MedDev Commercialization Centre
Centre de commercialisation MedDev
Regulatory Cycle and Certification

Agenda

Regulatory
  • Definition
  • Philosophy
  • Classification
  • Approval process (Canada, EU, USA)

Design controls
  • Rationale
  • Elements
  • Parts to be considered for early projects
    • Pre-spin off
Regulatory-Definition

Definition

‘Medical device’ means any instrument, apparatus, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings, for one or more of the specific medical purpose(s) of:

- diagnosis, prevention, monitoring, treatment or alleviation of disease,
- diagnosis, monitoring, treatment, alleviation of or compensation for an injury,
- investigation, replacement, modification, or support of the anatomy or of a physiological process,
- supporting or sustaining life,
- control of conception,
- disinfection of medical devices

and does not achieve its primary intended action by pharmacological, biological, immunological or metabolic means, in or on the human body, but which may be assisted in its intended function by such means.
Medical Devices Regulatory Philosophy

• **Origin**
  – Resulted from incident encountered in the medical
  – Regulation appeared in the USA mid-70’s
  – Regulation appeared in Canada and Europe in the mid-90’s

• **Regulatory authorities organized medical devices in several classes**
  – Product classification is based on the risk to patient injury
    – USA based its classification on three (3) levels: I-II et III
    – Canada et EU based their respective classification on four (4) levels
      » Canada classes I-II-III et IV
      » EU classes I-IIa-IIb et III
  – The higher the risk level, more demanding is the scientific or clinical/medical proof to support a product
    – Classes III et IV typically require a clinical trial to support a commercial approval application
Product Classification

- **Canada**
  - Class IV
  - Class III
  - Class II
  - Class I

- **US**
  - Class III
  - Class II
  - Class I

- **EU**
  - Class III
  - Class II
  - Class I

**Increased risk, increased data requirements**
Medical Devices Classification

• EU/Canada
  – European Medical Devices Directives 93/42/EEC et Medical Devices Regulations form Health Canada structure the classification based on 18 rules

• USA
  – Le Code of Federal Regulations lists product groups of existing approved products
    • By comparison, it can be established if the product is Class I or
    • If the company can establish equivalence to an existing generic product, therefore a Class II often referred as a 510(k)
    • Or, an innovative product where there are no substantial equivalence therefore a pre-market approval (PMA) is required and will need to be supported by a clinical study via an investigational device exemption (IDE)
Classification Flow Chart

1. Not Invasive → Low Risk → Class I
2. Invasive? Yes → Term?
   - Yes → Long Term Invasive → Risk → Class IIb
   - No → Short Term Invasive → Moderate Risk → Class IIa
3. Invasive? No → Class IIa
Classification Flow Chart

NON INVASIVE DEVICES

Rule 1
Either do not touch patient or contact only intact skin

Class I

Rule 2
Channelling or storing for eventual administration

Class I

or

Rule 3
Modify biological or chemical composition of blood, body liquids, other liquids intended for infusion

Class Iib

or

Rule 4
In contact with injured skin (mechanical barrier - absorb exudates)

Class I

or

or

For use with blood, other body fluids, organs, tissues

Class Ila

May be connected to an active medical device

Class Ila

Only filtration, centrifugation or exchange of gas or heat

Class Ila

Intended for wounds which breach dermis and heal only by secondary intent

Class IIb

or

Intended to manage micro-environment of wound + others

Class IIa
Classification Flow Chart
Classification Flow Chart

ACTIVE DEVICES

Rule 9
Active therapeutic devices intended to administer or exchange energy
- Administer or exchange energy in potentially hazardous way
- Intended to control & monitor or influence directly a class lb active therapeutic device

Rule 10
Active devices for diagnosis. May supply energy for "imaging purpose" monitor vital physiological processes
- When used to monitor vital processes where variations could result in immediate danger
- If this is in a potentially hazardous way

Rule 11
Active devices to administer remove medicines & other substances to or from the body
- If this is in a potentially hazardous way

Rule 12
All other active devices
Classification Flow Chart

SPECIAL RULES

Rule 13: Devices incorporating integral medicinal product liable to act in an auxiliary way on human body

Rule 14: Devices used for contraception or prevention of sexually transmitted diseases

Rule 15: Specific for disinfecting, cleaning, rinsing devices for contact lenses

Rule 16: For disinfecting other medical devices other than by physical action

Rule 17: Devices utilizing animal tissues or derivatives (not devices in contact only with intact skin)

Rule 18: Blood Bags
Classification examples
Implantation d'un système qualité basé sur la norme ISO13485 et certifié par un organisme de certification reconnu par Santé Canada (CMDCAS)

Préparation de la soumission de la Demande d'homologation. Classe II est similaire au 510(k) et plusieurs Classe III. Les Classe IV sont similaires au US PMA.

Soumettre demande MDL, DC, certificat ISO 13485 +$

Sante Canada revoit les demandes MDL (Classes II, III et IV) et revoit les dossiers de revue pour les Classes III et IV.

