International Organization for Standardization
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Международная организация по стандартизации

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Form 1: Proposal for a new field of technical activity

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Proposer: SAC	**ISO/TS/P 277** Click here to enter text.

A proposal for a new field of technical activity shall be submitted to the Central Secretariat, which will assign it a reference number and process the proposal in accordance with the ISO/IEC Directives (part 1, subclause 1.5). The proposer may be a member body of ISO, a technical committee, subcommittee or project committee, the Technical Management Board or a General Assembly committee, the Secretary-General, a body responsible for managing a certification system operating under the auspices of ISO, or another international organization with national body membership. Guidelines for proposing and justifying a new field of technical activity are given in the ISO/IEC Directives (part 1, Annex C).

The proposal (to be completed by the proposer)

Title of the proposed new committee (The title shall indicate clearly yet concisely the new field of technical activity which the proposal is intended to cover.) Technical Committee on Human Phenome

Scope statement of the proposed new committee (The scope shall precisely define the limits of the field of activity. Scopes shall not repeat general aims and principles governing the work of the organization but shall indicate the specific area concerned.)

Standardization in the field of human phenome.

Note. Human phenome is defined at the complete set of all human characteristics. It is determined by the interaction between genes and environment. It includes many characteristics ranging from macro- to micro-scales, from external appearance to internal functions, from biochemical characteristics to psychological behaviour, etc.

Excluded: the fields covered by ISO/TC276 (Biotechnology), ISO/TC215 (Health Information), ISO/IEC JTC1/SC37 (Biometrics), ISO/IEC JTC 1/SC 29 (Coding of audio, picture, multimedia and hypermedia information) and ISO/TC249 (Traditional Chinese Medicine).

Proposed initial programme of work (The proposed programme of work shall correspond to and clearly reflect the aims of the standardization activities and shall, therefore, show the relationship between the subject proposed. Each item on the programme of work shall be defined by both the subject aspect(s) to be standardized (for products, for example, the items would be the types of products, characteristics, other requirements, data to be supplied, test methods, etc.). Supplementary justification may be combined with particular items in the programme of work. The proposed programme of work shall also suggest priorities and target dates.

The initial work on development of international standards on human phenome is carried out from three levels.:
1. Basic standards. To establish vocabulary, terminology and classification standards of human phenome, as well as map visualization.
2. Method standards. Including human phenome cohort design principles, human phenome measurement, phenotype spectrum feature construction, characterization methods, analysis tools, etc.
3. Evaluation standards. Including quality evaluation of characteristic parameters, association of gene, environment and phenotype, etc.
First of all, we need to standardize the large number of vocabulary, terminology and classification of human phenome, promoting the research, application, communication and sharing of human phenome with a unified language.
The second aspect is to standardize the systematic measurement and representation from macro to micro-scales, to obtain the characteristics of the whole phenotype spectra of systematic measurement and ensure the data quality of human phenome. This part will be the basis of evaluation standards. It is also urgently required.
Thirdly, the evaluation standards will promote the accurate analysis and interpretation of human phenome characteristics, improve the reliability and comparability of human phenome, ensure the accuracy of measurement results of human phenome, and provide support for application.
The new TC plans to put forward five international standard proposals for the first and second levels of work within three years.

Indication(s) of the preferred type or types of deliverable(s) to be produced under the proposal (This may be combined with the "Proposed initial programme of work" if more convenient.)

The vocabulary, terminology and classification of human phenome will be developed as International Standards (IS) firstly. Human phenome cohort design principles and standards on human phenome measurement will be formed as IS gradually. With development, new technologies and applications may form Technical Specifications (TS) or Technical Reports (TR).

A listing of relevant existing documents at the international, regional and national levels. (Any known relevant document (such as standards and regulations) shall be listed, regardless of their source and should be accompanied by an indication of their significance.)

At present, there are no direct standards and specifications for human phenome under ISO. However, China has established standards of traditional Chinese medicine related phenotypic data such as YY/T 1488-2016 Tongue features acquisition device.

International work on Human Phenotype Ontology (HPO) has been carried out (https://en.m.wikipedia.org/wiki/human_Phenotype_Ontology). The MAQC consortium evaluated the technical performance of several microarray and sequencing platforms and the advantages and limitations of different bioinformatics data analysis methods in identifying differentially expressed genes (or biomarkers) (Guo L, et al., *Nature Biotechnology*, 2006; Shi L, et al., *Nature Biotechnology*, 2006; Su Z, et al., *Nature Biotechnology*, 2014), and performance evaluation of class prediction models for predicting clinical endpoints and drug toxicity endpoints (Shi L, et al., *Nature Biotechnology*, 2010; Su Z, et al., *Genome Biology*, 2014; Zhang W, et al., *Genome Biology*, 2014), and played an active role in promoting the establishment of FDA guidelines to ensure the reproducibility of omics results. Nature Publishing Group published three special issues in 2006, 2010 and 2014. Consequently, The Massive Analysis and Quality Control Society (MAQC) (Shi L, et al., *Nature Biotechnology*, 2017, https://www.nature.com/articles/nbt.4029; http://www.maqcsociety.com) was established in 2017 to improve the reproducibility, reliability and standardization of high-throughput omics (including genomics, transcriptomics, proteomics, and metabonomics, etc.).

