Scope: To develop standards for the biomaterials used in tissue engineered medical products.

Task Groups:

F04.43.01 - Substrates Guide - Lilsa Kuhn (kuhn_l@a1.tch.harvard.edu)
F04.43.02 - Scaffolds - Debi Mukherjee (dmukhe@lsumc.edu)
F04.43.03 - Collagen - Jack Parr (jparr@wmt.com)
F04.43.04 - Alginate – David Kaplan (dsk@cdrh.fda.gov)
F04.43.05 - Skin - Fred Cahn (fred_cahn@integra-ls.com)
F04.43.06 - Cartilage - Carmelita Frondoza (cgfrondo@welchlink.welch.jhu.edu)
F04.43.07 - Bone – Floyd Larson/Angela Blackwell (flarson@paxmed.com; aeb@cdrh.fda.gov)
F04.43.08 - Soft Tissue -
F04.43.09 - Cardiovascular - Lloyd Wolfinbarger (altmolec@aol.com)
F04.43.10 – Chitosan – David Kaplan (dsk@cdrh.fda.gov)

Draft Documents and Status:

Subcommittee/ Task Group	Designation	Title	Status
F04.43.01 Kuhn	F2027-00	*Standard Guide for Characterization and Testing of Substrate Materials for Tissue Engineered Medical Products*	Approved standard
F04.43.02 Mukherjee	New draft	*Guide for Scaffolds Used for TEMPS*	Under development
F04.43.03 Parr	New draft	*Draft Guide for Characterization of Collagen for Surgical Implants*	Expect draft for discussion at 11/00 meeting
F04.43.04 Domish/Kaplan	Draft z8425z	*Draft Guide for Characterization and Testing of Alginates as Starting Materials Intended for Use in Biomedical and Tissue Engineered Medical Product Applications*	Issued to F04.43 subcommittee ballot, F04.43(00-2); may proceed to Main ballot, F04(00-2); expect resolution of comments and negatives at 11/00 meeting.
F04.43.05 Cahn	New draft	*Draft Classification of Biomaterials Used in TEMPS for Skin*	Under development
F04.43.06 Frondoza	New draft	*Draft Guide for the Characterization of Biomaterials Used for Articular Cartilage*	Under development
F04.43.07 Larson/Blackwell	Pre-draft	*Draft Guide for Fabricated Biomaterials Used in TEMPS and Substituted for Repaired or Regenerated Bone*	Under development
F04.43.10 Kaplan	New draft	*Draft Guide for the Characterization and Testing of Chitosan as Starting Materials Intended for Use in Biomedial and TEMPS Applications*	Under development

F04.44 on Biomolecules

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Scope: To develop standards for the biomolecules, natural and/or recombinant, used in tissue engineered medical products.

Task Groups:

F04.44.01 - Bone Morphogenetic Protein - Thomas Porter (tporter@genetics.com)
F04.44.02 – Proteins – Thomas Porter (tporter@genetics.com)

Draft Documents and Status:

Subcommittee/ Task Group	Designation	Title	Status
F04.44.01 Porter	New draft	*New Standard Test Method for Vitro Biological Activity of Recombinant Human Bone Morphogenetic protein-2 (Rhbmp-2) Using the @-20 mouse Stromal Cell Line*	Balloted to Main ballot F04(00-1); withdrawn from ballot to resolve open negatives. Future ballot expected.
F04.44.02 Porter	Pre-draft	*Draft Guide for Proteins Used in TEMPS*	Under development.

F04.45 on Cells

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Scope: To develop standards for cells in tissue engineered medical products that may contain a local and/or systemically-acting cellular or tissue component of autologous, allogeneic, or xenogeneic origin or genetically modified cells of any species which may be formulated with a synthetic or natural material and/or biomolecule.

