Introduction to US FDA CDRH Regulations, 510(k)

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The Transformation of Medical Device Industry for Thailand 4.0: Software Validation for Medical Devices

Novotel Bangkok Sukhumvit 20, 5th floor, Room Benjasiri 1-2
January 17, 2017, 1:45 pm – 3:30 pm
FDA?

- 1906, a few scientists started testing food and drug for safety and efficacy

- Pre-Market Approval is highly emphasized

- Recently, paradigm change for emphasizing more on post-market issue is being discussed (21st Century Cures Act: Use of Clinical Data for Efficacy Proof)

- Group of top scientists are reviewing – estimated FTE of 15,000
Why everyone wants FDA approval?

• Complete and thorough review by experts before offered in market – Highly authoritative proof of safety and efficacy (effectiveness)

• FDA approval is not difficult -> If you are confident in your product

• Reasonable communication with FDA reviewers is very important
FDA Organization (1)
FDA Organization (2)

- Center for Food Safety and Applied Nutrition (CFSAN, includes Cosmetics)
- Center for Drug Evaluation and Research (CDER)
- Center for Devices and Radiological Health (CDRH)
- Center for Biologics Evaluation and Research (CBER)
- Center for Veterinary Medicine (CVM)
- Center for Tobacco Products (CTP)
CDRH in Detail

• CDRH = Center for Devices and Radiological Health

• MISSION: The mission of the Center for Devices and Radiological Health (CDRH) is to protect and promote the public health.

• VISION: Patients in the U.S. have access to high-quality, safe, and effective medical devices of public health importance first in the world.

• SHARED VALUES:
  • Public Health Focus
  • Science-Based Decisions
  • Our People - Our staff is our most critical resource. We value individual excellence, teamwork, and personal and professional diversity.
  • Innovation
  • Transparency
  • Honesty and Integrity - We maintain the public trust by acting with integrity and honesty. Our actions adhere to the highest ethical standards and the law.
  • Accountability - We hold ourselves accountable for the actions we do and do not take. We acknowledge our errors and learn from them.
CDRH Organization

- Office of the Center Director (Jeff Shuren)
- Office of Communication and Education (OCE)
- Office of Compliance (OC)
- Office of Device Evaluation (ODE)
- Office of In Vitro Diagnostics and Radiological Health (OIR)
- Office of Management Operations (OMO)
- Office of Science and Engineering Laboratories (OSEL)
- Office of Surveillance and Biometrics (OSB)
ODE
Office of Device Evaluation
Medical Devices Definition

Section 201(h) of the Federal Food Drug & Cosmetic (FD&C) Act

• an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is:
  • recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them,
  • intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
  • intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes.
Selling Medical Devices in US

• Premarket Requirements
  • Step One: Classify Your Device
  • Step Two: Choose the Correct Premarket Submission
  • Step Three: Prepare the Appropriate Information for your Premarket Submission to the FDA
  • Step Four: Send your Premarket Submission to the FDA and Interact with FDA Staff during Review
  • Step Five: Complete the Establishment Registration and Device Listing
Classification

• **Class I – Lowest Risk**  An example of a Class I device is a manual toothbrush. Class I devices are subject to *general controls*.

• **Class II – Moderate Risk**  Examples of Class II devices are male condoms and non-invasive blood pressure monitors. Class II devices are subject to *general controls and special controls*.

• **Class III – Highest Risk**  An example of Class III device is a heart valve. Class III devices are subject to *general controls and premarket approval*. 
General Controls

- General controls are described in the following sections of the FD&C Act:
  - 501: Adulterated devices
  - 502: Misbranded devices
  - 510: Registration of producers of devices
    - Establishment registration and device listing
    - Premarket Notification (510k)
    - Reprocessed single-use devices
  - 516: Banned devices
  - 518: Notifications and other remedies
    - Notification
    - Repair
    - Replacement
    - Refund
    - Reimbursement
    - Mandatory recall