The International Human Phenome Consortium (IHPC) and the Human Phenome Consortium of China (HPCC) were established in Shanghai, China on October 31, 2018. The HPCC Standards and Technical Specifications Working Group was formally established in Shanghai, China on December 7, 2018 to promote the establishment of human phenome technical standards. Furthermore, Fudan University established the Human Phenome Institute in July, 2017, focusing on the research and technology development of human phenome (http://hupi.fudan.edu.cn/wp-content/uploads/2018/11/2018-11-1920.pdf).

These documents provide an important basis for the development and evaluation of human phenome standards.

A statement from the proposer as to how the proposed work may relate to or impact on existing work, especially existing ISO and IEC deliverables. (The proposer should explain how the work differs from apparently similar work, or explain how duplication and conflict will be minimized. If seemingly similar or related work is already in the scope of other committees of the organization or in other organizations, the proposed scope shall distinguish between the proposed work and the other work. The proposer shall indicate whether his or her proposal could be dealt with by widening the scope of an existing committee or by establishing a new committee.)

The Technical Committee on Human Phenome will work closely with the relevant committees, avoiding overlapping work of standardization activities, and will work closely with all other organizations interested in the standardization of human phenome to advance the work of the Technical Committee in order to meet the urgent needs of standardization in the field of human phenome.

The Technical Committee will not cover the work of other technical committees, including but not limited to ISO/TC276 (Biotechnology), ISO/TC215 (Health Information), ISO/IEC JTC 1/SC 29 (Coding of audio, picture, multimedia and hypermedia information), ISO/IEC JTC1/SC37 (Biometrics), and ISO/TC249 (Traditional Chinese Medicine).

A listing of relevant countries where the subject of the proposal is important to their national commercial interests.

The standardization of human phenome has important scientific and economic values, involving the interests of many countries, organizations and institutions around the world.

It has become the consensus of international community to carry out research and technology development of human phenome, another strategic field after the Human Genome Project. It will help to comprehensively interpret the key information coded in the human life. The development of human phenome standards will promote the international recognition of phenome data.

In October 2018, 24 internationally renowned research institutions and universities from 17 countries (China, the United States, Australia, the United Kingdom, Russia, Germany, Sweden, Finland, Singapore, Canada, Costa Rica, Ghana, Ethiopia, Japan, India, the Philippines and Kazakhstan) jointly sponsored to support the International Human Phenome Project, and The International Human Phenome Consortium (IHPC) and its Working Group on Standards and Specifications were formally established. Scientists from these countries have reached consensus on the importance of standardization of human phenome.

IHPC brings together the major research powers of major developed countries in Europe and the United States along with the developing countries. The 22 institutions include 10 internationally renowned research institutes, including:

1. Institute for Systems Biology, United States;
2. MRC-NIHR National Phenome Center, United Kingdom;
3. Vavilov Institute of General Genetics, Russian;
4. Chinese Academy of Medical Sciences;
5. National Center for Child Health and Development, Japan;
6. Nanyang Technology University, Singapore;
7. University Hospital Freiburg, Germany;
8. Leibniz Research Institute for Environmental Medicine, Germany;
9. Institute of Genomics and Integrative Biology, India;
10. National Center for Biotechnology, Kazakhstan.

and 14 internationally renowned universities, including:

1. Australian National Phenome Center, Murdoch University, Australia;
2. Imperial College London, United Kingdom;
3. University of Liverpool, United Kingdom;
4. Karolinska Institute, Sweden;
5. University of Helsinki, Finland;
6. Harvard University, United States;
7. University of Alberta, Canada;
8. University of Costa Rica, Costa Rica;
9. University of Health and Allied Sciences, Ghana;
10. Addis Ababa University, Ethiopia;
11. Fudan University, China;
12. University of Chinese Academy of Sciences, China;
13. University of Liverpool, United Kingdom;
14. University of the Philippines Manila, Philippines.

At the same time, the development of human phenome standards will meet the urgent needs of medical industry, health industry, hospitals, universities, and scientific research institutions for human phenome standards, improve the accuracy of human phenome detection, promote the comparability of human phenome data across technology platforms and countries, avoid repeated measurements and wrong decisions caused by the inaccuracy of measurement results, reduce

A listing of relevant external international organizations or internal parties (other ISO and/or IEC committees) to be engaged as liaisons in the development of the deliverable(s). (In order to avoid conflict with, or duplication of efforts of, other bodies, it is important to indicate all points of possible conflict or overlap. The result of any communication with other interested bodies shall also be included.)