Task Groups:

F04.45.01 - Living Cells - Lisa Christenson (lchristenson@earthlink.net)
F04.45.02 - Cells and Processing - Paul Price (pprice@lifetech.com)
F04.45.03 - Preservation – Hubel – ()
F04.45.04 – Impedence tests – Steve Szabo (steve.szabo@coulter.com)
F04.45.05 – Biomarkers – Joan Zeltinger (joanz@san.rr.com)
F04.45.06 – In vitro Production and Processing – Joan Zeltinger (joanz@san.rr.com)

Draft Documents and Status:

Subcommittee/ Task Group	Designation	Title	Status
F04.45.01 Christenson	New draft	*Draft Guide for the Development of TEMPS with Living Cells*	Under development
F04.45.02 Price	New draft	*Draft Guide for Classification of Cells and Cell Processing*	Expect draft for ballot after 11/00 meeting
F04.45.03 Hubel	Pre-draft	*Draft Guide for Preservation of Cells*	Under development
F04.45.04 Szabo	New draft	*Draft Impedence Test Method for Cell Counting*	Expect draft for review at 11/00 meeting.
F04.45.05 Zeltinger	Pre-draft	*Draft Guide for Biomarkers of Visibility*	Under development
F04.45.06 Zeltinger	Pre-draft	*Draft Guide for In vitro Production and Processing*	Under development

F04.46 on Delivery Systems

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F04.46 on Delivery Systems (Continued)

Scope: To develop standards for the systems used to deliver to the intended site, cells and/or biomolecules for tissue engineered medical products.

Task Groups:

F04.46.01 - In-vivo Delivery Systems – Michael May (maymi@chem-eng.vtoronto.ca)
F04.46.02 – Encapsulation – Jan Stegmann (gte938f@prism.gatech.edu)

Draft Documents and Status:

Subcommittee/ Task Group	Designation	Title	Status
F04.46.01 May	New draft	*Draft Standard Guide for the Classification of In-Vivo Delivery Systems*	Expect draft for discussion at 11/00 meeting
F04.46.02 Stegemann	New draft	*Draft Standard Guide for Classification of Encapsulation*	Expect draft for ballot at 11/00 meeting

F04.47 on Assessment

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Vice-chair:
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Scope: To develop standards for the pre-clinical evaluation of tissue engineered medical products.

Task Groups:

F04.47.01 - Bone - Barbara Boyan (boyanb@uthscsa.edu)
F04.47.02 - Cardiovascular – Carlyle
F04.47.03 - Liver - Linda Custer (custer@alum.mit.edu)
F04.47.04 - Islets - Jack O'Neill (oneilj@joslab.harvard.edu)
F04.47.05 - Skin - Eliane Schutte (eliane.schutte@isotis.com)
F04.47.06 – Implantable Devices - Ron Ingram (ron_ingram@integra-ls.com)
F04.47.07 - Soft tissue/ligaments/tendon - Karen Ohland (ohlandk@asm.org)
F04.47.08 – Bone – Barbara Boyan (boyanb@uthscsa.edu)
F04.47.09 – Assessment framework and template – Barbara Boyan (boyanb@uthscsa.edu)
F04.47.10 –Meniscus – Malaviya
F04.47.11 – Pancreas – Jack O'Neill (oneilj@joslab.harvard.edu)

Draft Documents and Status:

Subcommittee/ Task Group	Designation	Title	Status
F04.47.01 Boyan	New draft	*Draft Guide for the Assessment of Bone Inductive Materials*	Under development
F04.47.02 Carlyle	New draft	*Draft Standard Guide for the Assessment of Cardiovascular Cells*	Selection of TG participants
F04.47.03 Custer	Pre-draft	*Draft Guide for Assessment of Liver TEMPS*	Under development
F04.47.04 O'Neill	Pre-draft	*Draft Standard Test Method for Assessment of Islets*	Selection of TG participants
F04.47.05 Schutte/Ritter	Pre-draft	*Draft Standard Test Method for Assessment of Skin Cells*	Selection of TG participants
F04.47.06 Ingram	New draft	*Draft Standard Test Method for Cartilage*	Under development
F04.47.07 Ohland	Pre-draft	*Draft Standard Test Method for Assessment of Ligament and Tendon Cells*	Selection of TG participants

F04.47.08 Boyan	New draft	*Draft Guide for Assessment of Bone TEMPS*	Under development
F04.47.09 Boyan	New draft	*Draft Guide for an Assessment Framework*	Expect draft for ballot after 5/00 meeting
F04.47.10 Malaviya	Pre-draft	*Draft Guide for Assessment of Meniscus TEMPS*	Under development
F04.47.11	Pre-draft	*Draft Guide for Assessment of Pancreas TEMPS*	Under development

F04.48 on Clinical Testing

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Scope: To develop standards for clinical trials associated with tissue engineered medical products.

