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Organisation internationale de normalisation
International Organization for Standardization
Международная Организация по Стандартизации

TO THE ISO MEMBER BODIES

Our ref. TS/P 235 (REV)

Date 2013-02-27

ISO/TS/P 235 – *Cell-combined medical products*

Dear Sir or Madam,

Please find attached a proposal for a new field of technical activity on *Cell-combined medical products* submitted by KATS (Rep. of Korea).

According to subclause 1.5.6 of Part 1 of the ISO/IEC Directives, you are kindly invited to complete the ballot form (Form 02) which can be downloaded at www.iso.org/forms and send it (preferably in Word format) to the Secretariat of the ISO Technical Management Board at *tmb@iso.org* before **27 May 2013.**

Yours faithfully,

Sophie Clivio,
Secretary of the Technical Management Board

Encl.: TS/P 235
Form 1 (REV)
Annex

PROPOSAL FOR A NEW FIELD OF TECHNICAL ACTIVITY	
Circulation date: Closing date for voting:	Reference number (to be given by Central Secretariat)
Proposer KATS	**ISO/TS/P**

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 or subcommittee, 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.)

Cell-combined medical products (CCMPs)

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 of guidelines for the cell-combined medical products(CCMPs) which consist of therapeutic cells and biomaterials designed to be delivered into the body to restore, replace defects and/or regenerate physiological functions is necessary.

The standards and guidelines include the terminology, specification, procedures in producing therapeutic cell expansion, cell-biomaterial hybridization, in vitro and in vivo experiments, and clinical trials for the cell-combined medical products(CCMPs).

These standards exclude 1)minimally manipulated cells/tissues/organ medical products (CTOMPs) intended for transplantation; 2)gene therapy; 3)blood transfusion; 4)extracorporeal devices containing living cells.

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.

Main components of the CCMPs are 1)autologous or allogeneic cells and 2) biomaterials (synthetic or natural)which are hybridized with the cells to provide and promote cellular functions necessary for the treatment goal.

The CCMPs are manufactured in forms of 1)injectable single cell suspension or 2)artificially manufactured multicellular structures that are named as tissue engineered medical products (TEMPs).

The standards for the CCMPs may include
-terminology
-categories and/or classification
the technologies of
-general requirements
-risk management
-cell harvestment (autologous or allogeneic)
-manipulation of therapeutic cells (e.g., gene modification, cell expansion)
-biomaterials for CCMPs (e.g., for single cell encapsulation or TEMPs)
a. bioinert or biodegradable
b. synthetic or natural (autologous, allogeneic or xenogeneic)
-procedures of cell hybridization with biomaterials
-in vitro analysis of CCMPs (e.g., cell viability, immunology)
-in vivo trial (e.g., animal experiments)
-clinical trials
other technologies appropriate to manufacture CCMPs to be developed in the future

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.)

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.)

Please refer to the Annex

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.)

TC150/SC7 (Tissue engineered medical products, TEMPs) has a very limited scope on the medical products consist of therapeutic cells hybridized with non-biological synthetic polymers that covers only a part of the CCMP. Representative type of CCMP is the injectable single cell suspension hybridised with natural/synthetic polymeric vehicle but that product is out of the scope of TC150/SC7. Furthermore, TEMPs manufactured by cells combined with natural polymeric materials which provide biological functions are also out of the committee. And the TC150/SC7 is less activated since the experts participated in TC150 are mainly from non-vital surgical implants.

TC194/SC1 (Tissue product safety) is working on standardization of preventing/protecting biologically-driven substances from contamination and/or infection. In 2012, the committee published a standard document "ISO 13022 Application of risk management to health care products containing viable human cells" which provides requirements for viable cell manipulation that shall be handled under aseptic condition, because it is impossible to sterilize cells with maintaining viability. This standard is applicable to the related standards which are whithin the scope of this new technology committee.

