to get to know each other. Groups tend to work better if the members are familiar with one another. If members don't get along well, the leader must not allow those members to impede the flow of the meeting. A quick solution is not to allow the conflicting people to sit near each other or in the direct line of fire.

Members of workgroups should be carefully selected. These are the people who will help resolve issues for the relevant specialty. They should be knowledgeable in the area of the group's responsibility. Members should be a diverse group without being incompatible. Try to recruit people from different perspective on the committee – when these people agree on the solution, you know it's a good one.

Remind members that they should be receptive and open to new ideas and other people's opinions as work is accomplished in a committee through the give and take of an open, uninhibited discussion.

- Always lead by example
- Carefully plan your agenda; think of an agenda as a roadmap that will ensure your meeting serves its purpose
- Know where you are going; review the meeting objectives and desired outcomes in your opening remarks
- Make sure everyone participates in the discussion
- Anyone who voices a problem must also offer a potential solution... meetings should not be constructive, and not a forum for complaining about everything and everyone
- Ensure that committee members take ownership in desired outcomes by inviting them to do something to support the goals of the committee
- Delegate but have realistic expectations of the amount of work that should be asked from each members given their respective responsibilities
- Provide an agenda at least 4 days prior to the meeting date
- Indicate business items to be discussed versus decided upon
- Circulate minutes no later than 10 days following the meeting.
- Chairs can also send a quick "to do list" summary the day after the meeting by email

- Evaluate your group from time to time by asking members about their experience on the group

Committees are an integral part of every successful organization. A committee with a clear purpose, a well-informed leader and dedicated members is on its way toward success.

Workgroups are an integral part of the revision. A working group with a clear purpose, a well-informed leader and dedicated members is on its way toward success.

DECLARATION OF INTERESTS FOR WHO EXPERTS

The assistance of distinguished authorities knowledgeable in a variety of medical and scientific fields is essential to WHO's work on global health issues. **It is expected that individuals who are qualified to serve as an expert for WHO may have private interests related to their expertise. But, at the same time, it is imperative that situations are avoided in which such interests may unduly affect, or may be perceived to affect, an expert's impartiality.**

To assure the highest integrity, and hence public confidence, in its activities. WHO policies require that all experts serving in an advisory role agree to disclose any circumstances which could give rise to a **potential conflict of interest** (i.e., any interest which may affect, or may reasonably be perceived to affect, the expert's objectivity and independence). Since you have been selected as a WHO expert in the activity described below, you are requested to disclose in this Declaration of Interest (DoI) form any financial, professional or other interest relevant to the subject of the work or meeting in which you will be involved and any interest that could be significantly affected by the outcome of the meeting or work. You are also asked to declare relevant interests of others who may, or may be perceived to, unduly influence your judgment (such as immediate family members, employers, close professional associates or any others with whom you have a substantial common personal, financial or professional interest.)

Kindly complete this form and submit it to WHO Secretariat, well in advance of the meeting or work. You are also asked to inform the Secretariat if any change in this information occurs before or during the course of the meeting or work. Non-completion of a DoI form at any stage precludes participating as an expert.

It should be clarified that the giving of affirmative answers to questions in a DoI form would not automatically disqualify or limit your participation as an expert. Rather, your answers will be screened by the Secretariat to determine if a potential conflict of interest may exist or may be perceived to exist. One of several outcomes can occur, depending on the circumstances (i.e., the nature and magnitude of the interest, its timeframe, the availability of sufficient measures to safeguard the integrity of the decision-making process if the expert is permitted to participate).

After reviewing the disclosures in the DoI form, the Secretariat may conclude that no potential conflict exists or that the interest is irrelevant or insignificant. If it appears that a conflict of interest exists and is potentially or clearly significant (or may be reasonably perceived to be so), one of the following three options, or a combination of these options, may be applied by the Secretariat: (i) you may be invited to continue to participate in the meeting or work, provided that your interest would be publicly disclosed; (ii) you may be asked not to take part in the portion of the meeting, discussion or work related to your interest, or not participate in related decisions; or (iii) you may be asked not to take part in the meeting or work altogether.

Any relevant conflicts will be **publicly disclosed** to other participants at the start of the activity and in the resulting report or other work product. The Secretariat will assume that you consent to such a disclosure, unless you check "no" in the space provided on the last page of this form. **In a later audit or investigation,** the contents of your DOI form may be made available to persons outside of WHO if the objectivity of the work or meeting in which you are involved is questioned and the Director-General considers disclosure to be in the best interests of the Organization, although only after discussion with you. By completing this DoI form, it is assumed that you agree to these conditions.

Name: Institution: Email:

Date and title of meeting or work, including description of subject-matter to be considered (if a number of substances or processes are to be evaluated, a list should be attached by the organizer of the activity):

_____

_____

Please answer each of the questions below. If the answer to any of the questions is "yes", briefly describe the circumstances on the last page of the form.

The term "you" refers to yourself and your immediate family members (i.e., spouse (or partner with whom you have a similar close personal relationship) and your minor children). "Commercial entity" includes any commercial business, an industry association, research institution or other enterprise whose funding is significantly derived from commercial sources with an interest related to the subject of the meeting or work. "Organization" includes a governmental, international or non-profit organization. "Meeting" includes a series or cycle of meetings.

EMPLOYMENT AND CONSULTING
Within the past 3 years, have you received remuneration from a commercial entity or other organization with an interest related to the subject of the meeting or work? Please also report any application or negotiation for future work.

1a Employment — Yes ☐ No ☐

1b Consulting, including service as a technical or other adviser — Yes ☐ No ☐

RESEARCH SUPPORT
Within the past 3 years, have you or your research unit received support from a commercial entity or other organization with an interest related to the subject of the meeting or work? Please also report any application for future research support.

2a Research support, including grants, collaborations, sponsorships, and other funding — Yes ☐ No ☐

2b Non-monetary support valued at more than US$1000 overall (include equipment, facilities, research assistants, paid travel to meetings, etc.) — Yes ☐ No ☐

INVESTMENT INTERESTS
Do you have current investments (valued at more than US$10 000 overall) in a commercial entity with an interest related to the subject of the meeting or work? Please also include indirect investments such as a trust or holding company. You may exclude mutual funds, pension funds or similar investments that are broadly diversified.