Task Groups:

F04.48.01 - Clinical Outcomes - Michael Sabolinski (msabolinski@organo.com)
F04.48.02 – Clinical Trials – David Watkins (watkinswd@msx.upmc.edu)

Draft Documents and Status:

Subcommittee/ Task Group	Designation	Title	Status
F04.48.01 Watkins	New draft	Draft Standard Guide for Clinical Testing	Selection of TG participants
F04.48.01 Watkins	Pre-draft	Draft Guide for Surrogate Endpoint Analyses in Clinical Trials for TEMPS	Under development

F04.49 on Microbiological Safety and Adventitious Agents

Chair:

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Vice-chair:
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Scope: To develop standards which identify and minimize/eliminate the microbiological risk in the manufacture and use of tissue engineered medical products.

Task Groups:
F04.49.01 - Framework – Mark Citron ()

Draft Documents and Status:

Subcommittee/ Task Group	Designation	Title	Status
F04.49.01 Citron	Pre-draft	*Draft Guide to the Framework for Microbiological Safety and Adventitious Agent for TEMPS*	Under development

Communications - Mary Fuka (Quetzal Computational Associates) (mary@quetzalcoatl.com)

Publicity/Public Relations - Mrunal Chapekar (NIST) (mrunal.chapekar@nist.gov)

Appendix B

Commercially Available Bone Substitutes used for Orthopaedic Reconstruction, Maxillofacial or Cranial Surgery

The following list was compiled by the UK Medical Devices Agency in 1999. It should be noted that the product details/descriptions have been obtained from product literature and scientific journals. The accuracy of the information has not been fully verified however the table does confirm the wide variety of biomaterials that are utilised in the manufacture of bone substitutes.

The starting materials for bone substitutes is quite diverse and varies from coral, bovine or human bone, and compositions of calcium phosphate/hydroxyapatite, with or without growth factors. The majority of products provide mechanical support in reconstructive surgery for damaged or diseased bone. The presentational form includes a wide variety of sizes and configurations for either load bearing or non-load bearing applications. Those that utilise raw materials of animal origin fall within the scope of the Medical Device Directive (93/42/EEC), such as Lubboc, Surgibone and Oxbone, which are of bovine origin. Those made of bone of human origin are excluded from the regulatory controls of the Directive but may well fall within the scope of other pre-existing controls.

Allogran-N (Biocomposites/Corin)

Crystalline structure derived from bovine bone for use in maxillofacial and cranial applications.

Bio-Gide (Biomaterials Geistlich)

Resorbable collagen membrane of porcine origin for use in maxillofacial and cranial applications.

Bio-Oss (Biomaterials Geistlich)

Bovine based implant for use in orbital and cranial applications.

Biosel 2 (Biomaterials Bioland)

Porous HA/TCP ceramic composite for fractures, bone unions and void replacements.

Body Parts (Tissue International Inc)

Range of human bones harvested from screened and tested cadavers.

Bonesource (Osteogenic Inc)

Hydroxyapatite bone cement for fractures, with FDA clearance.

Bone products (Pacific Coast Bank)

Range of human bones harvested from screened and tested cadavers.

BOP Biocompatible osteoconductive polymer (Norbridge Medical)

PVP/PMMA for spinal applications.

Bone Products (Pacific Coast Bank)

Range of human bones, blocks or granules harvested from screened and tested cadavers.

Calciresorb (Ceraver Osteal)

Resorbable tricalcium phosphate in granule form for orthopaedic applications.

Cerapatite (Ceraver Osteal)

Blocks of hydroxyapatite for fractures and bone unions.

Collagraft (Collagen Corp)

Ceramic/Collagen/ HA/TCP implant with autogenous marrow for fracture repair.

Endobon (Biomet Merck)

Bovine material converted to hydroxyapatite form for spinal applications.