The scope of a new TC titled “Biotechnology” is very valuable to avoid any conflict with the proposal for a new TC of “Cell Combined Medical Products” from KATS. We could understand that TC “Biotechnology” may cover “Terms and definitions, Analytical methods in the realm of -omics" technologies, Computing tools,bioinformatics for international comparability and integrability of data, Bioresources, Biobanking, Bioreactors, Metrology aspects of biotechnology (e.g. enzymology). The subjects are mainly related to analysis technologies at the genetic levels for biopharmaceuticals, but not to the living cell-combined medical products which are directly delivered into body. Of course, some related technologies in the TC “Biotechnology” are applicable at the very initial step of isolating, selecting, and gene-modifying “therapeutic cells” which are combined with the biomaterials for producing CCMPs. As TC “Biotechnology” noted that “The committee will not pursue standardization of forensic science, research, as well as applications for the agricultural-, food-, and medical industries”, it is clear that TC “CCMPs”, distinctly manufactured by Medical industries, is not under TC “Biotechnology. The new proposed TC “CCMPs” will mainly concern guidelines and standards for manufacturing processes applied to “Medical Products” definitely different from the “Pharmaceuticals” at TC “Biotechnology”.

Of course, this new TC “CCMPs” will not pursue scopes of TC 150, 194, 198, 212, and TC “Biotechnology”, but setup close cooperative activities through establishing official liaisons with them.

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

KATS (Kor), BSI (U.K.), ANSI (U.S.A.), JISC (Jap), DIN (Ger), Brazil, China, Holland, etc.

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.)

ISO TC150/SC7, TC194/SC1, TC198, TC210, TC212, VAMAS

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).

Governmental regulatory systems on biological- medical products.
Manufacturers producing cell integrated products.
Medical clinics using therapeutic cells.

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

KATS is ready to invite related experts from ISO member bodies as the TC secretariat.

Purpose and justification for the proposal. (The purpose and justification of the standard to be prepared shall be made clear and the need for standardization of each aspect (such as characteristics) to be included in the standard shall be justified. Clause C.4.12.1 through C.4.12.10 of Annex C of the ISO/IEC Directives, Part 1 contain 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.)

The CCMPs have been recently introduced, rapidly grown and expanded in medical markets, and regarded as the representative products that replace large part of the conventional drug or surgical implant markets that are intended to be used indistinctly. By using CCMPs, the philosophy of medical practice is changing from the conventional concept of medication and surgery to the personalized therapy that provides fundamental treatment of disease (including genetic diseases oriented from the individual genetic disorders) and defects (including both anatomical and physiological recoveries) to each patient. Drug is any chemical compound produced by chemical engineering or biotechnology, and surgical implant is designed and manufactured by non-viable biomaterials.

As CTOMPs are classified into type I (cell, tissue, organ transplants or grafts which are minimally manipulated after procurement from donors and transferred to recipients by medical practitioners) and type II (CCMP or cell-based implants which are manufactured by hybridizing therapeutic cells with biomaterials in forms of injectable single cell suspensions or TEMPs).

The main treatment efficacy of a CCMP comes from living cells in the product that are artificially manipulated in vitro for each patient, and shall be under the absolutely different conditions from conventional drugs and/or surgical implants. But it is not globally agreed that CCMPs shall be categorized in drugs (chemicals or biologics) and medical implants (made of non-viable biomaterials), and are regulated as the combination products in some nation. Differences in applying standards between drugs and medical devices result in various embarrassments in the global trade market, and furthermore, it is difficult to ensure the safety of the CCMPs.

In ISO TC150 (Surgical implants), SC7 (Tissue engineered medical products) is in activity, and scope of ISO TC150 SC7 declares the scaffolds only made by non-biological materials. The injectable single cell suspension products and TEMPs consist of therapeutic cells hybridized with biological materials are in exception.

In TC194 (Biological evaluation of the medical devices), SC1 (Tissue product safety) WG 1 (Risk assessment, terminology and global aspects) has developed a standard ISO 13022 “Application of risk management to health care products containing viable human cells” in association with viable cellular component(s) of products regulated as medicinal products, biologics, medical devices and active implantable medical devices or combinations thereof. It covers viable human materials of autologous as well as allogeneic human origin, obtained from living or deceased donors. It mainly concerns on protecting viable components of the products from extrinsic hazardous contamination. Furthermore, it does not include non-viable biological materials to be hybridized with cells.

