

# **Current Status of Regulatory Practices for Medical Devices in Korea**

**Moo-Song Lee, Won-Kyu Lee\***

**Department of Preventive Medicine, University of Ulsan &  
Asan Medical Center**

**\* Division of Safety, Device Headquarters, Korean FDA**

Good Morning. I am Moo-Song Lee from Asan Medical Center.

I will present current status of regulatory practices for devices. First of all,  
I should say that because my personal opinion is included, this  
presentation does not reflect official opinion of Korean FDA

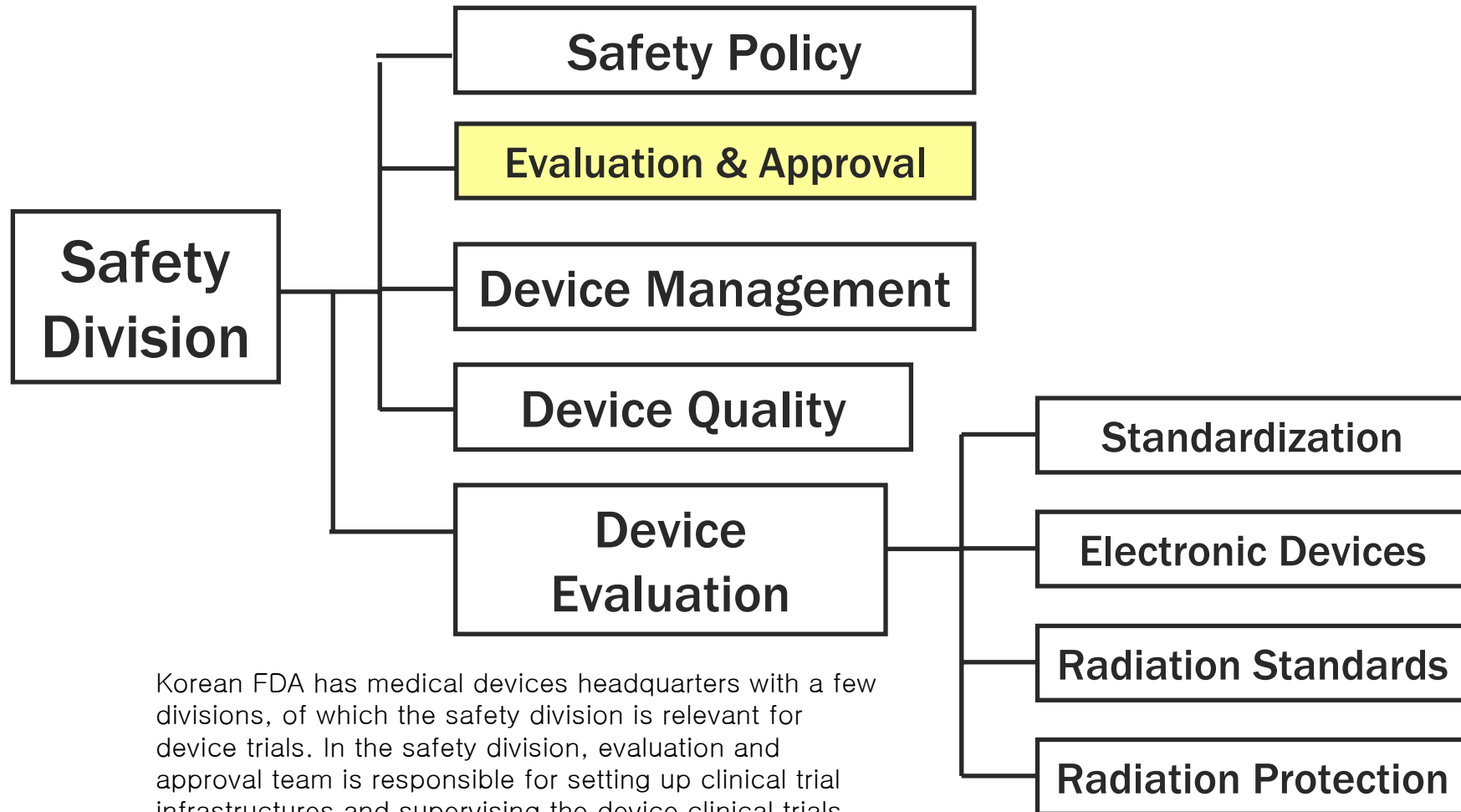
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I would proceed first the Korean situations of device industry with relevant regulations and review process for clinical trials of medical devices. Afterwards, limitations of current systems will be presented and ongoing as well as future projects follows.