Grafton (Osteotech Inc)

Human demineralized bone matrix for bone void filler and remodelling .

Healos (Orquest Inc)

Hydroxyapatite coated collagen fibres for spinal and fractureapplicatins

Lubboc (De Puy)

Bovine bone processed to blocks, wedges and cyclinders for spinal applications.

Neo-Osteo (Sulzer Orthopaedics Ltd)

Lyophilised bovine bone and collagen for use in spinal applications

OP-1 (Creative Biomolecules)

Osteogenic protein from recombinant technology for bone remodelling process in fractures etc.

Orthodyn (Dynagen Inc)

Resorable bone cement to encourage bone integration with joint replacements.

Ossigel (Orquest Ltd)

Hyaluronic matrix scaffold with fibroblast growth factor to stimulate the osseointegration process.

Osteoset (Wright Medical)

Resorable synthetic calcium sulphate bone replacement in pellet form, for fractures etc.

Oxbone (Bioland Ltd)

Bovine bone matrix structure for load bearing applications in bone fractures, spinal and unions.

Pro Osteon (Interpore Ltd)

Coralline hydroxyapatite porous structure for bone grafts in fracture and tumour applications

rh-BMP2 (Genetics Institute)

HA/TCP/Growth factor as bone substitute for bone repair

Super-Fixsorb (Takiron)

Artificial bone of bio ceramic particles and polylactic acid.

Surgibone (Unilab Inc)

Hydroxyapatite and tricalcium phosphate stucture for bone ingrowth in spinal applications.

ISO TC 150 WG 11 **N3**

ISO TC 150 WG 11

Tissue Engineering

Terms of Reference

"To develop specific new Work Item proposals for standardisation of tissue engineered implants and to recommend to ISO/TC 150 which technical group, either within ISO TC 150 or elsewhere, is most appropriate to conduct the work."

– ISO TC 150 Resolution 298 (Stockholm, 2000)

ISO TC 150 WG11 N5

EUCOMED
(Incorporating JAPM)

Industry Position on

Human Tissue Product[1] Regulation

Introduction

This *industry* Position has been prepared by EUCOMED which represents a large majority of the European medical technology industry, hereafter referred to as "*industry*". EUCOMED members comprise companies with European operations and national and pan-European organisations in the medical technology sector. Currently, EUCOMED represents more than 2,500 companies employing approximately 300,000 EU citizens that provide tens of thousands of healthcare products within the EU and globally. More than 85% of these companies are considered to be Small and Medium size Enterprises (SMEs).

The majority of medical technology products are already covered by existing community directives for medical devices (90/385/EEC, 93/42/EEC and 98/76/EEC) which provide a high level of patient safety for a wide range of products. The products and technologies being addressed in this *industry* Position are currently not regulated at community level.

This paper sets out *industry's* Position regarding the need for specific European regulation of medical technology products manufactured using or containing human tissues and/or their derivatives, hereafter referred to as "*human tissue products*". It analyses the current situation, the nature of the technology involved and proposes an approach that *industry* considers appropriate for European legislation to ensure patient safety, patient benefits and patient access on a community wide basis.

As part of the preparation of this *industry* Position, industry has considered the current status of national regulation within Europe and elsewhere in the world. It has also looked at other ongoing initiatives, such as the standardisation work in progress on human tissue engineered medical products. The *industry* task force continues to consult worldwide with healthcare professionals, regulatory authorities, tissue banks and other relevant organisations with a view towards achieving a global approach to regulation of these products.

The Need for European Regulation

In Europe there exist diverse national approaches to the regulation of *human tissue products*. This presents a confused and difficult community-wide environment for consistent and safe development, registration, and marketing of *human tissue products*. If not resolved, this will result in further discouragement of European R&D investment and deny patients access to benefits, many of which are life-saving provided, by these products.

[1] *Human Tissue Products* are defined within this position as medical technology products manufactured using or containing human tissues and/or their derivatives.

The rapid advances in the development of *human tissue products* are outpacing attempts to provide appropriate regulation. Any European regulation developed needs to be capable of addressing the particular requirements of these products and provide a streamlined process for their timely introduction into public health systems.