3a Stocks, bonds, stock options, other securities (e.g., short sales) — Yes ☐ No ☐

3b Commercial business interests (e.g., proprietorships, partnerships, joint ventures) — Yes ☐ No ☐

INTELLECTUAL PROPERTY
Do you have any current intellectual property rights that might be enhanced or diminished by the outcome of the meeting or work?

4a Patents, trademarks, or copyrights (also include pending applications) — Yes ☐ No ☐

4b Proprietary know-how in a substance, technology or process — Yes ☐ No ☐

PUBLIC STATEMENTS AND POSITIONS (during the past 3 years)

5a As part of a regulatory, legislative or judicial process, have you provided an expert opinion or testimony, related to the subject of the meeting or work, for a commercial entity or other organization? — Yes ☐ No ☐

5b Have you held an office or other position, paid or unpaid, where you may be expected to represent interests or defend a position related to the subject of the meeting or work? — Yes ☐ No ☐

ADDITIONAL INFORMATION

6a If not already disclosed above, have you worked for the competitor of a product which is the subject of the meeting or work, or will your participation in the meeting or work enable you to obtain access to a competitor's confidential proprietary information, or create for you a financial or commercial competitive advantage? — Yes ☐ No ☐

6b To your knowledge, would the outcome of the meeting or work benefit or adversely affect interests of others with whom you have substantial common personal, financial or professional interests (such as your adult children or siblings, close professional colleagues, administrative unit or department)? — Yes ☐ No ☐

6c Is there any other aspect of your background or present circumstances not addressed above that might be perceived as affecting your objectivity or independence? — Yes ☐ No ☐

7. **TOBACCO OR TOBACCO PRODUCTS** *(answer without regard to relevancy to the subject of the meeting or work)* — Yes ☐ No ☐

Within the past 3 years, have you had employment or received research support or other funding from the tobacco industry or had any other professional relationship with an entity, directly involved in the production, manufacture, distribution or sale of tobacco or tobacco products or representing the interests of any such entity?

EXPLANATION OF "YES" RESPONSES: If the answer to any of the above questions is "yes", check above and briefly describe the circumstances on this page. **If you do not provide, the amount or value of the interest, where requested, it will be assumed to be significant.**

Nos. 1 - 4: 7 **Type of interest, question number and category (e.g., Intellectual Property 4.a copyrights) and basic descriptive details.**	**Name of company, organization, or institution**	**Belongs to you, a family member, employer, research unit or other?**	**Amount of income or value of interest (if not disclosed, is assumed to be significant)**	**Current interest (or year ceased)**
Nos. 5-6: Describe the subject, specific circumstances, parties involved, time frame and other relevant details				

CONSENT TO DISCLOSURE. The Secretariat will assume that you consent to the disclosure of any relevant conflicts to other meeting participants and in the resulting report or work product, unless you check "no" in the space provided here. If you check "no", the Secretariat will not disclose the information without your prior approval, although this may result in your not being able to participate in the meeting or conference. **No:** ☐

DECLARATION. I hereby declare on my honour that the disclosed information is true and complete to the best of my knowledge.

Should there be any change to the above information, I will promptly notify the responsible staff of WHO and complete a new declaration of interests which describes the changes. This includes any change which occurs before or during the meeting or work itself and through the period up to the publication of the final results.

Date: _____ Signature_____

Annex 4 Roles and workflows

Basic roles are:

Member of the RSG or a TAG	Access to all domains and layers, commenting at all stages in own domain
Member of a Workgroup	Access to own domain, commenting there at all stages, access to all other domains but commenting only in public layer.
Recommended contributor	Highlighted comments and contributions, access to public layer
Unknown contributor	Commenting at public layer
Linearization editor	Commenting at all layers and groups, direct editing access to the linearization editing frontend.

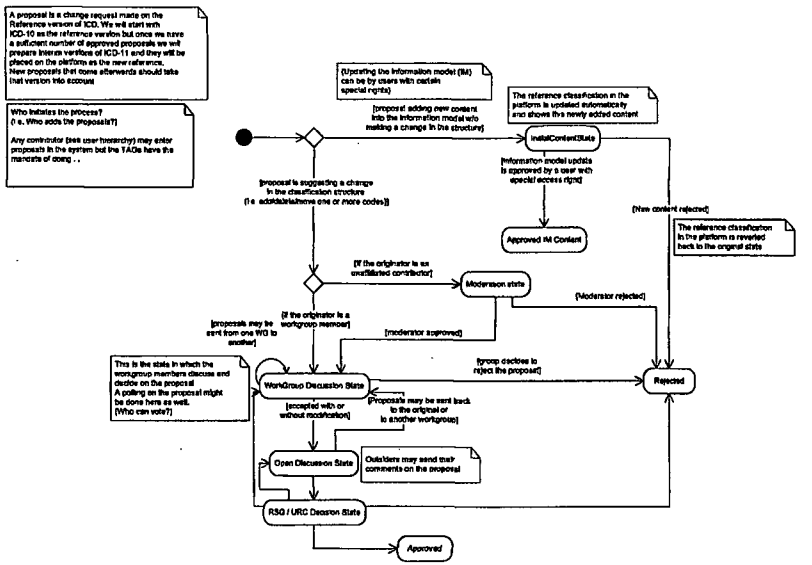
A recommended contributor is identified by valid, evidence based contributions, or has been constructively working actively for at least 3 months, or is identified to be a sound expert by his affiliation or scientific publications.

Unknown contributor is any person not included in one of the groups above.