# Medical Device Headquarters, KFDA



Korean FDA has medical devices headquarters with a few divisions, of which the safety division is relevant for device trials. In the safety division, evaluation and approval team is responsible for setting up clinical trial infrastructures and supervising the device clinical trials.

# Device Industries

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- **Current status**

Characteristics	2004년	2010년	2015년
Rank (Production)	13th	10th	5th
Production	\$1.5 billion	\$3.6 b	\$7.5 b
Exportation	\$0.65 b	\$2.1 b	\$5.5 b

- **For commercialization of new BT, IT Products**

- Safety and efficacy evaluation by quality clinical trials are needed.

- **Two aspects in conducting clinical trials**

- Promoting device industry

- Human protection by assuring safety and efficacy of devices

In Korea, device industry ranks thirteenth in production with medical devices of one point five billion dollars and growing rapidly. As we all know, for successful new devices, good clinical trials are essential. The most serious obstacles is the size of device companies. The majority is so small that cannot sponsor good trials. So the role of the government is much needed.

# Surroundings of Device Industry

## Market

- Sharp increase by aging society and seeking well-beings
  - An important industry for the next generation
    - a presidential election pledge
- ※ Market size in year 2009: \$3 billion, 2015: \$7 billion

## Technology

- Fusion industry, having potential for growth
  - Governmental R&D is expanded.
- ※ Department of Health & Welfare: \$130 million ('06 ~), D of Industry: \$150 million('05~'09), D of Technology: \$30 m ('05~)

## Commercialization

- Infrastructure for clinical trial of devices is scarce.
- ※ Focused on prescription drugs

Considering the aging of Korean population and seeking well-being, the market is expected to increase. Furthermore, advanced BT and IT technology in Korea would play an important role in developing promising products. However, the infrastructure for clinical trials are too shallow to achieve good clinical practices.

# SWOT Analysis for Device Industry

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## Strength

- ◇ Medical personnel and hospitals
- ◇ Consensus for well-being
- ◇ Investment for new devices

## Opportunity

- ◇ Importance of clinical infrastructures is stressed (esp. in governmental agencies)
- ◇ Importance of IRB ...
- ◇ Investment to industries ...

## Weakness

- ◇ Scarce clinical infrastructure
- ◇ Scarce investment to clinical R&D for commercialization
- ◇ Few educated clinical personnel & few educational program
- ◇ Few governmental support systems including regulatory activities

## Threat

- ◇ Clinical trials in Asia are mainly done in Australia or ...
- ◇ Late commercialization induces industrial fatigue.
- ◇ Poor clinical trials are obstacles for high-technology products.

SWOT analysis could be skipped. In summary, we have strengths as well as opportunities. But the weakness and threat are also deep especially for the medical institutions, personnel, and governmental support.

# **Device Clinical Trials, Approved by KFDA**

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- **Human trials for evaluating safety and efficacy of medical devices**
  - **Therapeutic usage of unapproved devices for clinical trials**
    - **should be approved**
  - **Emergency usage of unapproved devices for clinical trials**
    - **should be reported**
    - **Devices for clinical trials : Devices of which the clinical trials are approved**
    - **Life-threatening diseases, no alternative devices, or therapeutics alternatives**
- ***Excluded***
  - **Conducting trials for already approved products as approved indication or regimen**

We will focus on the device clinical trials in Korea. FDA don't regulate trials for already approved devices as the approved regimen and indication. For unapproved products, FDA approval is needed.

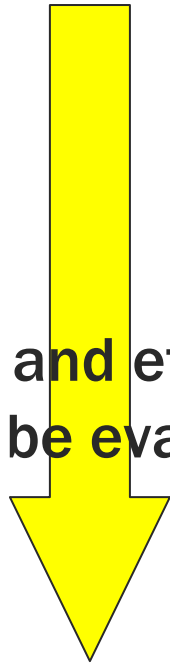
# Tracks of Approval

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Newly developed

Already approved



Safety and efficacy  
should be evaluated



Safety &  
efficacy  
changed

**Clinical trials should be approved.**

For already approved devices, if changes of safety and efficacy for example by different indication would be expected, clinical trials by FDA approved protocol should be conducted.