In developing this proposal *Industry* has recognized the need for European regulators to utilize expertise from multi-disciplinary regulatory areas, ie., biologics, medical devices. This is highlighted in the USA, where the unique nature of these products has triggered FDA to begin development of a new regulatory scheme to address their specific needs through the combined efforts of the Center for Biologics Evaluation and Research (CBER) and the Center for Devices and Radiological Health (CDRH).

In the interest of harmonizing approaches as far as practicable, this *Industry* Position has taken due account of the FDA's proposal and is intended to facilitate future global harmonization, whilst focusing on specific European regulatory needs.

The Technology, Stake-holders and Key Issues

A set of agreed terms for global application needs to be developed. For the purposes of this *Industry* Position, human tissues are defined as constituent parts of the human body such as: bones, skin, heart valves, cornea, tendons, cartilage, arteries, veins, dura mater, placenta and umbilical cord. This *Industry* Position also covers human cells intended for grafting, tissue repair and cell lines from cell cultures.

This *Industry* Position excludes:

- solid organs for traditional transplantation
- blood and blood products, where they are currently regulated or regulation is under consideration,
- gametes, reproductive tissues and embryos, which are covered by specific national rules and give rise to specific ethical issues; and
- tissues stored in genomic banks for obtaining genetic information (DNA).

The number of *human tissue products* is increasing and ranges from minimally manipulated products such as cornea, to highly manipulated products such as cultured and modified cell lines and tissues with or without systemic effect. *Industry* proposes that the following types of products should be within the scope of future European regulation:

- autologous *human tissue products* (i.e., the cells or tissues utilised in the product are implanted, transplanted, infused or transferred back to the individual from whom the cells or tissues were obtained)
- allogeneic *human tissue products* (i.e., the cells or tissues utilised in the product are derived from a different individual to the recipient of the product)

There are a number of stakeholders involved in the collection, handling, storage, manipulation, distribution, access and use of *human tissue products*.

These include:

- donors and their families
- procurement/collection organisations
- organisations involved in development, production or distribution of *human tissue products*
- health technology assessors
- healthcare professionals
- recipient patients and their families
- healthcare providers
- regulators

There are key issues including:

- safety
- quality
- traceability
- effectiveness of the product for its intended use
- ethical considerations including consent, confidentiality, data protection and non-profit donation
- commercial aspects
- surveillance of donors and recipients

all of which need to be carefully addressed in the course of developing appropriate regulation.

A Risk/Benefit Based Approach

Industry favours a risk/benefit based "multi-tiered" approach to European regulation of *human tissue products* which would provide a high level of protection of public health. In a multi-tiered approach, the level of regulation and its supporting processes would increase in proportion to the product risk, and thus ensure patient safety, product quality and effectiveness.

A risk/benefit approach would take into consideration a number of factors such as:

- tissue type (considering specific risks associated with the type of tissue)
- source of tissue (autologous or allogeneic)
- degree of manipulation (minimal to high)
- mode of action (local to systemic)
- intended use (elective to life saving treatment)
- quality of life (maintain to significantly improve)

Certain *human tissue products* may only require infectious disease testing and effective controls for collection, handling, storage, labelling, etc., whereas others may additionally require design control and demonstration of clinical effectiveness.

Industry favours the use of technical tools such as standardisation or other consensus-based guidance to support regulation. There is already extensive work within ASTM (American Society for Testing and Materials) on engineered *human tissue products* which could form the basis for a European/international system of standardisation. The technologies involved are fast-moving and diverse, therefore technical details should not be included into the regulations themselves. It is desirable to gain the acceptance of all relevant stakeholders in a consensus-based process, in order to develop technical tools that are open-ended and which do not inhibit innovation and patient accessability.

Proposed Elements for European Regulations

Industry proposes that specific future European regulation for *human tissue products* should as far as practicable, facilitate a globally harmonized approach covering the following elements:

- *Scope* - All *human tissue products* (i.e. autologous and allogeneic), both non-viable and viable and including combined tissue/non-tissue type products, but excluding solid organs for traditional transplantation, blood and blood products, gametes, reproductive tissues and embryos, and tissues stored in genomic banks for obtaining genetic information (DNA).