519: Records and reports on devices
- Adverse event report
- Device tracking
- Unique device identification system
- Reports of removals and corrections

520: General provisions respecting control of devices intended for human use
- Custom device
- Restricted device
- Good manufacturing practice requirements
- Exemptions for devices for investigational use
- Transitional provisions for devices considered as new drugs
- Humanitarian device exemption
Special Controls

- Performance standards
- Postmarket surveillance
- Patient registries
- Special labeling requirements
- Premarket data requirements
- Guidelines
After Classification – Premarket Submission

• Premarket notification [510(k)]
  • For Class I devices exempt from [510(k)] the submission of a [510(k)] and marketing clearance from FDA is not required.
  • If your Class I (or certain class II) device is exempt, subject to the limitations on exemptions, from the 510(k) process, this will be stated in the classification regulation.
  • However, other General Controls such as registration and listing, labeling, and good manufacturing practices (GMP) may apply.

• PMA
### User Fees

**MDUFMA:** Medical Device User Fee Modernization Act  
**MDUFA III (2012):** Medical Device User Fee Amendment

#### FY17 User Fees (in U.S. Dollars)

<table>
<thead>
<tr>
<th>Application Type</th>
<th>Standard Fee</th>
<th>Small Business Fee†</th>
</tr>
</thead>
<tbody>
<tr>
<td>510(k)‡</td>
<td>$4,680</td>
<td>$2,345</td>
</tr>
<tr>
<td>513(g)</td>
<td>$3,166</td>
<td>$1,583</td>
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<tr>
<td>PMA, PDP, PMR, BLA</td>
<td>$234,495</td>
<td>$58,624</td>
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<tr>
<td>panel-track supplement</td>
<td>$175,871</td>
<td>$43,968</td>
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<tr>
<td>180-day supplement</td>
<td>$35,174</td>
<td>$8,794</td>
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<tr>
<td>real-time supplement</td>
<td>$16,415</td>
<td>$4,104</td>
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<tr>
<td>BLA efficacy supplement</td>
<td>$234,495</td>
<td>$58,624</td>
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<tr>
<td>PMA annual report</td>
<td>$8,207</td>
<td>$2,052</td>
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<tr>
<td>30-day notice</td>
<td>$3,752</td>
<td>$1,876</td>
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OIR
OIR

• regulates in-home and laboratory diagnostic tests (in vitro diagnostic devices, or IVDs);
• regulates radiological medical devices;
• regulates radiation-emitting non-medical products; and
• implements the Mammography Quality Program authorized by the Federal Mammography Quality Standards Act of 1992

• CLIA
CLIA

- Clinical Laboratory Improvement Amendments

- FDA
  - Categorizes tests based on complexity
  - Reviews requests for Waiver by Application
  - Develops rules/guidance for CLIA complexity categorization

- CMS (Center for Medicare and Medicaid Services)
  - Issues laboratory certificates
  - Collects user fees
  - Conducts inspections and enforces regulatory compliance
  - Approves private accreditation organizations for performing inspections, and approves state exemptions
  - Monitors laboratory performance on Proficiency Testing (PT) and approves PT programs
  - Publishes CLIA rules and regulations

