Global Standards : Do They Exist?
ORS Industry Connect
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My disclosure is listed in the disclosure index on the ORS website. My disclosure is that I am a paid employee of Zimmer Biomet. The opinions expressed herein are not necessarily endorsed by Zimmer Biomet.
Standards within the Global Regulatory Framework

• **Overview of Standards**

• **Use of standards in regulatory planning**
  – US
  – EU
  – Global Perspective

• **Maintenance and Review of Standards**
  – Varying market requirements
  – “State of the Art”
Overview of Standards
Overview of Standards

Definitions and Terms

• Established norm or requirement, uniformity in areas such as engineering/technical criteria, methods, processes.

• Common and repeated use of rules, conditions, guidelines or characteristics

• Types of Standards -
  – Vertical- apply to specific product groups/device types
  – Horizontal – apply across multiple product groups/device types (e.g. sterilization)
  – Test Methods
  – Material Specifications
  – National, International, Regional

Why do we use Standards?

• Consistency, Credibility, Predictability

• Harmonization of Requirements

• Streamline regulatory review
Overview of Standards

Standards Organizations and Standard Adoption

- Standards Organizations*
  - International Organizations
    - International Organization for Standardization (ISO)
    - American Society for Testing and Materials (ASTM)
  - Regional Standards Organizations
    - European Committee for Standardization (CEN)
    - Pacific Area Standards Congress (PASC)
  - Local Standards Organizations
    - British Standards Institute (BSI) – UK
    - American National Standards Institute (ANSI) – USA
    - Association for the Advancement of Medical Instrumentation (AAMI) – USA

*List includes examples for discussion.

Standard developed/published by ISO, Standard considered by CEN and published as an EN standard unmodified, Standard considered by BSI and published as a British standard unmodified, e.g. BS EN ISO 14630:2012.
Use of Standards in Regulatory Planning
Use of Standards in Regulatory Planning

US - FDA

• Use and conformance to standards may vary but can be used in all pre-market submissions
  – Determination of Classification and Product Code
  – Identify Special Controls
  – Determine relevance and incorporate requirements into design controls, design specifications

• De Novo
  – Defining the Special Controls (Class II only)
  – Written into the new regulation
  – Legally required for all devices of the same type (Sets the precedent)

Sec. 888.3660 Shoulder joint metal/polymer semi-constrained cemented prosthesis.
(a) Identification. A shoulder joint metal/polymer semi-constrained cemented prosthesis is a device intended to be implanted to replace a shoulder joint. The device limits translation and rotation in one or more planes via the geometry of its articulating surfaces. It has no linkage across-the-joint. This generic type of device includes prostheses that have a humeral resurfacing component made of alloys, such as cobalt-chromium-molybdenum, and a glenoid resurfacing component made of ultra-high molecular weight polyethylene, and is limited to those prostheses intended for use with bone cement (888.3027).
(b) Classification. Class II. The special controls for this device are:
(1) FDA’s:
   (ii) "510(k) Sterility Review Guidance of 2/12/90 (K90-1),"
   (iii) "Guidance Document for Testing Orthopedic Implants with Modified Metallic Surfaces Opposing Bone or Bone Cement,"
   (iv) "Guidance Document for the Preparation of Premarket Notification (510(k)) Application for Orthopedic Devices," and
(2) International Organization for Standardization’s (ISO):
## Use of Standards in Regulatory Planning

**US - FDA**

- Final Guidance – “Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices” (US FDA, Document issued September 14, 2018)

- FD&C Act 514(c) amended by 21st Century Cures Act & adoption of ISO/IEC 17050-1 and 17050-2

<table>
<thead>
<tr>
<th>Change/Update</th>
<th>Impact</th>
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</thead>
<tbody>
<tr>
<td>Form 3654 no longer needed</td>
<td>General use vs declaring conformity</td>
</tr>
<tr>
<td>Declaration of Conformity (DoC) to a Standard required when a submitter declares conformity</td>
<td>DoC – attestation that the device is in conformance to all normative requirements of the standard, testing conducted prior to submission on finished or final finished device -May reduce the amount of supporting info to be submitted to FDA</td>
</tr>
</tbody>
</table>

**Transition Period**

- Standard revisions are not retroactive
- Implementation period
- Consideration for device modifications
- Note: Does the revision address a safety or effectiveness issue?
- Revision is not automatically an FDA Consensus Standard

Don’t forget to check the Supplemental Information Sheet (SIS) – Part B of the FDA Consensus for the extent of recognition
Use of Standards in Regulatory Planning