- *Terminology* - Recognition of an internationally accepted set of terms.

- *Technical requirements* - should be multi-tiered and based on a risk-benefit approach, so as to provide a level of control appropriate to the risks inherent in the use of the *human tissue product* and also providing a high level of safety to the patient and other stakeholders.

  Technical instruments such as standards or similar consensus-based guidance should be promulgated, to permit flexibility in the approach to compliance with legal requirements. These instruments should take into account the rate and high degree of technological innovation in the field, whilst ensuring the safety of the patient and other stakeholders.

  Technical requirements should address quality, safety and where appropriate, effectiveness, taking into account in particular:

  - screening of donors
  - collection of tissues from donors
  - testing
  - processing
  - storage
  - labelling
  - packaging
  - distribution
  - traceability
  - clinical benefit
  - surveillance of donor and recipient
  - environmental impact

- Any future regulation should, wherever possible, allow for consideration of existing technical data or market experience which is available for established *human tissue products*.

- *Ethical considerations.* It is essential that the ethical basis for future European regulation should be based on:
  - the Council of Europe Convention on Human Rights and Biomedicine[2]
  - the Opinions of the European Group on Ethics and New Technologies to the European Commission[3]

  and consider the opinions of recognized professional and patient interest groups.

Industry recommends that the European Commission, the Council of Ministers and the European Parliament move immediately to propose and adopt Community legislation for regulation of *human tissues products* based on the above outlined position.

Information is available on the types of products, technologies, their applications and benefits upon request.

For further information on this *Industry* Position or questions please contact:

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[2] Council of Europe - European Treaties ETS N°. 164, Oviedo, 04.IV.1997
[3] European Group on Ethics in Science and new Technologies to the EC - Press Dossier - Adoption of an Opinion on Human Tissue Banking, 21 July 1998

厚生科学研究費補助金（医薬安全総合研究事業）
分担研究報告書

承認申請時に用いる基準、資料の要求範囲に関する研究

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研究要旨　ＧＨＴＦにおいて基準の活用についてのガイダンスドキュメントが作成されたことを踏まえ、わが国での医療用具承認審査の効率化、迅速化及び質の向上を図るため各種基準の調査及びその活用方策について検討を行った。また、同じくＧＨＴＦにおいて、技術概要文書（ＳＴＥＤ）のガイダンスドキュメントが作成されたことを踏まえ、わが国の医療用具承認審査へのＳＴＥＤ導入方策についても検討を行った。

Ａ．目的

医療用具承認申請に関する国際ハーモナイゼーション推進のための協議がＧＨＴＦ及びＩＳＯ／ＴＣ２１０において進められているが、これらの活動から生まれた成果を十分に活用し、わが国の医療用具の承認審査について、効率化、迅速化を図るとともに、国際整合性のとれた承認審査体制の整備を図る。

Ｂ．方法

１）承認申請資料、基準に関する調査

欧米の医療用具の認証制度において使用されている各種基準（米国：Recognized Consensus Standard 欧州：Harmonized Standard）について、インターネット、刊行本等を用いて調査し、一覧表を作成する。作成した一覧は、今後、わが国の承認審査のための基準作成に資することを念頭に、その分類わけ等の整備を図る。さらに、欧米において、それらの基準の位置づけ、活用方法の実態、また、承認審査に必要な資料の範囲等の調査を行う。

２）承認審査にかかる基準について

わが国承認審査において、基準策定の必要性の高いもの（申請品目が多い

もの、確立された技術であり、将来的に第三者認証の可能性が考えられるもの、リスクが高く一定の技術水準が必要なもの、横断的な基準で広く使われることが想定されるもの）から、海外基準を入手し、翻訳を行い、わが国の基準として作成する場合の方策を検討する。

3）承認申請に必要な資料要求範囲について

ＳＴＥＤと現行の資料概要について比較を行い、また、諸外国のＳＴＥＤ活用状況を調査し、わが国の承認審査においてもＳＴＥＤを活用するための方策を検討する。

（倫理面の配慮）

医療用具の市販前評価の国際ハーモナイゼーションの推進により、不要な動物試験や臨床試験を避けることができ、かつ低コストで安全な医療用具を提供することが期待される。このことは、本研究の推進が倫理面にも貢献することを示している。なお、本件では、動物実験、ヒトの試験は予定されていない。