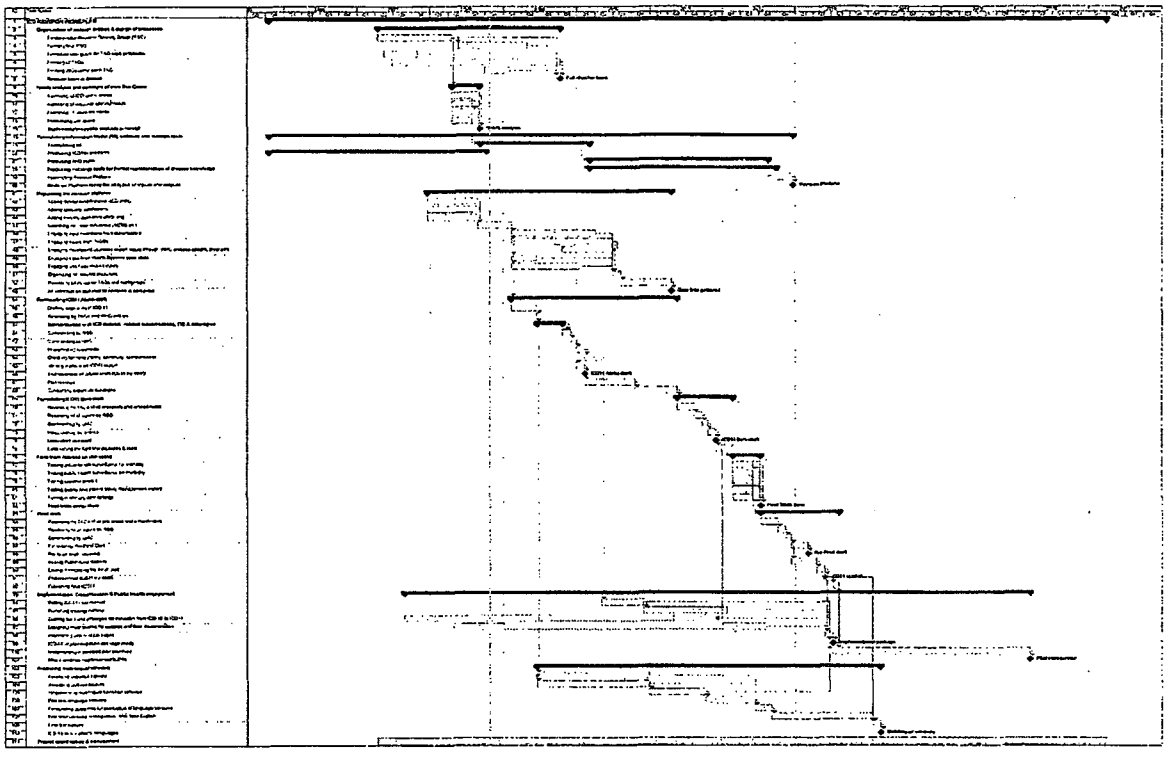
Contributions consist of comments, suggestions to structure of one or more linearizations, suggestions to definitions and to conceptual clustering for different usecases. Additional input comes for the rule base of ICD.

Access paths include submission of proposal to open discussion layer and forwarding to the relevant TAG by a moderator, and direct submission to the relevant TAG. Forwarding to a workgroup is task of the TAG.

Proposals for update of ICD can be generated by Workgroups, or everybody accessing the revision platform. The proposals can relate to modifications of the structure of ICD, to modification of definitional content of ICD or to both. Any structural changes will be decided before definitional content is formulated. In some cases definitions will exist from previous versions of ICD, IND, and other internationally agreed sources, thus guiding decisions that may lead to structural changes. The graphics below depicts the flow of a proposal:



Annex 5 Gant chart of the project



Annex 6 Roles and responsibilities

WHO Headquarters coordinates the overall ICD revision in consultation with the WHO Member States, the WHO-FIC Network, and multiple professional organizations to ensure that the final revision is broadly responsive to the many different aspects of health care. The work will be mainly carried out by the Revision Steering Group and the Workgroups as shown in the figure and further described below:

ICD-10 Revision Organization Structure

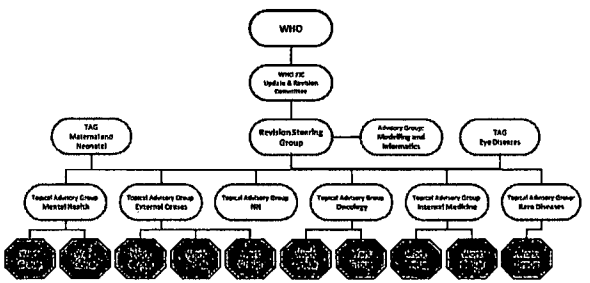


Figure 7 – ICD-10 Revision Organization Structure

16.1 WHO

WHO coordinates the overall revision process in conjunction with the relevant stakeholders? WHO is the secretariat of the World Health Assembly (WHA) and ensures the products from the revision process are acceptable to the WHA. The RSG assists WHO in this task. Daily business is done in a small executive group consisting of WHO, the chair of the RSG and a project manager

16.2 Update and Revision Committee

The committee was established to coordinate, decide, and advise WHO about updates to ICD-10. Its tasks now include updates for ICF, as well. In the revision process, the committee would deal with coordination of transition between ICD-10 and ICD-11, in conjunction with the last update to ICD-10 in 2010. The committee will verify, in cooperation with Mortality and Morbidity Reference Groups that the core linearizations of ICD-11 (mortality and morbidity) are fit for purpose. Assisting in design and evaluation of field tests of ICD-11 will provide the necessary evidence.

16.3 The Revision Steering Group (RSG)

The Revision Steering Group has been established as an oversight mechanism. Each main area of revision will be worked through a topic advisory group and multiple workgroups. For more detail see Annex ToR of RSG.

The Revision Steering Group will communicate on an ongoing basis by email, have regular conference calls, and will convene at least twice annually for an in-person meeting.

16.4 Topic Advisory Groups

Topic Advisory Groups will serve as the planning and coordinating advisory body for specific issues which are key topics in the update and revision process, namely Oncology, Mental Health, External Causes of Injury, Communicable Diseases, Non-communicable Diseases, Rare Diseases and others to be established.

The primary charge of each group will be to advise WHO in all steps leading to the revision of topic sections of ICD in line with the overall revision process. In particular:

- *Advise on particular topic revision steps and establish workgroups and partners to involve* - The TAGs will advise WHO on constitution of working groups to undertake generation of necessary evidence, to develop proposals for changes and to focus on specific issues as needed. Each TAG will (a) determine the number and content areas of the workgroups, (b) identify the members and chairs of the workgroups, (c) present an initial mandate to each workgroup, (d) establish procedures for the activities of the workgroups, and (e) facilitate cross-fertilization of ideas and reducing redundant efforts by making workgroups aware of one another's activities.
- *Advise in developing various drafts of topic segments in line with the overall production timeline of ICD-11* TAGs will review initial recommendations of the workgroups and consolidate those to achieve consistency in proposals across groups and areas.
- *Advise in developing protocols for and in implementing field trials* - TAGs will also assist WHO in identifying appropriate representatives of various stakeholders and in establishing effective collaboration/consultative mechanisms.