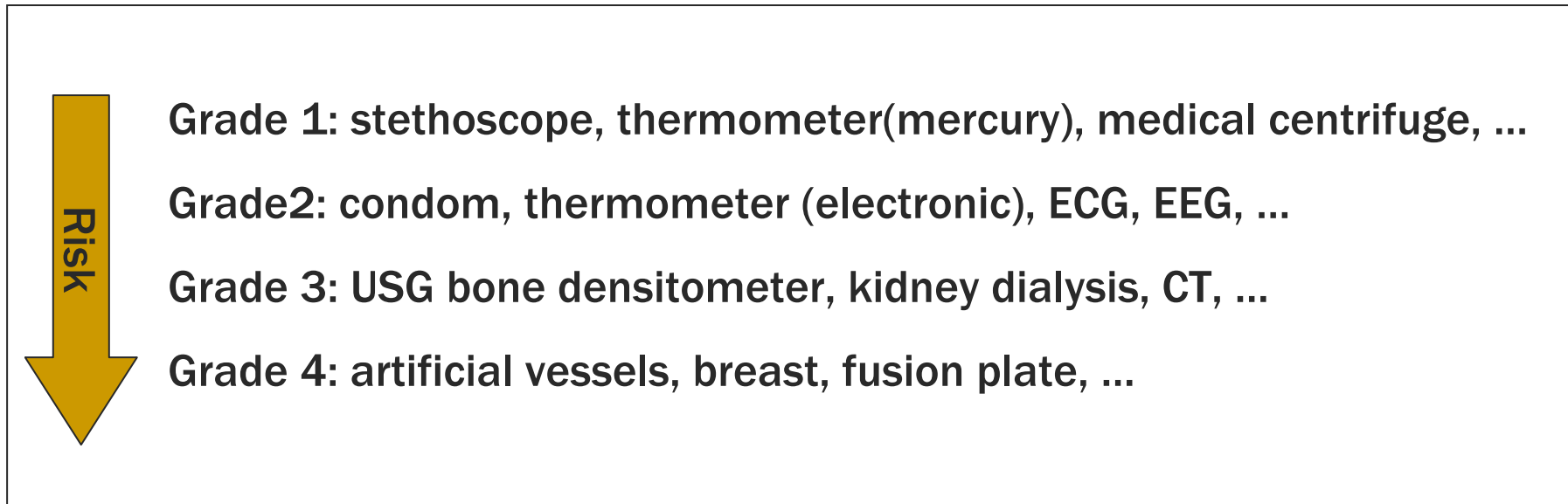


# Grading of Devices

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## By purpose of use & potential risk



Grading of devices also affects the review track of clinical trials. For Grade 4 device such as fusion plate with highest risk, conducting clinical trials is essential for product approval.

## **Products to be Approved for Safety & Efficacy**

- **Compared to already approved or noticed products**
  - **Different totally or in part, in aspects of**
    - **indication, mechanism, design**
    - **materials, chemical constituents, Energy source used (or transmitted)**
    - **performance, manufacturing process**
    - **technical properties**
  - **For which the safety or efficacies are expected to be different.**
    - ※ **Regulations for technical documents**
    - ※ **Division of Medical Devices Evaluation**

In summary, clinical trials evaluating safety and efficacy should be needed in cases of new products with different indication, mechanism, design, and so on.

## Approved Devices in Korea, 2001-2006, by Trials

Clinical Department	Approved products	Items
Surgery	16	implants, bone grafts, ...
Internal Medicine	14	glucometer, endoscope, stent, ...
Urology	9	urination controller, foreskin remover, ...
ENT	5	adhesion check, ...
Dermatology	5	Wrinkles check, suture, wound clothing, ...
Dentistry	4	implants, GTR, bone grafts, ...
Ophthalmology	2	IOL, contact lenses, ...
OBGY	1	labor inducer
Clinical Pathology	1	microarray chip analyzer
<b>Total</b>	<b>57</b>	

From year two thousand one to two thousand six, 57 devices were approved after conducting clinical trials. As you can see, major therapeutic departments use the devices.

