Study Group 1
Roles of Standards in Assessment of Medical Devices SG1(PD)/N044R6

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Definition

- **Conformity assessment:** The systematic examination to determine the extent to which a medical device fulfils specified requirements
- **Conformity Assessment Body (CAB):** A body engaged in the performance of procedures for determining whether the relevant requirements in technical regulations or standards are fulfilled. A CAB is authorized to undertake specified conformity assessment activities by a RA that will ensure performance of the CAB is monitored and, if necessary, withdraw designation

Definition (cont'd)

- **Regulatory Authority (RA):** A government agency or other entity that exercises a legal right to control the use or sale of medical devices within its jurisdiction, and may take enforcement action to ensure that medical products marketed within its jurisdiction comply with legal requirements
- **Risk:** Combination of the probability of occurrence of harm and the severity of that harm

Standards

- **Basic safety standards (horizontal standards):** Standards indicating fundamental concepts, principles and requirements with regard to general safety aspects applicable to all kinds or a wide range of products and/or processes
- **Group safety standards (semi-horizontal standards):** Standards indicating aspects applicable to families of similar products and/or processes making reference as far as possible to basic safety standards
- **Product safety standards (vertical standards):** Standards indicating necessary safety aspects of specific products and/or processes, making reference, as far as possible, to basic safety standards and group safety standards
- **Recognised standards**: Standards deemed to offer the presumption of conformity to specific essential principles of safety and performance (Essential Principles)

General Principles

- Regulatory Authorities and industry should encourage, support and contribute to the development of international standards for medical devices to demonstrate compliance with the essential principles of safety and performance of medical devices" (referred to hereafter as the Essential Principles).
- Regulatory Authorities developing new medical device regulations should encourage the use of international rather than national standards, whenever feasible.
- Regulatory Authorities should provide a mechanism for recognizing international standards to provide manufacturers with a method of demonstrating compliance with the Essential Principles. This mechanism should include also withdrawal of recognition.
- If a manufacturer chooses not to apply a recognised standard in part or in full, then this is acceptable if an appropriate level of compliance with the Essential Principles can be demonstrated.

General Principles

- While it may be preferable for harmonization purposes to use international standards, it may be appropriate for Regulatory Authorities to accept the use of global, national/regional standards or industry standards as a means of demonstrating compliance.
- Standards Bodies developing or revising standards for use with medical devices should consider the suitability of such standards for demonstrating compliance with the Essential Principles and should identify which of the Essential Principles they satisfy. They should only undertake such work when there is a clearly identified need and should take account of technology and practice existing at the time of development compatible with a high level of protection of health and safety.
- Standards should not discourage the use of new technologies.
- Standards should represent the generally acknowledged state of technology. Not all devices, or elements of safety and/or performance, may be addressed by recognised standards, especially for new types of devices and emerging technologies.

General Consideration

- Standards represent the opinion of experts from all interested parties, including industry, regulators, users and others.
- Standards are based on current scientific knowledge and experience.
- Preference should be given to standards developed in accordance with principles of procedural transparency, and rules that require public comment, periodic revisions, and the consideration and resolution of all negative votes.
- Innovation may present unanticipated challenges to experience.
- Because standards are based on experience, their rigid and mandatory application could become a barrier to innovation.
- Operation of a quality system, subject to assessment, has become widely acknowledged as a fundamental and effective tool for the protection of public health.
- Quality systems include provisions that address both innovation and experience.
- Such provisions include field experience, risk analysis and management, phased reviews, documentation and record keeping as well as the use of product and process standards.

International Standards

Building block for harmonized regulatory processes

Use of Standards

- Voluntary except deemed mandatory
- Compliance to “Recognized Standard”
- Free to select alternative solutions to demonstrate compliance
  - National and International standards
  - Industry standards
  - Internal SOP
  - Current state of art techniques related to performance, material, design, processes

Declaration of Conformity

- Documented in STED in lieu of technical documentation submission
- Retain documentation to demonstrate device compliance to selected standard or other means to meet Essential Principles
  - How standard was applied with test results.
  - Deviations
    - other means to compliance
    - when not applicable

Revision or Replacement of Recognized Standards

- Updated standard become “recognized”
- Transition Period
  - Should allow enough time for manufactures to response
  - Max < 5 years; unless exceptional circumstances
- During Transition Period
  - Both existing and revised version give presumption of conformity to Essential Principles
  - Unless safety implication, devices on market is OK
- After Transition Period
  - Superseded document may be withdrawn after transition period
  - Manufacturer using superseded version may do so but should perform and document risk assessment

Case 1: Implantable Pacing Lead Standard

Background

- Country X developed a local industry standard
- Standard hierarchy
  - National
  - Industry
  - Manufacturer
- Standards are mandatory minimum requirement
- Premarket Approval requires type testing based on standard

Case 1: Implantable Pacing Lead Standard

1. Scope

The Standard prescribes the technical specifications, testing procedures, labeling, packaging, transporting and storing of implantable pacing lead (hereinafter shortened as “lead”).