Topic Advisory Groups will consist of experts within each major domain of the classification chapters. Currently there are following:

- Mental Health : S. Hyman
- External Causes : J. Harrison
- Rare Diseases : S. Aymé
- Oncology : IARC Editor(s)
- Internal Medicine : K. Sugano
- Ophthalmology S. Kashii/A. Colenbrander
- Dermatology R. Chalmers/M. Weichenthal
- Others: *to be formed e.g. Child and Adolescent Health etc.*

Topic Advisory Groups (TAG) will lead the work in different fields of expertise. Such fields can be vertical, as cancers (oncology) or horizontal, as rare diseases that can be found in every chapter. The TAG will organize **workgroups** to deal with relevant subtopics, such as diabetes in internal medicine.

The TAGs will communicate on an ongoing basis by email, have regular conference calls, and will convene at least twice annually for an in-person meeting.

TAG Health informatics and modelling (HIM)

This TAG is established to ensure the consistency and usefulness of disease modelling and revision tooling environment. The TAG HIM will advise the Revision Steering Group, and will act after consultation with the RSG: For more detail see Annex ToR TAG HIM.

Communication will be the same as for the other TAGs. Involvement of modelling experts of SNOMED will be an asset.

16.5 Workgroups

Work Groups will serve as the key functioning unit for the review of evidence and generation of main proposals at a specific topic in the classification. For example, the TAG in the Mental Health Area will be responsible for the whole of chapter V and its linkages, whereas it may generate 5-10 working groups to carry out the systematic reviews on special sections of the chapter such as schizophrenias and psychosis; mood and anxiety disorders or topics such as children and youth, common brain disorders, etc. For more detail see Annex Instruction Manual for TAGs and Workgroups.

16.6 Ontology and terminology working groups

Ontology work means editing linkages of the drafted categories of ICD-11 inside ICD, rendering the analogue classification knowledge explicit and computable. The ontology work also consists of editing linkages to existing ontologies that relate to the descriptive dimensions of concepts in ICD.

At the current stage ontology experts are rare and it can not be assumed that such knowledge is widespread among other groups. The tooling environment of the revision will facilitate establishing such linkages by content-only experts, with a thorough review is done by ontology experts in conjunction with classification specialists.

Similar challenges and opportunities apply to terminology linkages. However, two main tasks are foreseen for the working group:

1. Terminological consistency inside ICD (particularly for diseases)
2. Terminological consistency and linkages to selected reference terminologies (anything except diseases)

Ongoing mapping processes between SNOMED and ICD are relevant to this part of the revision.

Annex 7 Standards

Standards, initiatives, and projects relevant to the revision of ICD are described for their field of activity, implementation, maturity, and problems. Present environment

1 Classifications

Members of the family of international Classifications, as core classifications, related, and derived classifications overlap with fields that are covered by current ICD. Alignment of fields of overlap requires consideration of such classifications.

16.7 ICPC

The International Classification for Primary Care shares concepts with ICD. Both classifications are being reviewed and will align common concepts.

WHO has accepted ICPC-2 within the WHO FIC mainly as a reason for encounter classification, and users may use it as a classification for primary care or general practice wherever applicable. ICPC-2 classifies patient data and clinical activity in the domains of General/Family Practice and primary care, taking into account the frequency distribution of problems seen in these domains. It allows classification of the patient's reason for encounter (RFE), the problems/diagnosis managed, interventions, and the ordering of these data in an episode of care structure. The ICPC-2 has a biaxial structure and consists of 17 chapters, each divided into 7 components dealing with symptoms and complaints (comp. 1), diagnostic, screening and preventive procedures (comp. 2), medication, treatment and procedures (comp. 3), test results (comp. 4), administrative (comp. 5), referrals and other reasons for encounter (comp. 6) and diseases (comp. 7).

The classification was developed in an international effort by the classification working group of the World Organisation of National Colleges, Academies, and Academic Associations of General Practitioners/Family Physicians (WONCA). An updated second edition has been published in 2003. A revised edition, the ICPC-3 is under preparation. WHO and WONCA are collaborating to align ICD and ICPC during the respective revision processes, as well as aligning ICPC and ICF. The ICPC-2 has been translated into more than 20 languages and is in use world wide.

16.8 Clinical modifications of ICD-10

Although some countries found ICD-10 sufficient for clinical reporting, reimbursement and resource allocation, many others felt that it did not provide adequate detail for clinical and administrative uses. Also, neither ICD-9 nor ICD-10 provided codes for classification of operative or diagnostic procedures. As a result, clinical modifications of ICD were developed, often along with procedure classifications (Australia, Canada, France, Germany, Thailand, Korea, and USA). These modifications will inform the revision of ICD-10.

16.9 Adaptations of ICD-10

Adaptations of ICD for Dentistry and Stomatology, Dermatology, Mental Health, Neurology (NA), Oncology (ICD-O), Paediatrics, Orthopaedics and Rheumatology, and other disciplines accommodate the need for more detail in these specialities. The detail added in these adaptations will inform the revision of ICD-10.

16.10 ICF

The overall aim of the ICF is to provide a unified and standard language and framework for the description of health and health-related states of an individual. It defines components of health and some health-related components of well-being (such as education and labour). The ICF therefore contains health domains and health-related domains. These domains are described from the perspective of the body, the individual, and the society in two basic lists:

(1) Body Functions and Structures

(2) Activities and Participation

As a classification, ICF systematically groups different domains for a person in a given health condition. Functioning is an umbrella term encompassing all body functions, activities, and participation; similarly, disability serves as an umbrella term for impairments, activity limitations, or participation restrictions.

ICF also lists

(3) Environmental factors

Those interact with all these constructs. In this way, it enables the user to record useful profiles of individuals' functioning, disability and health in various domains, as for pre-treatment and post-treatment assessment (e.g. for outcome measurement) or social insurance assessment.

The International Classification of Impairments, Disabilities, and Handicaps (ICIDH) was first published by the World Health Organization for trial purposes in 1980. Developed after systematic field trials and international consultation over five years, it was renamed ICF and endorsed by the Fifty-fourth World Health Assembly for international use in 2001. ICF is translated in over 38 languages and can be accessed online in the 6 official languages at WHO.

16.11 ATC/DDD

Revision of ICD will align categories that relate to drugs with the ATC/DDD.