## **New Clinical Trials for Devices: Application and Approval**

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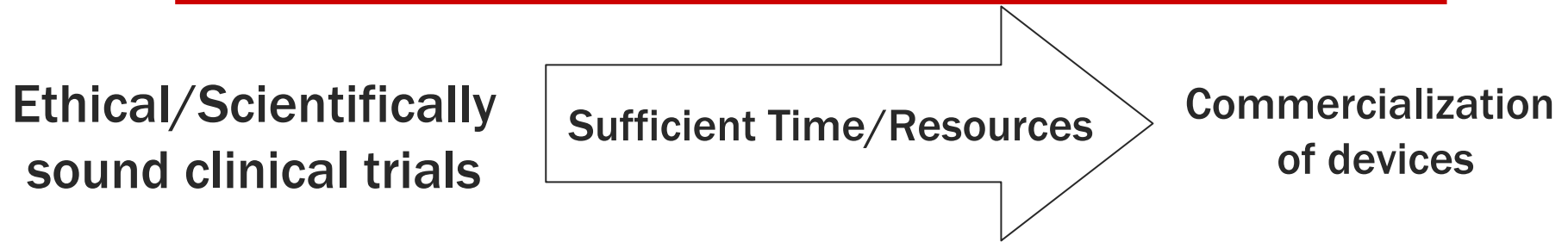
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<b>Year</b>	<b>Applied Protocols</b>	<b>Approval (No)</b>	<b>Approval(%)*</b>
<b>2001</b>	<b>16</b>	<b>3</b>	<b>18</b>
<b>2002</b>	<b>29</b>	<b>9</b>	<b>31</b>
<b>2003</b>	<b>23</b>	<b>9</b>	<b>39</b>
<b>2004</b>	<b>24</b>	<b>13</b>	<b>54</b>
<b>2005</b>	<b>18</b>	<b>9</b>	<b>50</b>
<b>2006</b>	<b>33</b>	<b>14</b>	<b>42</b>
<b>Total</b>	<b>140</b>	<b>57</b>	<b>40</b>

※ **Self-withdrawal or rejected due to insufficient pre-clinical data, trials methods without scientific rationale, etc.**

In total, sixty percent of clinical trial protocols have not been approved because of insufficient pre-clinical data, poor scientific quality.

# Ethics/Scientific Integrity in Clinical Trials



## Roles of Sponsor, Investigator, IRB, FDA

This slide stress the ethical, and sound clinical trials, in which sponsors, investigators, IRB, and FDA has its role. And the sufficient time and resources are needed for marketing approval.

# Flowchart of Protocol Review

Sponsor/Investigator  
Preparing protocols



IRB  
Review/Approval

FDA  
Review/Approval

<b>Preparing protocols</b>
Clinical protocol (Investigators)
Technical documents (Sponsor)
Scientific methodology Ensuring safety

<b>Reviewing protocols</b>
Clinical protocol (IRB)
Reviewing scientific methodology

<b>Reviewing safety</b>
Clinical protocol (FDA IRB)
Technical documents
Scientific methodology Ensuring safety

In parallel

For protocol approval, sponsor and investigators develop the protocol. IRB reviews and approves the protocol. FDA also reviews the protocol.

# Flowchart of Trial Conduct

Investigator/Sponsor/IRB  
**Management**



**IRB**  
Monitoring conduct  
& Approving Results

**FDA**  
Monitoring conduct  
& Approving Results

<b>During trials</b>
Conducting trials (Investigator)
Monitoring (Sponsor)
Management (IRB, FDA)
<b>Conducting trials with scientific rationale Monitoring/Management</b>

<b>Reviewing results</b>
Results (IRB)
<b>Ensuring scientific conduct of trials</b>

<b>Reviewing results</b>
Results, ... (FDA)
<b>Approving scientific conduct of trials</b>

In parallel

During the trials, the relevant bodies also has their roles.

# **Limitations of Device Clinical Trials in Korea**

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- **Facilities**
  - **Limiting clinical trials to big hospitals with more than 200 beds.**
    - **Specialized small clinics, research institutes are not allowed to conduct trials (2006).**
    - **IRB's are not possible in such small clinics.**
  - **Just a few big hospitals have specialized facilities and personnel.**
    - **Governmental support for device clinical trial center is needed.**

As we will see, Korea has also limitations of which some are very serious. Most important is the scanty infrastructure for which governmental support is most needed.