- CDC
### Examples of Radiation-Emitting Electronic Products

<table>
<thead>
<tr>
<th>Use</th>
<th>Ionizing (x-ray)</th>
<th>Optical (visible, UV, IR, laser)</th>
<th>RF, Microwave, VLF/ELF, magnetic</th>
<th>Acoustic (sonic, ultrasonic)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medical: Diagnostic</strong></td>
<td>General radiography</td>
<td>Slight</td>
<td>Magnetic resonance imaging</td>
<td>Doppler ultrasound</td>
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<td></td>
<td>Dental radiography</td>
<td>Retinal acuity</td>
<td></td>
<td>Color doppler ultrasound</td>
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<td></td>
<td>Fluoroscopy</td>
<td>Fluorescence spectroscopy</td>
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<td>Computed tomography</td>
<td>Transilluminator</td>
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<td></td>
<td>Mammoography</td>
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<tr>
<td><strong>Medical: Therapeutic</strong></td>
<td>Medical accelerator</td>
<td>Wound healing</td>
<td>Hyperthermia</td>
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<td></td>
<td>(Rad therapy)</td>
<td>Low-level laser therapy</td>
<td>Dathermy</td>
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<td></td>
<td></td>
<td>PUVA therapy</td>
<td>Bone healing</td>
<td>Bone healing</td>
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<tr>
<td><strong>Medical: Surgical</strong></td>
<td>Intra-operative electron beam</td>
<td>Surgical laser</td>
<td>Electrosurgery</td>
<td>Lithotripsy</td>
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<td></td>
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<td>Ophthalmic, PRK laser</td>
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<td></td>
<td>Dental laser</td>
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<tr>
<td><strong>Medical: Other</strong></td>
<td>Bone density measurement</td>
<td>Germicide lamps</td>
<td>Blood warmers (microwave)</td>
<td>Bone density measuring</td>
</tr>
<tr>
<td></td>
<td>Cabinet x-ray</td>
<td>Dental resin curing</td>
<td>Sterilizer (plasma)</td>
<td>Geriatric bath (ultrasound)</td>
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<td></td>
<td>Veterinary imaging</td>
<td>Operating lights</td>
<td>Telemetry</td>
<td>Hearing aid</td>
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<tr>
<td><strong>Scientific, Other</strong></td>
<td>Analytical x-ray</td>
<td>Research lasers</td>
<td>Many scientific uses</td>
<td>Many scientific uses</td>
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<td></td>
<td>Oscilloscope</td>
<td>UV/R research uses</td>
<td>Nuclear magnetic resonance</td>
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<td>Weather doppler</td>
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<tr>
<td><strong>Industrial</strong></td>
<td>Cabinet x-ray</td>
<td>Ranging &amp; detection</td>
<td>Dielectric heater, sealer</td>
<td>Nondestructive tests</td>
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<td></td>
<td>Industrial x-ray</td>
<td>Alignment, surveying</td>
<td>Food processing</td>
<td>Gauging</td>
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<td>Check weld/metal integrity</td>
<td>Laser welder</td>
<td>Dryer</td>
<td>Detect motion/occupancy</td>
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<td>Laser material processing</td>
<td>Air traffic control</td>
<td>Cleaner</td>
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<td>Process control/machine vision</td>
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<td>Welder</td>
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<td></td>
<td>UV curing</td>
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<tr>
<td><strong>Business, Commercial, Security</strong></td>
<td>People (contraband) scanner</td>
<td>Suntan parlors</td>
<td>Police radar</td>
<td>Jewelry cleaners</td>
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<td>Fluorescent lamp</td>
<td>Pest controllers</td>
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<td></td>
<td>IR detector or security</td>
<td>EAS, metal detector</td>
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<td></td>
<td>Fiberoptic communication</td>
<td>Security system (microwave)</td>
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<td>Reprographics</td>
<td>Walkie-talkies</td>
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<td>Mercury vapor lamp</td>
<td>Clothes dryer</td>
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<td>UPC readers</td>
<td>Communication</td>
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<td>Laser pointer</td>
<td>Microwave LAN</td>
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<td>IR data transmitt/control</td>
<td>RF-excited lighting</td>
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<tr>
<td><strong>Consumer (household, entertainment, sports)</strong></td>
<td>Television receiver</td>
<td>Halogen lamp</td>
<td>Cellular telephone</td>
<td>Ultrasonic toothbrush</td>
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<td>Video monitor</td>
<td>Laser light shows</td>
<td>Microwave oven</td>
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<td>Night vision scope</td>
<td>Laser printer</td>
<td>Electric blanket</td>
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<td>Suntan bed, lamps</td>
<td>CB/ham radio</td>
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<td>CD and CD-ROM player</td>
<td>Intrusion/anti-theft</td>
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<td>Laser toys/velites</td>
<td>Remote controller</td>
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<td>Laser gunsight</td>
<td>Video monitor</td>
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<td></td>
<td></td>
<td>Remote controller</td>
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<td>Autofocus camera</td>
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<td></td>
<td></td>
<td>Digital display/monitor</td>
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Introducing Radiation-Emitting Products to US Market