The ATC/DDD system classifies therapeutic drugs. The purpose of the ATC/DDD system is to serve as a tool for drug utilization research in order to improve quality of drug use. In the ATC classification system, the drugs are divided into different groups according to the organ or system on which they act and their chemical, pharmacological and therapeutic properties. Drugs are classified into five different levels. Drug consumption statistics (international and other levels) can be presented for each of these five levels. The Daily Drug Doses reflect an average of international dosage to get an estimate of consumption.

The system has been since 1975. The classification is updated on an annual basis. So far, the ATC contains no reference to the ICD.

16.12 ICECI

The ICECI classifies external causes of injuries. First published in May 1998, ICECI is designed to help researchers and prevention practitioners to describe measure and monitor the occurrence of injuries and to investigate the circumstances of occurrence. The classification has a separate coding axis for each main concept. It aims to be useful for injury prevention, useable in many types of settings

(different parts of the world; emergency departments and other places where data are collected) and to ensure comparability and complementarity with the ICD-10.

The ICECI has a multi-axial and hierarchical structure: a core module including seven items (mechanism of injury, objects/substances producing injury, place of occurrence, activity when injured, the role of human intent, use of alcohol, use of (other) psycho-active drugs) and five additional modules to enable collection of additional data on special topics (violence, transport, place of occurrence, sports, occupational injury). A set of short ICECIs been proposed for use in countries or societies with limited resources for injury surveillance.

It has been developed as a related classification with respect to ICD-10 chapter XX. An aim in developing ICD-11 is to increase compatibility between ICD and ICECI, with ICECI possibly being a derived classification from ICD in the future.

Custodianship and responsibility for maintenance and updating lies with an international group of experts: ICECI Coordination and Maintenance Group that includes WHO; a group of three persons act as the executive committee. The ICECI is available for free download on the internet in English, Spanish, and Portuguese

17 Terminologies

Although all of the items within this category may not meet the technical definition of a terminology, it remains important for ICD to coordinate and interface with them to reduce duplication and discontinuities in use and meaning, as well as support efficient processing. Terminologies play an increasing role in health, where electronic reporting of individual data is in place, e.g. electronic health records, cancer registration, and death certificates

17.1 SNOMED

SNOMED CT® (Systematized Nomenclature of Medicine-Clinical Terms) is a clinical healthcare terminology joint development between the NHS in England and the College of American Pathologists (CAP) to develop an international clinical terminology and was formed in 1999 by the convergence of SNOMED RT and the United Kingdom's Clinical Terms Version 3 (formerly known as the Read Codes). It has greater depth and coverage of healthcare than the versions of Clinical Terms (Read Codes) that it replaces.

The historical strength of SNOMED RT was its terminologies for specialty medicine and methods for distributed collaborative development, while the strength of Clinical Terms Version 3 was its terminologies for general practice. By combining these two systems, SNOMED CT is the most comprehensive clinical vocabulary available with concepts of unique meanings and formal logic-based definitions organized into hierarchies. It covers most aspects of clinical medicine with over 357,000 concepts for the electronic health record (EHR). SNOMED CT cross-maps to such other terminologies as ICD-9-CM, ICD-O3, ICD-10, Laboratory LOINC, and OPCS-4. It supports ANSI, DICOM, HL7, and ISO standards.

http://www.ihtsdo.org/

http://en.wikipedia.org/wiki/SNOMED_CT

17.2 OMIM

Online Mendelian Inheritance in Man (OMIM™) is a continuously updated catalogue of human genes and genetic disorders. OMIM focuses primarily on inherited or heritable, genetic diseases. It is also considered to be a phenotypic companion to the human genome project. OMIM (Online Mendelian Inheritance in Man) is a computerized database version of Victor McKusick's book, Mendelian Inheritance in Man, provided through the National Center for Biotechnology Information. The primary difference between the two resources is that the online version is more current. The online database is updated daily, whereas the book contains all the information that was available online at the time of print. The online version also provides links to a variety of related resources.

The text Mendelian Inheritance in Man, authored and edited by Dr. Victor A. McKusick and a team of science writers and editors at Johns Hopkins University and elsewhere, is now in its 12th edition. See McKusick, V.A.: Mendelian Inheritance in Man. 12th ed., Baltimore: Johns Hopkins University Press, 1998.

http://www.ncbi.nlm.nih.gov/Omim/omimfaq.html

17.3 MeSH

MeSH is the US National Library of Medicine's controlled vocabulary thesaurus. It consists of sets of terms naming descriptors in a hierarchical structure that permits searching at various levels of specificity.

MeSH descriptors are arranged in both an alphabetic and a hierarchical structure. At the most general level of the hierarchical structure, there are very broad headings such as "Anatomy" or "Mental Disorders." More specific headings are found at more narrow levels of the eleven-level hierarchy, such as "Ankle" and "Conduct Disorder." There are 24,767 descriptors in 2008 MeSH. In addition to these headings, there are more than 172,000 headings called Supplementary Concept Records (formerly Supplementary Chemical Records) within a separate thesaurus. There are also over 97,000 entry terms that assist in finding the most appropriate MeSH Heading, for example, "Vitamin C" is an entry term to "Ascorbic Acid."

The MeSH thesaurus is used by NLM for indexing articles from 4,800 of the world's leading biomedical journals for the MEDLINE/PubMED® database. It is also used for the NLM-produced database that includes cataloguing of books, documents, and audiovisuals acquired by the Library. Each bibliographic reference is associated with a set of MeSH terms that describe the content of the item. Similarly, search queries use MeSH vocabulary to find items on a desired topic.

http://www.nlm.nih.gov/pubs/factsheets/mesh.html

17.4 UMLS

The purpose of US NLM's Unified Medical Language System® (UMLS) is to facilitate the development of computer systems that behave as if they "understand" the meaning of the language of biomedicine and health. To that end, NLM produces and distributes the UMLS Knowledge Sources (databases) and associated software tools (programs) for use by system developers in building or enhancing electronic information systems that create, process, retrieve, integrate, and/or aggregate biomedical and health data and information, as well as in informatics research. By design, the UMLS Knowledge Sources are multi-purpose. They are not optimized for particular applications, but can be applied in systems that perform a range of functions involving one or more types of information, e.g., patient records, scientific literature, guidelines, and public health data. The associated UMLS software tools assist developers in customizing or using the UMLS Knowledge Sources for particular purposes. The lexical tools work more effectively in combination with the UMLS Knowledge Sources, but can also be used independently.