# **Educational Center or Programs are Needed**

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- **Just a few university hospitals provide educational program focused on medicinal products.**
- **No governmental educational program**
  - ❖ **US, for example, provide governmental support for clinical trial centers.**
- **Clinical trial personnel in medical institutions do not have enough**  
**Insufficient understandings for clinical trials regulations**
  - ❖ **Few specialized educational programs for investigators, sponsors, and IRB's**
- **Specialists in preparing protocols are needed.**
  - ❖ **among sponsors or investigators**

Educating clinical trial personnel is critical. Few hospitals are running educational program for device-specific clinical trials as well as the Korean FDA until two years ago. As a result, there are almost no well-educated trial personnel as well as specialist for developing protocols.

# **Insufficient Support and Trial Management System**

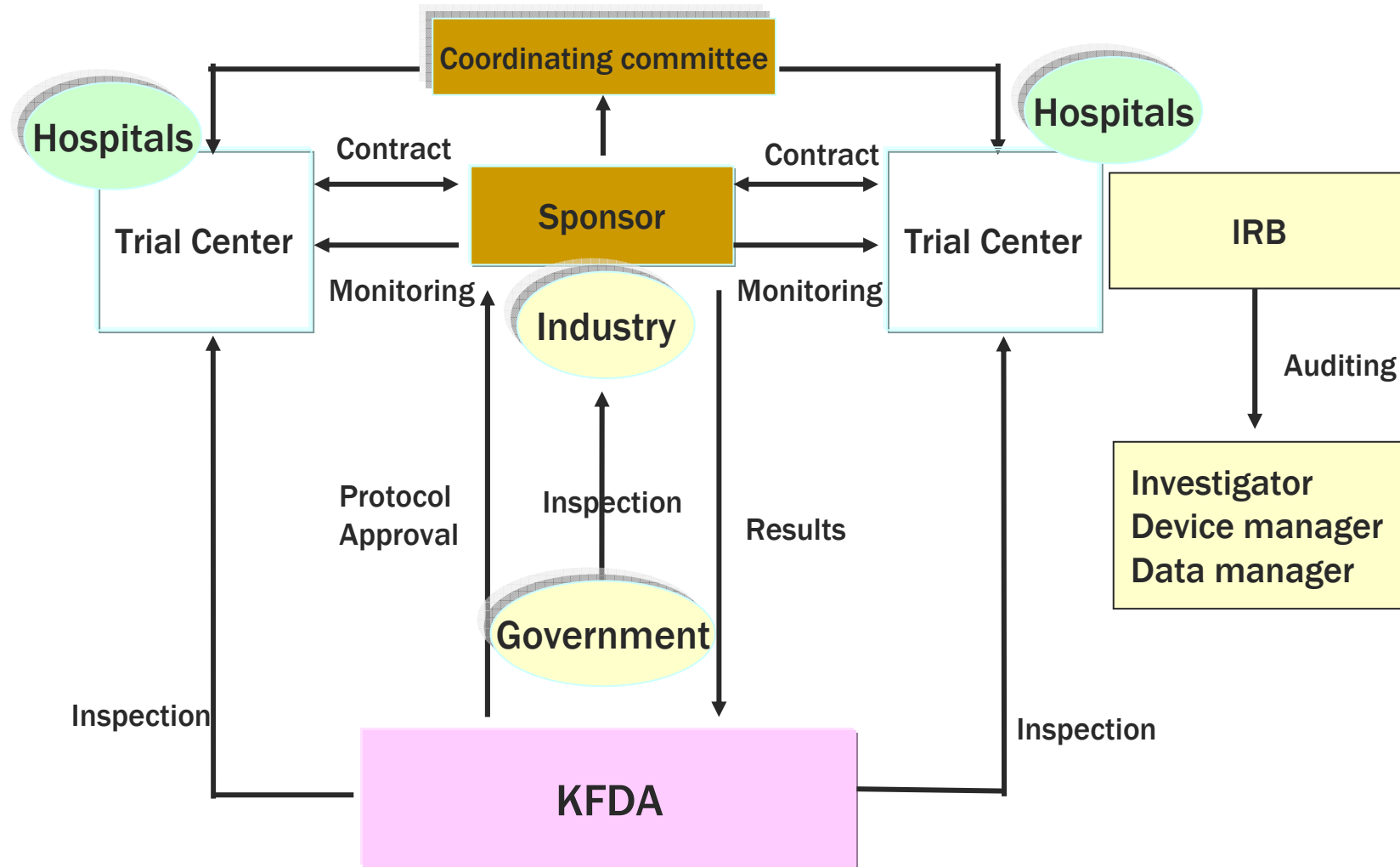
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- **Standardization of Protocol for Device Trials**
- **Standardization of SOP for Clinical Trial Centers**
- **Clinical support for commercialization**
  - ※ **Financial support for conducting device trials**
- **Comprehensive Trial management and support systems**
  - ※ **Efficient, comprehensive management system, allowing for Korean situation**
  - ※ **Specialist group (clinical and engineering) are needed.**

For standardization of protocols and SOP's for institutions conducting trials, there is much to be done. And for small companies, financial support for conducting clinical trials are also needed.