C．研究結果

1）承認申請資料、基準に関する調査

欧米の医療用具の認証制度において使用されている各種基準及びガイダンスをすべて調査し、一覧表を作成した。また、各種基準名の翻訳、基準の性格の区別等を行うとともに、日医機協関係工業会の協力を得て、国際基準に対応するＪＩＳ及びわが国の承認基準を盛り込み、一覧表の整備を図った。これらの作業は、今後の研究に資することが期待される。

2）承認審査にかかる基準について

諸外国の基準に関する調査において作成されたリストに基づき、現在、翻訳がすでになされているものの調査を行い、一部を入手した。また、横断的な基準で医療用具に広く使われることが想定される国際規格（Horizontal International Standard）の原本（英文）をすべて入手した。

3）承認申請に必要な資料要求範囲について

ＳＴＥＤのわが国への導入可能性に関する検討を行う目的で、ＳＴＥＤと現行資料概要との比較検討を行い、比較表を作成した。また、諸外国におけるＳＴＥＤ導入状況を調査したが、いずれも今後１年を視野に入れたパイロット計画を推進中であり、その情報をＧＨＴＦにフィードバックし、ＳＴＥＤガイダンスドキュメントの再検討を行うことが明らかとなった。

D．考　察

1）承認申請資料、基準に関する調査

米国の Recognized Consensus Standard、ＦＤＡ各種ガイダンス、欧州の Harmonized Standard について、それぞれ 487、505、163 種類もの基準が承認審査において用いられてい

ることが明らかになった。それらのすべてについて、基準名の翻訳、また、それが医療用具の特異的な基準であるか（Vertical）、横断的な基準であるか（Horizontal）を明らかにし、さらに各基準についてキーワードを盛り込んだ。また、すべての医療機器を対象にして、日医機協関係18団体に、これらの基準に対応するＪＩＳの識別番号及びわが国の承認審査基準の標題について調査を依頼した結果、ほとんどの工業会より必要な情報を入手することができ、それらを一覧表に追加した。今後、さらに各基準の分類わけなどの充実を図る必要があるが、この基準一覧表を承認審査にかかる基準作成に活用することとしたい。

２）承認審査にかかる基準について

一部の基準の翻訳を入手したが、ほとんどの基準についてわが国において翻訳文が存在しないのが現状である。今後、できる限り、翻訳を入手するとともに、翻訳のない基準については、重要度の高いものから順次翻訳を行うこととしたい。また、それぞれの領域の専門家、関係業界、行政担当者とも連携し、例示的に基準案を策定する予定である。特に、制度改正に伴う第三者認証において、基準適合性審査が必要となってくることから、性能基準等の要素を考慮した基準案づくりにも注力することとしたい。それらの際には、ＧＨＴＦにおいて作成されている基本要件への適合性、ＳＴＥＤの導入を視野に入れ、国際的に整合のとれた基準のテンプレートを検討することとしたい。

３）承認申請に必要な資料要求範囲について

米国及びカナダにおいて検討されているＳＴＥＤの試行的受け入れは、その審査対象医療用具を限定していることが明らかになったが、わが国では、特に対象用具を絞る必要性がないことから、すべての医療用具を対象として試行的な受け入れを行うべきものと思われる。また、ＳＴＥＤと現行の資料概要との比較検討を行った結果、要求項目は両者において大きな差異がないものの、①イの１「起源または発見の経緯および開発の経緯」、②イの２「外国における使用状況」、③ロの３「規格及び試験方法」については、ＳＴＥＤにおいて要求項目が希薄か、或いは存在しないことから、ＳＴＥＤの試行的な受け入れの際には追加的に当該項目も資料の要求をせざるを得ないものと思われる。

なお、ＳＴＥＤの導入は、国際整合性を保つためにも、非常に重要な課題であり、関係業界からも積極的な導入を進めるべきである旨の意見が出ているが、申請者側の作業負担も大きく、当面は、試行錯誤の繰り返しになるものと予想される。このため、試行的受け入れの際には、現行の治験相談や一般面接等の場を活用し、申請者側の相談受け入れを密にし、申請者側の膨大な作業量を考慮して迅速な審査を行うべきものと思われる。