There are three UMLS Knowledge Sources: the Metathesaurus®, the Semantic Network, and the SPECIALIST Lexicon. They are distributed with flexible lexical tools and the MetamorphoSys install and customization program.

http://www.nlm.nih.gov/research/umls/

17.5 International Nomenclature of Diseases (IND)

Confusion in disease nomenclature constitutes a severe barrier to communication and to the storage and retrieval of information. Few diseases have a single recognized name: most have several different--often widely different--names, and some have thirty or more. Many of these names are strict synonyms; others, however, are not, but may represent only a single clinical manifestation of a given disease rather than the disease itself. The confusion is aggravated by the fact that the same name, or very similar names, may be applied to two or more different conditions, or be used in different ways by different authors. Moreover, very similar names may be used in different senses in different languages.

In 1970 the Council for International Organizations of Medical Sciences (CIOMS) began the preparation of an International nomenclature of diseases (IND), with the assistance of its member organizations, and five volumes of provisional nomenclature were issued during 1972-1974. It was soon realized, however, that such a nomenclature, if it was to be truly international, necessitated much wider consultation than was possible solely through the CIOMS member bodies. In 1975 the IND became a joint project of CIOMS and the World Health Organization (WHO), guided by a Technical Steering Committee composed of representatives of both organizations. Preparation of the International nomenclature of diseases is supported by grants to CIOMS from the Kuwait Foundation for the Advancement of Sciences and the Kuwait Ministry of Public Health. However, funding stopped with the first gulf war.

For each volume, a first draft was prepared by consultants working under the guidance of the WHO Technical Terminology Service, taking into account existing recommendations and in consultation with CIOMS and WHO experts. This draft is distributed to a large number of individual experts throughout the world. Subsequently the draft is revised in the light of their comments, and the revised text is again distributed for review. If problems involving differences of interpretation should arise, meetings of experts may be convened in Geneva or elsewhere in order to resolve the

difficulties. When a consensus has been reached, the text is published as a first edition of the International nomenclature of diseases of the organ or system involved.

The principal objective of the IND is to provide, for every morbid entity, a single recommended name. The main criteria for selection of this name are that it should be specific (i.e., that it should apply to one and only one disease), unambiguous, as self-descriptive as possible, and as simple as possible. However, many widely used names do not fully meet these criteria, and to propose new names might well increase, rather than eliminate, confusion. Consequently, names that are in almost universal usage are retained, even if they do not fully meet the criteria listed above, provided they are not seriously incorrect. Eponyms are avoided to the maximum possible extent, since they do not meet the criterion of self-descriptiveness; however, many of these also are in such widespread use that they must be retained.

Each disease or syndrome for which a name is recommended is defined as unambiguously, and yet as briefly, as possible. To the definition is appended a list of synonyms--that is, terms other than the recommended term that have been applied to the morbid entity in question. These lists, which are invaluable for information retrieval, are made as complete as possible, and they are supplemented, where necessary, by notes explaining why certain synonyms are rejected or why an alleged synonym is not in fact a synonym at all.

A final objective of the IND is that is should serve as a complement to the WHO International Classification of Diseases (ICD). This calls for a brief explanation of the difference, and the relationship, between the two. The ICD is designed for the statistical classification of diseases, and it is not a nomenclature: that is, the terms used in the ICD are not recommended names. The IND, on the other hand, is a nomenclature, and not a classification: it is a list of recommended names (with definitions and rejected synonyms) for diseases, without any attempt to specify the manner in which those diseases should be classified for the purposes of statistical reporting. The names recommended in the IND will be used, as appropriate, instead of the present ICD names in the 10th revision of the ICD.

Early volumes of the International nomenclature of diseases included the ICD code for each disease. It was found, however, that this gave rise to a certain amount of confusion, some readers assuming that the IND was intended to replace the ICD. Furthermore, the 10th revision of the ICD will use a different (alphanumeric) system of coding. ICD codes are therefore no longer included in the International nomenclature of diseases.

Both CIOMS and WHO aimed at facilitating communication between health workers throughout the world by providing a truly international language of diseases and thus eliminating one of the barriers to communication that at present hamper efforts to improve the health of mankind.

18 Data models

A consensus data model will support the effective use and reuse of ICD data for multiple purposes. The definition of disease and of external causes of diseases has been approached in various ways, and several initiatives have created their own model accommodating a specific use. The differences result in incompatible conceptualization and hamper development of specialty and business overarching use of information.

19 Ontological standards

The linkage to and use of ontological concepts and practices will enable ICD to be computable. This is expected to support the global exchange of semantic data. Ultimate interoperability would mimic or exceed that of the financial services industry. Ontologies in the field of information technology aim at representation of specific knowledge. Evolution in this field is fast. A set of standards for representation of ontologies, and tools for handling ontologies have been developed.

19.1 OWL

The Web Ontology Language (OWL) is a family of knowledge representation languages for authoring ontologies, and is endorsed by the World Wide Web Consortium. This family of languages is based on two semantics: OWL-DL and OWL-Lite semantics are based on Description Logics which have attractive and well-understood computational properties, while OWL-Full uses a novel semantic model intended to provide compatibility with RDF Schema. OWL ontologies are most commonly serialized using RDF/XML syntax. OWL is considered one of the fundamental technologies underpinning the Semantic Web, and has attracted both academic and commercial interest.

19.2 RDF

Resource Description Framework (RDF) is a family of World Wide Web Consortium (W3C) specifications originally designed as a metadata model but which has come to be used as a general method of modelling information, through a variety of syntax formats.

The RDF metadata model is based upon the idea of making statements about resources in the form of subject-predicate-object expressions, called triples in RDF terminology. The subject denotes the resource, and the predicate denotes traits or aspects of the resource and expresses a relationship between the subject and the object.

20 Technological standards

20.1 SQL3

SQL3 development includes temporal relationships that could be used in the context of ICD revision tracking and management.