The Standard is applicable to implantable pacing lead. …

4. Technical Requirements

4.3 Appearance

The surface should be smooth; there should be no material overflow at the compressed joint

4.7 Simulation Life Test

After six months of simulation life test, the lead should conform to 4.4.2 and 4.4.3.

WHAT ABOUT THESE REQUIREMENTS?

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4. Technical Requirements

Case 1: Implantable Pacing Lead Standard

4. 9. 2 Biological Evaluation

4.9.2.1 The lead should not release any material with side effect to patients. Appropriate tests or evaluation should be adopted to prove the toxicity of the material of lead; and such tests or evaluation should show that the material is free from toxicity. XXnnnnn.1-2001 (ISO 10993-1) has presented the basic principle of the biological evaluation of Medical Device.

4.9.2.2 The lead should be free from pyrogenicity.

4.9.2.3 The lead should be free from cytotoxicity.

4.9.2.4 The lead should not be stimulating or cause allergy.

4.9.2.5 The lead should be free from acute systemic toxicity

4.9.2.6 The lead should be free from hereditary toxicity.

4.9.2.7 The lead should not cause hemolysis.

4.9.2.8 The lead should not cause implantation reaction.

4.9.2.9 The lead should not cause cancer.

WHAT ABOUT THESE REQUIREMENTS?

Case 1: Implantable Pacing Lead Standard

4. 9. 2 Biological Evaluation

4.9.2.1 Biological Evaluation should be **conducted per XXnnnnn.1-2001.**

Case 1: Implantable Pacing Lead Standard

5. Testing Procedure

The testing procedure provided by the Standard is the evaluation test for in-conformity, equivalent testing approaches can also be taken. However, for disputed items, the testing procedure provided here should be adopted.

5.5 Compliance Test

Experiment I:

Special fixture should be used; and the inner diameter of fixture should not exceed 110% of the diameter of the tested lead. The inner surface of the lower end of fixture should be belled fillet; thus when the tested lead is inserted along the frame of fixture, the center line of lead will form a bend with a radius of 6mm±0.1mm. The unit (see to figure 1) can be installed in a machine; vibrating fixture can be fixed vertically so that the tested lead section may bend in the bell mouth of fixture. In the unit, after the tested lead section has been installed at the fixture, the lead section should be hanged vertically due to gravity to represent the testing situation at worst conditions. A pliant string (flexible cord) should be tied at the lower end of the tested lead section, and the other end of the string should be tied with a weight with a certain weight to ensure that the center line of the tested lead section corresponds to the bending radius; or the lead whose tube chamber is difficult to disassemble can be used as the tested section directly and bent along with the fillet.

Above-mentioned unit should swing at a θ of 90o±2o with vertical direction as axle with a vibration frequency of 2Hz±0.5Hz for at least 47,000 cycles. The center of rotation of the testing device and the tested lead section should be adjusted well to diminish vibration. For each separate, even and flexible section of lead, the test should be conducted.