Les demandes d’Homologation approuvées sont affichées sur le site web de Sante Canada et les Certificats d’Homologation sont envoyées par courriel au demandeur.

Les ventes et distribution peuvent débuter au Canada. Les Licenses n'expirent pas mais vous devez payer les rais annuel, sinon votre License pourrait être révoquée.
### Health Canada – Review time

<table>
<thead>
<tr>
<th>Class</th>
<th>Review and approval time</th>
<th>Certificat expiry</th>
<th>Time to renew certificat</th>
<th>Complexity</th>
<th>Cost to approval</th>
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<tr>
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<td>2-4 months</td>
<td>1 year</td>
<td>2 months</td>
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<td>+</td>
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<tr>
<td>Classe II</td>
<td>1-2 months</td>
<td>1 year</td>
<td>2 months</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Classe III</td>
<td>4-5 months</td>
<td>1 year</td>
<td>2 months</td>
<td>+++++</td>
<td>+++</td>
</tr>
<tr>
<td>Classe IV</td>
<td>6-8 months</td>
<td>1 year</td>
<td>2 months</td>
<td>++++++</td>
<td>++++++</td>
</tr>
</tbody>
</table>
USA FDA – Processus d'homologation

Utiliser le FDA Classification Data Base en recherchant Predicate Device et noter aux 3 lettres du Code Produit et Regulation Number. Dans la négative suivre le De Novo process, et Significant Risk or Not (SR ou NSR)

Classe I

Classe II

Classe III

Implantation d'un système qualité basé GMP américaine 21CFR 820 (similaire à ISO 13485)

Les produits innovants de classes II et III requièrent généralement des études cliniques donc la soumission d'un Investigational Device Exemption (IDE)

Préparation et soumission du 510(k) + et $CV

Préparation et soumission du dossier PreMarket Approval (PMA) et paiement pour la revue

FDA émet l'autorisation 510(k) sur le Web

FDA émet une lettre d'approbation du PMA et affiche sur le site Web FDA

S'assurer de la conformité aux GMPs, enregistrer l'instrument sur le FDA web site 21 CFR 807 et sélectionner un agent si la société n'a pas de présence aux USA. Débuter la mise en marché.
## USA FDA – Review time

<table>
<thead>
<tr>
<th>Class</th>
<th>Review and approval time</th>
<th>Certificate expiry</th>
<th>Renewal</th>
<th>Complexity</th>
<th>Cost</th>
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<tr>
<td>Classe I</td>
<td>1 month</td>
<td>illimited</td>
<td>SO</td>
<td>+</td>
<td>+</td>
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<tr>
<td>Classe II</td>
<td>3-6 months</td>
<td>illimited</td>
<td>SO</td>
<td>+++</td>
<td>+++</td>
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<tr>
<td>Classe III</td>
<td>18-30 months</td>
<td>illimited</td>
<td>SO</td>
<td>+++++++++++</td>
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Other requirements

• Canada/Europe
  – Implementation and certification of a quality system based on ISO 13485
  – Class I, IIA et IIB or classe III (Canada) are respectively a self certification, a need for a technical file with the addition of a review of medical literature
  – Class III (EU) et Classe III (USA) et IV (Canada) requires a clinical trial and
    • Design dossier, manufacturing procedures validated
    • EU authorities will issue a certificate that allows sales in 26+ member state countries of the enlarge EEC

• USA
  – Implementation and certification of a quality system based USFDA quality system cGMP, similar to ISO 13485
  – Classe I requires a simple notification
  – Classe II or a 510(K) requires the filing of a technical file and possibly a clinical trial for a novel technology where patient risk has not been established
  – Classe III requires a clinical trial to be conducted under IDE and followed by the filing of a PMA as well as an inspection of manufacturing facility prior to approval.
# Certification Costs

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<td>ISO certification</td>
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<tr>
<td>Class IV</td>
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</table>
Design control
Design Controls

What is it?
Design Controls are an
• integrated set of management practices (policies, processes and procedures)
• which are applied to control design activities
• while assessing quality and correcting errors through an iterative process of development.

Why does it exist?
• To ensure regulators can properly assess a product and
• for medical professional and patients to benefit from a safe and effective product
Design Controls

Why start early?

• Help inventors to properly document their inventions in a systematic way
• Identifies the unique key attributes of the devices
• Helps define the risks associated with the device
• Facilitates the documentation from an Intellectual Property point of view
Design Control Elements

1) Design Control – States that when manufacturers or suppliers develop a product subject to design controls, they shall establish and maintain the proper documentation to ensure the specified design requirements are met.

2) Design and Development Plan – Describes the overall development plan and defines design activities and responsibilities. It establishes roles of all contributors to the development process including marketing, purchasing, manufacturing, R&D, Regulatory Affairs, and others. The Plan also defines design elements, intended use, and interfaces associated with the overall design process.