# Systems of Device Trials

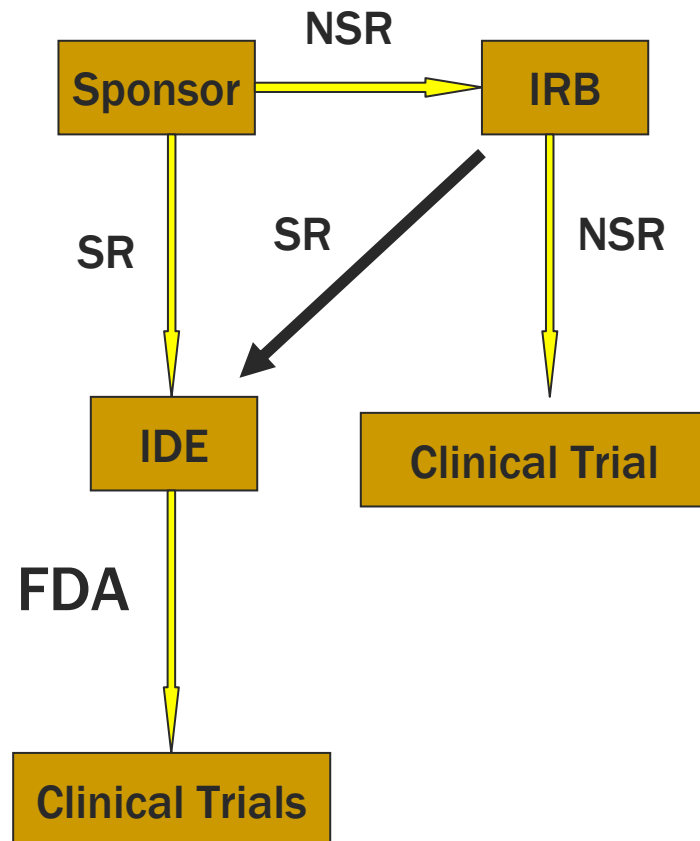


In Korea, for every party in clinical trials are not prepared to conduct good clinical trials. In summary, infrastructures and systems are lacking until recently.

# In US

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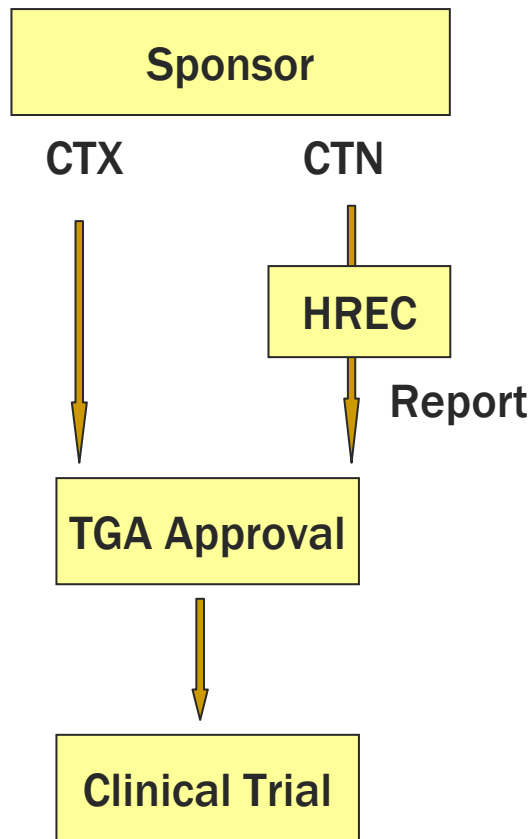
- \* SR (Significant Risk) : FDA approval needed
- \* NSR (Non-Significant Risk) : IRB approval needed
- \* Sponsors classify the device as SR or NSR
- \* IDE (Investigational Device Exemption)
- CFR 21.82
- Standards for device trials