IHPC, MAQC, HPCC, and the International Institute of Human Phenome of China can be engaged as liaisons in the development of deliverable(s). There is no conflict or overlap with other ISO/IEC committees. ISO/TC276, ISO/TC215, ISO/IEC JTC1/SC37 and ISO/TC249 will be communicated and can play coordinating roles in the process of standardization of human phenome.

A simple and concise statement identifying and describing relevant affected stakeholder categories (including small and medium sized enterprises) and how they will each benefit from or be impacted by the proposed deliverable(s).

Twenty-four research institutions from 17 countries around the world are conducting human phenome research within the “International Human Phenome Consortium (IHPC)". The standards on human phenome to be developed will provide a unified yardstick for research institutions and enterprises in various countries, promote information exchange and lead to mutual trust in the field of human phenome research, producing great social benefits, and promote the international equivalence and consistency of global human phenome research.

At present, world-renowned pharmaceutical companies and new drug R&D enterprises have begun to use phenome measurement data to help them objectively evaluate the efficacy and safety of drugs, so as to improve the efficiency of new drug R&D. The results of human phenome standardization will bring huge economic and social benefits for drug research and development, clinical applications, and so on.

An expression of commitment from the proposer to provide the committee secretariat if the proposal succeeds.

Should ISO approve the establishment of a Technical Committee on Human Phenome, China is committed to providing the committee secretariat.

We would actively contact interested relevant parties (such as IHPC), relevant countries (such as the United States, Germany, the United Kingdom and other countries);

We would actively contact other relevant ISO technical committees such as: ISO/TC276, ISO JTC 1/SC 29, JTC1/SC37, ISO/TC215, ISO/TC 249, ISO TC 212, ISO/REMCO, ISO/TC 12, ISO/TC 69, etc.

We would liaise with BIPM, IFCC, ILAC, WHO and other international institutions to jointly promote the work and development of the TC.

We would do our best to achieve the international standardization of human phenome.

Purpose and justification for the proposal. (The purpose and justification for the creation of a new technical committee shall be made clear and the need for standardization in this fieldshall be justified. Clause C.4.13.3 of Annex C of the ISO/IEC Directives, Part 1 contains a menu of suggestions or ideas for possible documentation to support and purpose and justification of proposals. Proposers should consider these suggestions, but they are not limited to them, nor are they required to comply strictly with them. What is most important is that proposers develop and provide purpose and justification information that is most relevant to their proposals and that makes a substantial business case for the market relevance and the need for their proposals. Thorough, well-developed and robust purpose and justification documentation will lead to more informed consideration of proposals and ultimately their possible success in the ISO IEC system.)

Through systematic characterization of the human features, the multi-level association, integration and holistic applications of the interrelationships between genes, environment and phenotypes can be discerned. Standardization of the process for the discovery of the intrinsic laws governing the formation of phenotypic characteristics such as human health and disease and the discovery of biomarkers will bring a revolutionary impetus to the bio-industry and pharmaceutical research and development.

The goal of the Technical Committee on Human Phenome is to standardize the whole process from cross-scale convergence to fusion analysis of big data sets of human phenotypes. Through the establishment of the standardization system, the global sharing of human phenome standards can be achieved.

The scope of the technical committee includes terminology and classification of human phenome; measurement results and data quality of human phenome (such as macro measurement, data analysis and quality requirements); reference standards of human phenome (such as establishment of reference maps, characteristics and requirements of materials); standards for the systematic characterization and construction of human phenome; application of human phenome, etc.

The human phenome study has become a global focus. It is the study of the entire set of human characteristics (phenotypes) as they change in response to genetic mutations and environmental influences. From the breadth, depth and longitudinal dimensions, from micro- to macro-level, it systematically measures and characterizes the internal and external characteristics of organisms. It uses macro-measurement technology (high-throughput phenotypic analysis technology) combined with big data mining methods to describe the multi-scale relationship among genotypes, environments and phenotypes, and constructs a cross-scale, highly complex and dynamic knowledge map of human phenome data. Faced with the new paradigm of life sciences research, human phenome research in the world is still on its own. It is necessary to establish a standardized system of human phenome to facilitate a new breakthrough for human biomedical research. It has tremendous market and clinical application potentials (Zheng Y, et al., *Biomarkers in Medicine*, 2015).

Because of the cross-scale and high complexity nature of human phenome research, the lack of standards will inevitably lead to problems, for example, tens of thousands of human phenotypes entries cannot be expressed probably and uniformly, different measurement methods and data results cannot be mutually integrated, which will limit the development of human phenome research (Baker M, *Nature*, 2016). Under the framework of unified scale and standardization system, it will facilitate the integration, sharing, and mining of global data, thus accelerating the development and application of this innovative field.

Signature of the proposer LI Yubing

Further information to assist with understanding the requirements for the items above can be found in the Directives, Part 1, Annex C.