3) Design Input – Establishes the requirements that will ensure the device will meet the needs of the intended users. This is often in the form of a Product Requirements document or a Device Specification document; et al. Design input does not come in a box and is not a tangible entity, but is a process of gathering all available information about how a device might fulfill one or more user needs, while defining requirements which characterize the device. A requirements document is the tangible embodiment of user needs and is “the” document that comprises all fundamentals to help decide how to implement the design. Requirements should specify what is needed, not the solution, and act as a basis for verification of the design. It is not a trivial document and requires time and effort.
4) **Design Output** – Applies to all stages of the design process. These are the final technical documents that constitute the Design History File (DHF). This information shows that the device was developed according to the Design Plan and Design Inputs. It ensures that the Design Output meets the Design Input requirements and specifications. Design output is the accumulated information and instructions for building and maintaining the product. If followed, the result will be a device that consistently meets specified user need(s).

5) **Design Review** – These are planned, formal, and documented reviews of the design results conducted at appropriate stages of the device's design development. Formal Design Reviews (minimum of two) require the participation of representatives of all functions concerned with the design stage being reviewed and an individual(s) who does not have direct responsibility for the design stage being reviewed, as well as any specialists needed. The formal reviews ensure that Design Outputs are meeting the Design Input requirements and are being recorded.

6) **Design Verification** – Assesses conformance to the requirements and confirms and documents (in reports) that the design output has met design input requirements. It verifies that the product was "made right".
7) **Design Validation** – Validation follows successful Verification and is performed under defined operating conditions on initial production units, lots, or batches, or their equivalents. It shall determine, by objective evidence, that devices conform to defined user needs and intended uses and shall include testing of production units under actual or simulated use conditions. Design validation shall include software validation and *risk analysis, where appropriate. It confirms that only safe and effective devices are produced for their intended use and therefore validates the "right product" was made.

8) **Design Transfer** – Ensures that the design specifications of the device is correctly translated into production specifications.

9) **Design Changes** – Design Changes are to be documented and validated or where appropriate, verified (again). They are also to be reviewed and approved again before their implementation.

10) **Design History File (DHF)** – Each manufacturer shall establish and maintain a DHF for each type of device. The DHF shall contain or reference the records necessary to demonstrate the design was developed in accordance with the approved design plan and the requirements of this part (21CFR820.30). It is a collection all outputs derived from the previous categories listed above.
Design Controls

**Feasibility**
- User requirements
- Functional & performance requirements
- Market and communication input
- Regulatory requirements
- Design requirements

**Design**
- Concept design
- Sub system design
- Detailed design

**Verification**
- Risk analysis
- Static code analysis
- Failure mode effect analysis
- Biocompatibility testing
- Design and code review
- Verification testing as per requirements

**Validation**
- Mechanical testing
- Clinical trials
- Sterilization validation
- Environmental testing
- Labelling validation
- End user testing in actual or simulated environment

**Design changes**
- Post-market surveillance
- Document feedback and changes identified
- Change request and risk review

**Design transfer**
- Documentation
- Packaging and labelling
- Master device record
- Training of end users
- Bill of material
- Process worksheets

**Review**
Design Controls

How does it apply to you at the university level?

• It is not a requirement for you, it is for industry

HOWEVER
• Adhering to its principles will help you structure your idea
• Adhering to its principles will help you structuring your IP
• Adhering to its principles will help you with forming a company and attract investments
Design Controls

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Where do I start? PLANNING

• Document! Document! Document!

• Get a notebook
  • Identify your note book to yourself and with a unique number
  • Ensure you sign and date the bottom of every page
  • If you have computer drawings, print them and glue them inside your notebook, sign and date them
Things I should remind myself? FEASIBILITY

• Your idea should have a purpose?
• What problem/issue are you trying to resolve?
• Is there a need, a market for your idea?

• Define the user needs and define some high level specifications

• Document it in your notebook
Things I should remind myself?  

**DESIGN PLAN**

- You have defined the user need....

- Define now how you can demonstrate your product can work
  - What are the tests you need to conduct to demonstrate your idea/product does work?
  - Write the hypothesis?
  - Imagine the test sequences you need to achieve?
  - Put them in a flow chart

- **Document in your notebook**
Design Controls

Things I should remind myself? VERIFI

✓ You defined the user needs
✓ You defined your plan and a flow chart of the test sequences

It is time for the actual verification testing

For each test
- Clearly state the test objective
- Define the test methodology
- Define the number of samples to be tested and why
- Identify the test equipment required

• Document in your notebook
Design Controls

Things I should remind myself? VERIFICATION

Proceed with verification testing

For each test
- Take note of the test equipment model, serial, calibration
- Conduct the testing
- Gather all raw data

- Document in your notebook
Design Controls

Things I should remind myself?  VERIFICATION

Write the report

For each report use the following structure

• Report number
• Title
• Purpose
• Methodology
• Data interpretation and discussion
• Conclusion

• Document in your notebook the report #, where it is and when produced
Q & A