US - FDA

- Stay Tuned in 2020

<table>
<thead>
<tr>
<th>Update – ASCA Pilot</th>
<th>Impact</th>
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<tbody>
<tr>
<td>Accreditation Scheme for Conformity Assessment Pilot Program</td>
<td>• FDA Guidance expected end of 2020</td>
</tr>
<tr>
<td></td>
<td>• Uses FDA-recognized accreditation bodies to accredit test labs to</td>
</tr>
<tr>
<td></td>
<td>certain FDA-recognized standards</td>
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<tr>
<td></td>
<td>• Standardized test reports – enhanced consistency and predictability</td>
</tr>
<tr>
<td></td>
<td>in pre-market reviews</td>
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<td></td>
<td>• Pilot program will include a minimum of five FDA-recognized</td>
</tr>
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<td></td>
<td>consensus standards, at least one will be device specific.</td>
</tr>
</tbody>
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Use of Standards in Regulatory Planning

EU

• Use of Standards is voluntary, as other methods may be used to show conformance to the requirements of the directives, however:
  – Medical Device Directive (93/42/EEC) states that a device must “conform to the generally acknowledged state of the art.”
  – Medical Device Regulation (2017/745) – “state of the art” similarly referenced

How to define:
  – Specific definition not in the regulations
  – ISO 14971:2012 Standard for medical device risk management describes state of the art as “best practices as used in other devices of the same or similar type.”
  – What is currently and generally accepted as good practice

  – Compliance to the latest revisions of standards is often a point of review when establishing “state of the art”
Use of Standards in Regulatory Planning

EU

- Standards in the EU
  - Standards that can be used to give a presumption of conformity to the MDD are listed in the Official Journal of the European Union (OJEU)
  - All of the standards in the OJEU are EN standards and are “harmonized”
    - Older standards may not have the Annex ZA or equivalent
  - What is the Annex ZA?
    - For each clause of the standard, the clauses in the relevant part of the MDD are listed where a “presumption of conformity” can be claimed
- Example

<table>
<thead>
<tr>
<th>Clause(s)/sub-clause(s) of this European Standard</th>
<th>Essential Requirements (ERs) of Directive 93/42/EEC</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>1, 2nd indent</td>
</tr>
<tr>
<td>4, 5, 8 and 10</td>
<td>5</td>
</tr>
<tr>
<td>7.1 and 7.2</td>
<td>6a</td>
</tr>
<tr>
<td>5 a), 5 f), 6 a) and 6 b)</td>
<td>7.1, 1st indent</td>
</tr>
<tr>
<td>5 a), 6 a) and 6 b)</td>
<td>7.1, 2nd indent</td>
</tr>
<tr>
<td>7.2 c)</td>
<td>7.1, 3rd indent</td>
</tr>
<tr>
<td>5 f), 5 r), 7, 8 and 10</td>
<td>7.2</td>
</tr>
<tr>
<td>5 h) and 6</td>
<td>7.3</td>
</tr>
</tbody>
</table>
Use of Standards in Regulatory Planning

Global Perspective

• Rest of World Requirements
  – ANVISA GMP
  – China National Standards, Testing Requirements
  – Russia / EEU Requirements

• Establish a Regulatory Strategy
  – Define Key Markets
    • Don’t sacrifice long-term impact for potential short-term benefit
  – Understand requirements and regional or local standards
    • Early planning = efficiency

ANVISA – Suture Anchor standard (ABNT/CB-026 STANDARD PROJECT P 26070.05-013-1 NOV 2018)

Global - Electrical Standard IEC 60601 – Must consider target market’s local electrical codes e.g. Canada CSA C22 and Brazil’s INMETRO certification.
  • Early planning in development saves money, time, and potential unnecessary redesign.
Maintenance and Review of Standards
Varying Market Requirements

- How does the revision of a standard impact your device?
  - US
    - Dependent on when the standard changes in product development, i.e. before FDA review, during review, or after review (clearance/approval)
    - Changes to standards after review are not retroactive
    - The Agency encourages use of pre-submission (“Q-sub”) meetings before review when there are questions regarding standard changes
    - Note – did the standard revise to address issues of safety or effectiveness?
    - Consideration of standard revisions in device modification assessment
  - EU
    - Review of “state of the art”
    - CE Renewal period
  - Global Perspective
    - Consider timing of global market submissions
    - Renewal timeframes

Standards review occurs throughout the Total Product Lifecycle
Maintenance and Review of Standards

Managing the Chaos

• Establishing a standards review process
  – Who?
  – How often?
  – Notifications?

• Defining impact
  – Process?
  – Procedure?
  – Product?

• Implementation
Role of Standards within the Global Regulatory Framework

• Overview of Standards
  – Established the terminology, types, organization, adoption and why we use standards
• Use of Standards in Regulatory Planning
  – Defined areas of take-away for US and EU
  – Importance of understanding key markets and the global requirements early
• Maintenance and Review of Standards
  – Standard review and conformance is not a one-time review
  – Total product lifecycle review
  – Establishment of a process is key
Resources
Resources

• US – FDA Standards
    • Module 1: Standards Overview
    • Appropriate Use of Voluntary Consensus Standards
  – Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices (Guidance for Industry and Food and Drug Administration Staff):
  – Accreditation Scheme for Conformity Assessment Pilot Program

• EU