ANSI (X3H2) and ISO (ISO/IEC JTC1/SC21/WG3) SQL standardization committees have for some time been adding features to the SQL specification to support object-oriented data management. The current version of SQL in progress including these extensions is often referred to as "SQL3" [ISO96a, b].SQL3 object facilities primarily involve extensions to SQL's type facilities; however, extensions to SQL table facilities can also be considered relevant. Additional facilities include control structures to make SQL a computationally complete language for creating, managing, and querying persistent object-like data structures. The added facilities are intended to be upward compatible with the current SQL92 standard (SQL92).This and other sections of the Features Matrix describing SQL3 concentrate primarily on the SQL3 extensions relevant to object modelling. However, numerous other enhancements have been made in SQL as well [Mat96]. In addition, it should be noted that SQL3 continues to undergo development, and thus the description of SQL3 in this Features Matrix does not necessarily represent the final, approved language specifications.

http://etrij.etri.re.kr/Cyber/servlet/GetFile?fileid=SPF-1041761245678

21 Reference projects and initiatives

The projects and initiatives below will inform the development of ICD from tooling to content to structure.

21.1 The National Center for Biomedical Ontology

The goal of the Center is to support biomedical researchers in their knowledge-intensive work, by providing online tools and a Web portal enabling them to access, review, and integrate disparate ontological resources in all aspects of biomedical investigation and clinical practice. A major focus of the work involves the use of biomedical ontologies to aid in the management and analysis of data derived from complex experiments.

The Center is organized into six core components:

Core 1: Computer science research

Core 2: Bioinformatics research

Core 3: Driving biological projects and external research collaborations

Core 4: Infrastructure

Core 5: Education

Core 6: Dissemination

The Center is a US National center, assembling the expertise of leading investigators from across the country.

21.2 Organization of the Center

The Core 1 computer-science research and the Core 2 bioinformatics research involve the participation of Stanford University, Lawrence Berkeley National Laboratory, Mayo Clinic, University of Victoria, and University at Buffalo. Two Driving Biological Projects involve investigation of model-organism databases (FlyBase and ZFIN), while the third involves analysis of clinical-trial data stored in TrialBank.

The computer-science research in Core 1 delivers tools for accessing and unifying ontologies, and Core 2 concentrates on creating tools for using these ontologies to annotate large biomedical data sets, enabling data-set analysis, and integration. These tools enable the driving biological projects in Core 3. There is a direct flow of tools and technologies from Core 1 to Core 2 to Core 3, while the projects in Core 3 motivate the Center's research activities at all levels.

The Center achieves its objectives by advancing standards of good practice, by creating tools and theories that support a wide range of driving biological projects and collaborative research activities, and by training computational biologists, specialists in informatics, and computer scientists in the use of ontologies and of the Center's technologies in support of their research.

The National Center for Biomedical Ontology is part of the National Centers for Biomedical Computing supported by the NIH Roadmap. The Center is funded by the National Institutes of Health (NIH) and is part of the network of National Centers for Biomedical Computing.

21.3 Bioportal

BioPortal is a Web application to access the Open Biomedical Ontologies (OBO) library. This library contains a large collection of ontologies in biomedicine spanning many species from Arabidopsis to Homo Sapiens, and many scales, from molecules to whole organism. The ontology content includes the ontologies of the model organism communities, biology, chemistry, anatomy, radiology, and medicine.

BioPortal permits users to browse individual ontologies with three browsing paradigms--text, tree-view, and graph view. In addition, it permits search across all or specific ontologies according to term name or attribute content.

BioPortal will soon be providing a suite of tools for developers to integrate its functionality into their own applications, by providing URIs for all ontology content and Web services for accessing BioPortal functionality. It will also be providing tools to enable the community to comment on ontologies and their contents, to align and map them, as well as novel ways to visualize them and use them in applications. [2008]

http://www.bioontology.org/

21.4 FMA

The Foundational Model of Anatomy ontology (FMA) is an evolving computer-based knowledge source for bioinformatics; it is concerned with the representation of classes and relationships necessary for the symbolic modelling of the structure of the human body in a form that is understandable to humans and is also navigable, parseable, and interpretable by machine-based systems. Specifically, the FMA is a domain ontology that represents a coherent body of explicit declarative knowledge about human anatomy. Its ontological framework can be applied and extended to all other species.

The Foundational Model of Anatomy ontology is one of the information resources integrated in the distributed framework of the Anatomy Information System developed and maintained by the Structural Informatics Group at the University of Washington.

http://sig.biostr.washington.edu/projects/fm/AboutFM.html

21.5 Semantic health

To efficiently implement E-Health to meet the rising needs of mobile citizens, patients and providers, its fragmented interoperability initiatives must come together and coordinate with the increasing need to link clinical data to information from basic biological sciences and evidence of best clinical practice. Considering the need for interoperability at the Member State and cross-border level of the European Union - as expressed in the EU E-Health Action Plan - and for global interoperability - as represented by WHO - it is necessary to embark on a process that will prompt the divergent initiatives to join forces for the benefit of all citizens.

This SemanticHEALTH SSA develops a European and global roadmap for RESEARCH in health-ICT, focusing on semantic interoperability issues of E-Health systems and infrastructures. The roadmap will be based on consensus of the RESEARCH community, and validated by stakeholders, industry, and Member State health authorities. It

identifies key short-term (2-5 years) and medium-term (4-10 years) RESEARCH needs to achieve semantic interoperability of E-health systems (including issues of nomenclatures presently in use, classifications, terminologies, ontologies, EHR and messaging models, public health and secondary uses, and decision support, their relationships, mapping needs, limitations)

analyses unsolved research issues arising in the context of realistic approaches to priority clinical and public health settings (reflecting on models of use, benefits expected, concrete application experience and lessons learned; relevance of open source model)

takes into account the impact of non-technological (health policy, legal, socio-economic) aspects

reflects and integrates results of related FP6 (E-health ERA, I2-Health and other) studies.

The consortium and associated experts represent centres of excellence from four continents and the WHO.

http://www.semantichealth.org/

21.6 Disease ontology

Disease Ontology is a controlled medical vocabulary developed at the Bioinformatics Core Facility in collaboration with the NuGene Project at the Center for Genetic Medicine. It was designed to facilitate the mapping of diseases and associated conditions to particular medical codes such as ICD-9CM, SNOMED and others. This mapping is useful if efforts like the NuGene Project because it allows request for particular tissue type requests to be mapped quickly and with high fidelity to a set of ICD-9 codes that can then be used to retrieve appropriate samples from the tissue bank. Without such a mapping, clinicians are forced to manually search through ICD-9CM coding booklets to find all possible applicable codes matching their request. Given the complex organization of ICD-9CM and difficulty of the manual process, codes and therefore tissue samples are often overlooked. In one sample case, an early version of the Disease Ontology doubled concept coverage while reducing the overall misclassification error percentage. Eventually we envision that the Disease Ontology can also be used to associate model organism phenotypes to human disease as well as medical record mining.