• Manufacturer’s responsibility
  • Manufacturer: Those who manufacture, assemble, and import radiation-emitting products
  • Maintain records and submit reports before marketing and annually
  • Once report is submitted
    • Accession number will be issued
    • Acknowledgement letter will be provided
• Certification
  • Meets FDA performance standards
  • Does not emit hazardous radiation
Performance Standards

- Performance Standards for Electronic Products: General (21 CFR 1010)
- Specific Performance Standards for Electronic Products (21 CFR 1020 - 1050)
- Television receivers (21 CFR 1020.10)
- Cold-cathode gas discharge tubes (21 CFR 1020.20)
- Diagnostic x-ray systems and their major components (21 CFR 1020.30)
  - Radiographic equipment (21 CFR 1020.31)
  - Fluoroscopic equipment (21 CFR 1020.32)
  - Computed tomography (CT) equipment (21 CFR 1020.33)
- Cabinet x-ray systems (21 CFR 1020.40)
- Microwave ovens (21 CFR 1030)
- Laser products (21 CFR 1040.10)
  - Specific purpose laser products (21 CFR 1040.11)
- Sunlamp products and ultraviolet lamps intended for use in sunlamp products (21 CFR 1040.20)
- High-intensity mercury vapor discharge lamps (21 CFR 1040.30)
- Ultrasonic therapy products (21 CFR 1050.10)
FDA Guidances

• Guidance represents the Food and Drug Administration's (FDA's) current thinking on the topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations.
When a Guidance is needed

• Example: Guidance for Industry and FDA Staff Guidance on Laser Products - Conformance with IEC 60825-1 and IEC 60601-2-22 (Laser Notice No. 50)

• What should manufacturers do in using this guidance?
• Use the following modified statement of compliance on the certification label: “Complies with FDA performance standards for laser products except for deviations pursuant to Laser Notice No. 50, dated (Insert date of this guidance.)” or “Complies with 21 CFR 1040.10 and 1040.11 except for deviations pursuant to Laser Notice No. 50, dated June 24, 2007”; and

• Submit product reports or supplemental reports to describe changes to products in accordance with this guidance.

• The effectiveness of this guidance will end on the effective date(s) of any amendments to the Federal regulations applicable to laser products under Chapter 1, Subchapter J of Title 21 of the Code of Federal Regulations.
Post-Market Regulations

• MDR (medical device reporting)

• **Mandatory Medical Device Reporting:**
  • The Medical Device Reporting (MDR) regulation (21 CFR 803) contains mandatory requirements for manufacturers, importers, and device user facilities to report certain device-related adverse events and product problems to the FDA.
  
• **Manufacturers:** Manufacturers are required to report to the FDA when they learn that any of their devices may have caused or contributed to a death or serious injury.

• **Importers:** Importers are required to report to the FDA and the manufacturer when they learn that one of their devices may have caused or contributed to a death or serious injury. The importer must report only to the manufacturer if their imported devices have malfunctioned and would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.
Other Post-Market Regulations

• Recalls
• Corrections
• Removals
OSEL

Office of Science and Engineering Laboratories
OSEL

- **Support CDRH for Science-Based Decisions**

- **Organization**
  - Division of Applied Mechanics (DAM)
  - Division of biology, chemistry, and material science (DBCMS)
  - Division of imaging, diagnostics, and software reliability
  - Division of biomedical physics
DBP

• biomedical and tissue optics,
• biophysics and electrophysiology,
• electrical engineering,
• functional device performance and human factors
• wireless communication and electromagnetic interference and compatibility.
Optics