当研究班での検討状況を踏まえつつ、厚生労働省審査管理課から、「医療用具承認審査におけるサマリー・テクニカル・ドキュメント（ＳＴＥＤ）の試行的受け入れについて」医薬審第0201010号が平成14年2月1日に発出された。本研究では、今後、ＳＴＥＤの記載内容及び必要資料を解説したガイダンスの作成に向けた検討を行う予定である。

Ｅ．結　論

本分担研究では、ＧＨＴＦ等の国際整合の動向を踏まえつつ、諸外国における承認申請時の基準活用状況を明らかにし、わが国において承認審査または第三者認証のための基準作成の推進を図ることとしている。そのような観点から、諸外国の基準リストの作成を行い、また、ＳＴＥＤの試行的な受け入れが開始されるなど、初年度としては本研究の目的を達成するための環境整備が整えつつあるものと考えている。今後、初年度の成果を踏まえ、ＳＴＥＤの導入に伴う課題、基本要件への適合性、適合性評価指針などのＧＨＴＦ活動状況等も十分に考慮して、基準案の作成及び資料要求範囲の検討に向けた作業を進める予定である。

Ｆ．健康危害情報

なし

Ｇ．研究発表

なし

Ｈ．　知的財産権の出願・登録状況

なし

資料１　　STED／国内申請資料　比較表

STED	申請書	資料概要
C.2 カバーページ その国の特殊な要求事項によってカバーページの中に含めるべき情報を詳述してもよい。	様式第10 (2)	・「品目の概要」 類別、一般的名称、販売名、クラス分類、申請者名、略号一覧表
C.3 概要説明 その国の特殊な要求事項によって概要説明の中に含めるものを指示してもよい。少なくとも以下の情報を推奨。		
(1) STED の大要		
・医療機器の紹介		・「品目の概要」 類別、一般的名称、販売名、クラス分類、申請者名、構造・原理、備考（新規性の説明）、カラー写真又は鮮明なカラー印刷物
・意図した使用		・「品目の概要」 性能・使用目的、操作方法又は使用方法
・医療機器の適応		・「品目の概要」効能又は効果
・新機軸の特徴		・新規要求事項（一部は、「イ.1. 起源又は発見の経緯及び開発の経緯」で要求）
・STED の内容一覧		・資料概要全体の目次
(2) 機器の販売経緯 ・機器の市販国 ・意図した使用 ・ラベリングの指示事項 ・市販前承認についての懸案事項（行政からの指摘） ・リコール／不具合事象		・「イ.2. 外国における使用状況」

7.1 関連基本要件及び適合性を立証するために用いる方法（付属書 B 参照） 7.1.1 一般事項 (1) 基本要件の識別（申請品目の基本要件を記載）		・新規要求事項 基本要件は、法・規則・通知・JIS 等にあるが、ひとつにまとまっていない。
(2) 適合性を立証するための方法の識別（基本要件に適合していることの立証方法を記載） ・認定規格基準 ・他の規格基準 ・最新技術／企業内部の方法 ・市販の類似機器との比較		・新規要求事項 JIS、日本薬局方、承認基準等から識別
(3) 用いた規格基準等の識別（用いた規格基準の明確化） ・規格基準の全標題 ・識別番号 ・規格基準の発行日 ・規格基準を作成した組織 ・企業の内部規格基準の詳述		・新規要求事項
7.1.2 基本要件及び適合性証拠（基本要件に適合する旨を証明する試験結果の一覧） ・支援文書を添付した一覧表		・新規要求事項
7.2 機器に関する記述 7.2.1 一般情報 ・機器の機能上の目的（意図した使用）	性能、使用目的、効能又は効果	・「品目の概要」 使用目的、効能又は効果
・意図した患者層と医療条件（適応）及び患者の選択基準	性能、使用目的、効能又は効果	・「品目の概要」 使用目的、効能又は効果
・機器が使用されてはならない、当然予見できる医療条件（禁忌）	使用上の注意	