Disease Ontology is implemented as a directed acyclic graph (DAG) and utilizes the Unified Medical Language System (UMLS) as its immediate source vocabulary to access medical Ontologies such as ICD-9CM. Using this standard, much of the process of updating the ontology can be handled by UMLS, freeing resources for clinicians to pursue more urgent tasks. For situations where the graph needs to be directly edited, the open source graph editor DAGEdit can be used. DAGEdit can readily manipulate and view the Disease Ontology because it is stored in Open Biomedical Ontologies (OBO) format in order to take advantage DAGEdit and any other OBO standards compliant tools. The screenshot of the Disease Ontology was taken using DAGEdit and show version 3 of Disease Ontology.

As a graph, the Disease Ontology can be thought of as a subset of UMLS. It fills a niche in the medical ontology world as a lightweight ontology offering context-free concept identifiers designed specifically to facilitate mapping to medical billing codes. Other Ontologies such as SNOMED and MESH lack these features.

The previous version of Disease Ontology (v2.1) is based almost entirely on ICD-9CM with additional concepts included that are useful for mapping common disease requests. It is a lightweight ontology containing 19136 concept nodes and is currently available for download. The newest version Disease Ontology 3 (revision 21) is based on primarily on freely available UMLS vocabularies (including ICD-9) and is currently under development.

http://diseaseontology.sourceforge.net/

http://ontology.buffalo.edu/bfo/BeyondConcepts.pdf

21.7 Knowledge bases

Several groups have compiled structured disease specific knowledge, as in clinical trial databases. However, the models differ across the groups. Aligning and feeding this content into ICD in the context of the revision process would fertilize the revision and allow world wide harmonization of the information model. Comparison of existing structures would allow distilling the most suitable model. Including a genetic axis would allow correlating genotypes and phenotypes of large population samples through data derived from routine data collection. Recruitment of best possible candidates for tests would become easier. Feeding in content from multiple sources will prevent possible bias to the revision.

21.8 caBIG

caBIG™ stands for the cancer Biomedical Informatics Grid™. caBIG™ is an information network enabling all constituencies in the cancer community – researchers, physicians, and patients – to share data and knowledge.

Molecular-based research is generating vast amounts of complex genetic data, and there is a need to integrate this information with separate and distinct clinical data. Furthermore, this research is based on disparate document and data formats, making it difficult to leverage in meaningful ways.

Research advances and clinical improvements face the following challenges:

A huge and growing volume of data – including genomic and proteomic information – that must be collected, analyzed, and made accessible

A multitude of "legacy" or previously developed information systems, most of which cannot be readily shared between institutions. Many of these systems continue to be paper-based, rather than electronic

An absence of common data formats

Few common vocabularies, making it difficult, if not impossible, to interlink diverse research and clinical results

An absence of tools to connect different databases

The mission of caBIG™ is to develop a truly collaborative information network that accelerates the discovery of new approaches for the detection, diagnosis, treatment, and prevention of cancer, ultimately improving patient outcomes.

The goals of caBIG™ are to:

Connect scientists and practitioners through a shareable and interoperable infrastructure

Develop standard rules and a common language to more easily share information

Build or adapt tools for collecting, analyzing, integrating, and disseminating information associated with cancer research and care.

Difficulty in identifying and accessing available resources, such as biospecimens and reagents

An absence of information infrastructure to share data within an institution, or among different institutions

http://cabig.cancer.gov/

22 Software

22.1 Lexgrid

LexGrid provides support for a distributed network of lexical resources such as terminologies and ontologies via standards-based tools, storage formats, and access/update mechanisms.

Currently, there are many terminologies and ontologies in existence. But just about every terminology has its own format, its own set of tools, and its own update mechanisms. The only thing that most of these pieces have in common with each other is their incompatibility. This makes it very hard to use these resources to their full potential. We have designed the Lexical Grid as a way to bridge terminologies and ontologies with a common set of tools, formats, and update mechanisms. The Lexical Grid is:

accessible through a set of common API's

joined through shared indices

online accessible

downloadable

loosely coupled

locally extendable

globally revised

available in web-space on web-time

cross-linked

http://informatics.mayo.edu/LexGrid/

22.2 Protégé

Protégé is a free, open source ontology editor and knowledge-base framework. It supports two main ways of modelling ontologies via the Protégé-Frames and OWL. Protégé is being developed at Stanford University in collaboration with the University of Manchester and is supported by a strong community of developers and academic, government and corporate users, who are using Protégé for knowledge solutions in areas as diverse as biomedicine, intelligence gathering, and corporate modelling.

22.3 ICD Update and Revision Platform

ICD Update and Revision Platform is a web based system that is designed to facilitate communication within expert workgroups. It has been operational since January 2006.

The basic functionality of the software can be summarized as follows:

This is a web application which means that the users access it from a web site without the need for downloading or installing any programs. All of the information collected and shared by the application resides on a central location in the WHO servers.

The application collects update and revision proposals in a structured and organized manner. This is done by asking the user to fill a form in which the user explains the proposal as well as the rationale behind the proposal. In addition to this, he/she can provide links to web pages such as publication references from PubMed or can upload documents that are relevant to the proposal.

The proposals are organized according to the existing ICD-10 structure. So the users may browse through the classification and see what is proposed in each and every part of the classification. They may post their comments on the proposals which are compiled and displayed with the proposals themselves

The application is not only for collecting the proposals but also works as a workflow engine which starts when the proposal is created and ends when it is removed from the system or it is implemented in the ICD. The workflow is in line with the present updating process.

Different users have different levels of authorization in the workflow. For example, standard users can submit proposals but cannot decide whether they are accepted or when they are going to be implemented, etc.

All old versions of proposals due to editing, all deleted and rejected proposals are stored in the system for review and cannot be edited any more.

http://extranet.who.int/icdrevision

22.4 Lexwiki

A collaborative terminology authoring platform based on Semantic MediaWiki which is currently under development at the Mayo Clinic.