- Biosensing, Ultrashort Laser Therapeutics and Nanobiophotonics
- High Resolution Optical Imaging
- Laser and Optical Safety
- Optical Spectroscopy and Spectral Imaging
- Optical Image Quality and Computational Biophotonics
Laser and Optical Safety (2)

• [http://www.fda.gov/MedicalDevices/ScienceandResearch/ResearchPrograms/ucm477386.htm](http://www.fda.gov/MedicalDevices/ScienceandResearch/ResearchPrograms/ucm477386.htm)

### Laser and Optical Safety

Contact

Do-Hyun Kim, Ph.D

Summary

This program supports the agency’s regulatory and guidance role by advancing our knowledge on the optical radiation safety of medical devices on human tissue. The program especially focuses on the understanding of light-tissue interaction for novel and emerging optical technologies, such as laser scanning confocal microscopy, two-photon microscopy, photoacoustic microscopy, and hyperspectral imaging. These technologies deliver lights on biological tissue in an unconventional way, so they require understanding of optical radiation damage mechanism.
Laser and Optical Safety (2)

- **Personnel**
  - *FDA Staff:*
    - Do-Hyun Kim, Ph.D.
    - Ilko K Ilev, Ph.D.
    - T Joshua Pfefer, Ph.D.
    - Dexiu Shi, Ph.D.
    - Quanzeng Wang, Ph.D.
  - *Research Fellow:*
    - Mio k Yun, Ph.D.

- **Relevant standards & guidances**
  - ISO 15004-2
  - IEC 60825-1
  - ANSI Z136.1
510(k) Exempt Devices

• Preamendment devices not significantly changed or modified
  • devices legally marketed in the U.S. by a firm before May 28, 1976 and which have not been significantly changed or modified since then
  • a regulation requiring a PMA application has not been published by FDA.
  • Devices meeting this description are referred to as "grandfathered" and do not require a 510(k).
• Class I/II devices specifically exempted by regulation.
510(k) types

• Traditional 510(k)

• Special 510(k)
  • Under the Special 510(k) option, 510(k) holders who intend to modify their own legally marketed device will conduct the risk analysis and the necessary verification and validation activities to demonstrate that the design outputs of the modified device meet the design input requirements.
  • The Special 510(k) allows the manufacturer to declare conformance to design controls without providing the data.

• Abbreviated 510(k)

• Third-Party 510(k)

• De Novo
510(k) Fee Exemption

<table>
<thead>
<tr>
<th>Category</th>
<th>Exemption or Waiver</th>
</tr>
</thead>
<tbody>
<tr>
<td>Third-party 510(k)</td>
<td>Exempt from any FDA fee; however, the third-party does charge a fee for its review.</td>
</tr>
<tr>
<td>Any application for a device intended solely for pediatric use.</td>
<td>Exempt from user fee. Please note that changing the intended use from pediatric use to adult use requires the submission of a new 510(k). The new 510(k) is subject to the 510(k) review fee at the time of submission.</td>
</tr>
<tr>
<td>Any application from a State or Federal Government entity.</td>
<td>Exempt from any fee unless the device is to be distributed commercially.</td>
</tr>
</tbody>
</table>
513(g)

- For devices that are innovative, it can sometimes be difficult to find an exact predicate device using the FDA classification database. In this case, you can submit a 513(g) “Request for Information” to the FDA. The 513(g) submission should outline the characteristics of your device and include rationale on why you believe it falls into a specific class.
De Novo

• Entirely new devices are automatically considered to be Class III in the US. However, many new products are not high risk. This is why the FDA has the *de novo* process. You may consider filing a “*de novo*” submission if the FDA determines, through means such as a 513(g) or Pre-Submission, that your device is a “novel” with no existing classification or predicate device on the market.

• Within 120 days after your *de novo* submission, the FDA will determine if your device is Class I or II and may issue an entirely new product code and regulation number. If rejected, your device will remain Class III.
Thank you