Case 1: Implantable Pacing Lead Standard

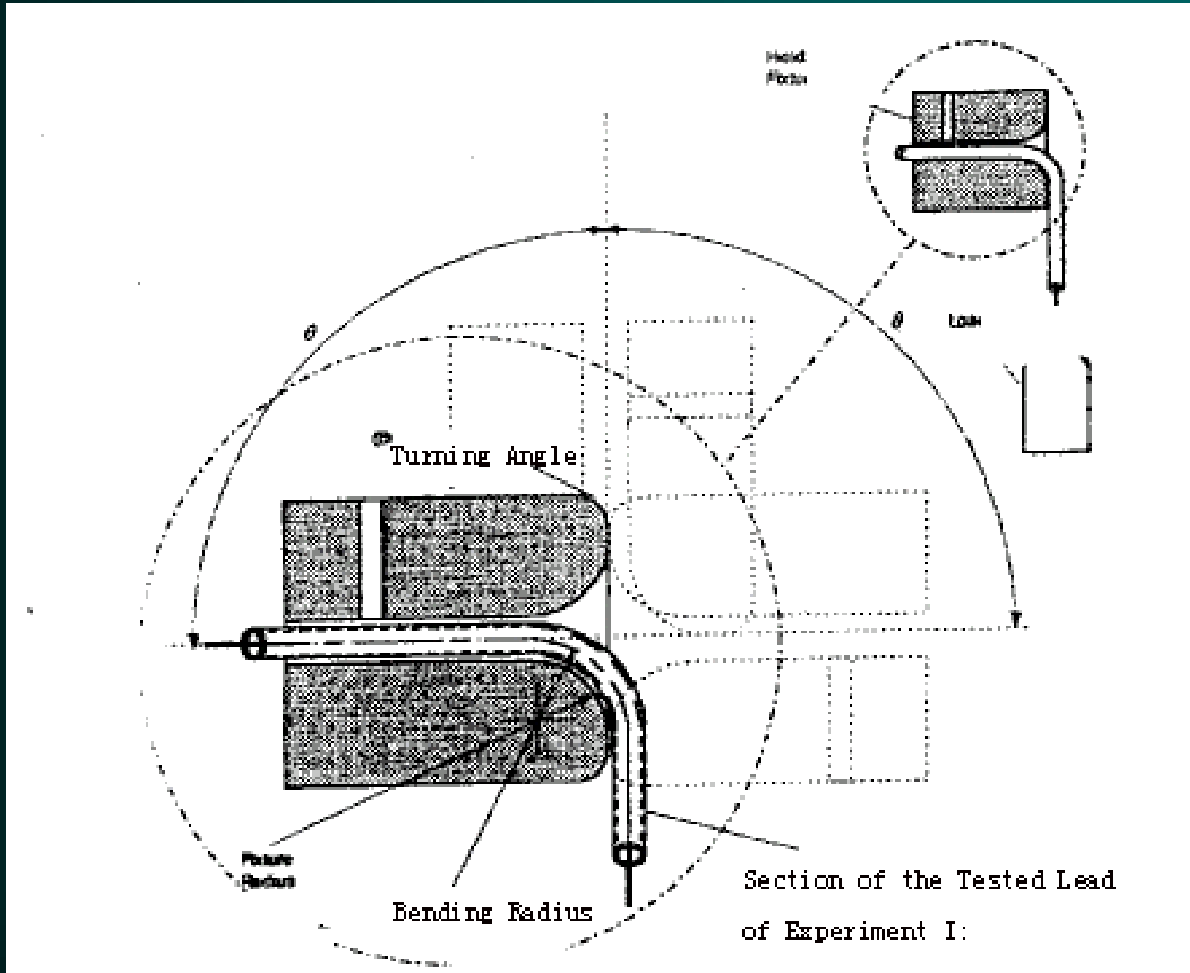

Figure 1 Testing Device for Lead Section Bending Test

Case 1: Implantable Pacing Lead Standard

ISO 14708-2:2005 (EN 45502-2-1:2003)

23 Protection of the active implantable medical device from mechanical forces

23.5

Test 1:

Use special holding fixture [see Figure 127]. The inside bore of the fixture shall be no greater than 110% of the diameter of the LEAD segment under test. At the lower end of the fixture, the inside surface shall be formed into a bell mouth having a radius such that when the test segment conforms to the contour of the fixture the centre-line of the test segment forms a 6 mm±0.1 mm centre-line bending radius [see Figure 127].

The fixture shall be mounted in a machine that can oscillate the fixture 90o from the vertical and forces the test segment to flex in the bell mouth of the fixture. The LEAD test segment shall be mounted to hang vertically under gravity in the holding fixture, oriented in the worst case test condition when the test segment allows multiple orientations.

A load sufficient to assure that the centre line of the test segment conforms to the bending radius shall be attached to the lower end of the thin, flexible line (cord) strung through the test segment. For lead bodies with no accessible lumen, a minimal tensile load may be applied directly to the test segment, so that it conforms to the bending radius.

The fixture shall be oscillated through an angle θ of 90o±2o each side of vertical at a rate of approximately 2 Hz for a minimum of 47 000 cycle.

Case 1: Implantable Pacing Lead Standard

5. Testing Procedure

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5.5 Compliance Test

The test involves two experiments, which shall be conducted following the requirements of ISO 14708-2.

Case Study 2
Phasing in / out of Standards

- Mature Standards replaced by newer standards
- Withdrawal of Recognized Standard
  - Impact to products in the market & legacy product designed to old standard but continue to market, e.g. Standard for prions in animal tissue devices
  - Products with “treat to public health” should be recalled
  - Another example

Case Study 2
Phasing in / out of Standards

ISO 5841-1:1989 Pacemaker Standards is being revised, target to be replaced by ISO/FDIS 14708-2 (approval stage – ballot initiated)

- Minor terminology change: End of Life (EOL) vs. End of Service (EOS)
  - Programmer software & manual change - design and distribution cost

HOW TO PHASE IN / OUT THESE STANDARDS?

Conclusion

- Standards compliance is one of the means to demonstrate compliance to Essential Principles
- Standards enforcement flexibility should be allowed
- Clear and consistent procedure for withdrawing recognized standards should be established
- Economies need to have better organized participation in development and use of international standards