Therefore, establishing a new technical committee of the cell-combined medical products(CCMPs)in ISO, and setting global standards for the products is extremely required at present

Signature of the proposer

SEO, Kwang-Hyun
Administrator
Korean Agency for Technology and Standards

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

Comments of the Secretary-General (to be completed by the Central Secretariat)

Signature

Annex

(A listing of relevant existing documents at the international, regional and national levels)

ISO 10993-1, Evaluation of biological safety of medical instrument -- Part 1: Evaluation and Testing
ISO 10993-7:1995, Biological evaluation of medical devices -- Part 7: Ethylene oxide sterilization residuals
ISO 11607-1:2006, Packaging for terminally sterilized medical devices -- Part 1: Requirements for materials, sterile barrier systems and packaging systems
ISO 11607-2:2006, Packaging for terminally sterilized medical devices -- Part 2: Validation requirements for forming, sealing and assembly processes
ISO 13022: 2012, Application of risk management to health care products containing viable human cells
ISO 13485:2003, Medical devices -- Quality management systems -- Requirements for regulatory purposes
ISO 14155-1:2003, Clinical investigation of medical devices for human subjects -- Part 1: General requirements
ISO 14155-2:2003, Clinical investigation of medical devices for human subjects -- Part 2: Clinical investigation plans
ISO 14630, Non-active surgical implant -- General requirements
ISO 14971:2000, Medical devices -- Application of risk management to medical devices

Korea
KSP 1600:2007 General guideline of safety test for the cell based therapeutic substances
KFDA Code of human cell/tissue/organ Bank
KFDA Code of cell engineered products
KFDA Code of biologics

United Kindom
Code of Practice for Tissue Bank
Code of Practice for Human Tissue Products

United States of America
21 CFR Parts 210 and 211 Drug Current Good Manufacturing Practices
21 CFR Part 312 IND regulations
21 CFR Parts 600-680 Biologics Regulations
21 CFR Parts 1270-1271 Human Tissue Regulations
FEDERAL REGISTER; Application of Current Statutory Authorities to Human Somatic Cell Therapy Products and Gene Therapy Products; Notice - 10/14/1993
FEDERAL REGISTER; Human Cells, Tissues, and Cellular and Tissue-Based Products; Donor Screening and Testing, and Related Labeling; Interim Final Rule - 5/24/2005
FEDERAL REGISTER; Current Good Tissue Practice for Human Cell, Tissue, and Cellular and Tissue-Based Product Establishments; Inspection and Enforcement; Final Rule - 11/18/2004
FEDERAL REGISTER; Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products; Final Rule - 5/25/2004
FEDERAL REGISTER Human Cells, Tissues, and Cellular and Tissue-Based Products; Establishment Registration and Listing; Interim Final Rule; Correction - 1/30/2004
FEDERAL REGISTER Human Cells, Tissues, and Cellular and Tissue-Based Products; Establishment Registration and Listing; Interim Final Rule; Opportunity for Public Comment - 1/23/2004
Guidance for Industry: MedWatch Form FDA 3500A: Mandatory Reporting of Adverse Reactions Related to Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) - 11/30/2005
Draft Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (HCT/Ps) - 5/20/2004
Public Health Service Guideline on Infectious Disease Issues in Xenotransplantation - 1/19/2001
Guidance for Industry: Source Animal, Product, Preclinical, and Clinical Issues Concerning the Use of Xenotransplantation Products in Humans - 4/3/2003
Draft Guidance for Reviewers: Instructions and Template for Chemistry, Manufacturing, and Control (CMC) Reviewers of Human Somatic Cell Therapy Investigational New Drug Applications (INDs) - 8/15/2003
ASTM F2312-04 Standard Terminology Relating to Tissue Engineered Medical Products
ASTM F2211-04 Standard Classification for Tissue Engineered Medical Products (TEMPs)
ASTM F2210-02 Standard guide for processing cells, tissues, and organs for use in tissue engineered medical products

ASTM F2027-00 Standard guide for characterization and testing of substrate materials for tissue engineered medical products
ASTM F2150-02 Standard guide for characterization and testing of biomaterial scaffolds used in tissue engineered medical products
ASTM F2212-02 standard guide for characterization of type I collagen as starting material for surgical implants and substrates for tissue engineered medical products (TEMPs)
ASTM F2315-03 Immobilization or encapsulation of living cells or tissue in alginate gels
ASTM F2383-05 Standard guide for assessment of adventitious agents in tissue engineered medical products
ASTM F2386-04 Standard guide for preservation of tissue engineered medical products (TEMPs)