We should skip the foreign situation which we should learn. They have different review track by the significance of the risk posed by the devices

# In Australia

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\* TGA : Therapeutic Goods Administration

\* CTX : Clinical Trial Exemption

- TGA review

\* CTN : Clinical Trial Notification

- HREC review → Institutional approval

- Report to TGA

- Roles of TGA decreased

\* HREC : Human Research Ethics Committee

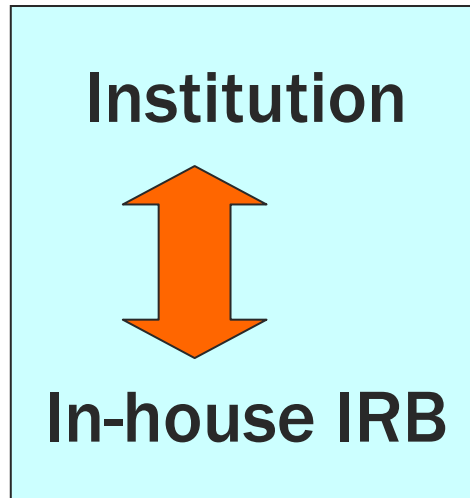
• Sponsor determines CTX/CTN

• Sponsor takes overall responsibilities for device safety.

They have different tracks which are clinical trial exemption and notification by the risk of devices determined by the sponsors.

# Managing Medical Institutions

## - Institutions with IRB's -



- Institutions have their IRB's.
- IRB's are responsible for trials conducted in their institutions.

I should now change the presentation to the recent significant changes in Korea. From two thousand six, guidelines for good clinical practices in medical devices come into effect as well as new initiative for promoting clinical trials.

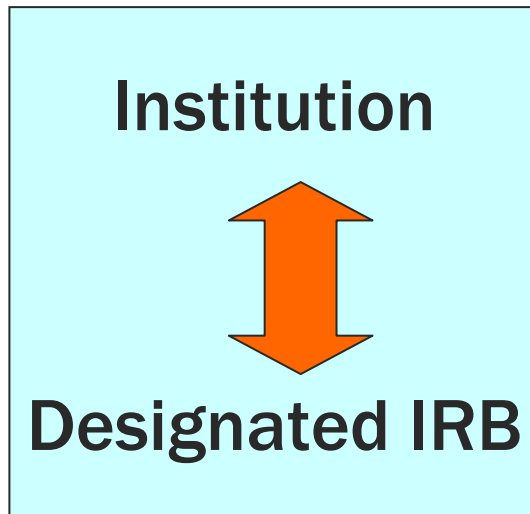
In the beginning, for managing medical institutions ensuring good clinical trials, the role of IRB is essential. In Korea there are three kinds of institutions regarding IRB's. The first one is the usual institutions which have their own IRB's.

# Managing Medical Institutions

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## - Institutions without IRB's -



- Institutions don't have their IRB's.
- Institutions conduct trials under outside IRB's (designated IRB's)

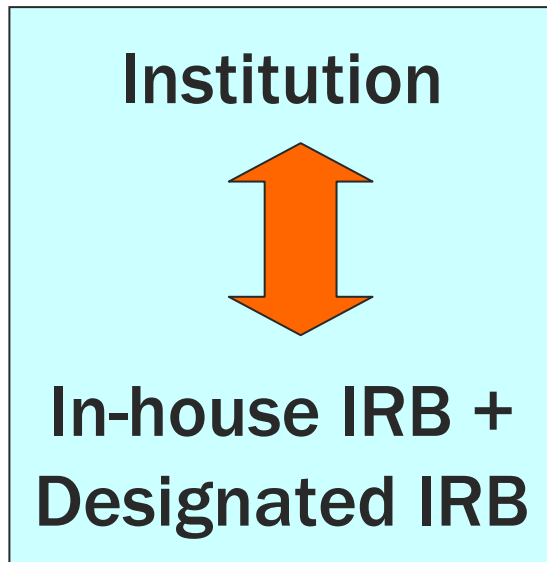
Small institutions might have outside IRB called designated IRB which is run by other institutions and reviewing protocols in behalf of the small institutions by contract.

# **Managing Medical Institutions**

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## **- Institutions with designated IRB -**

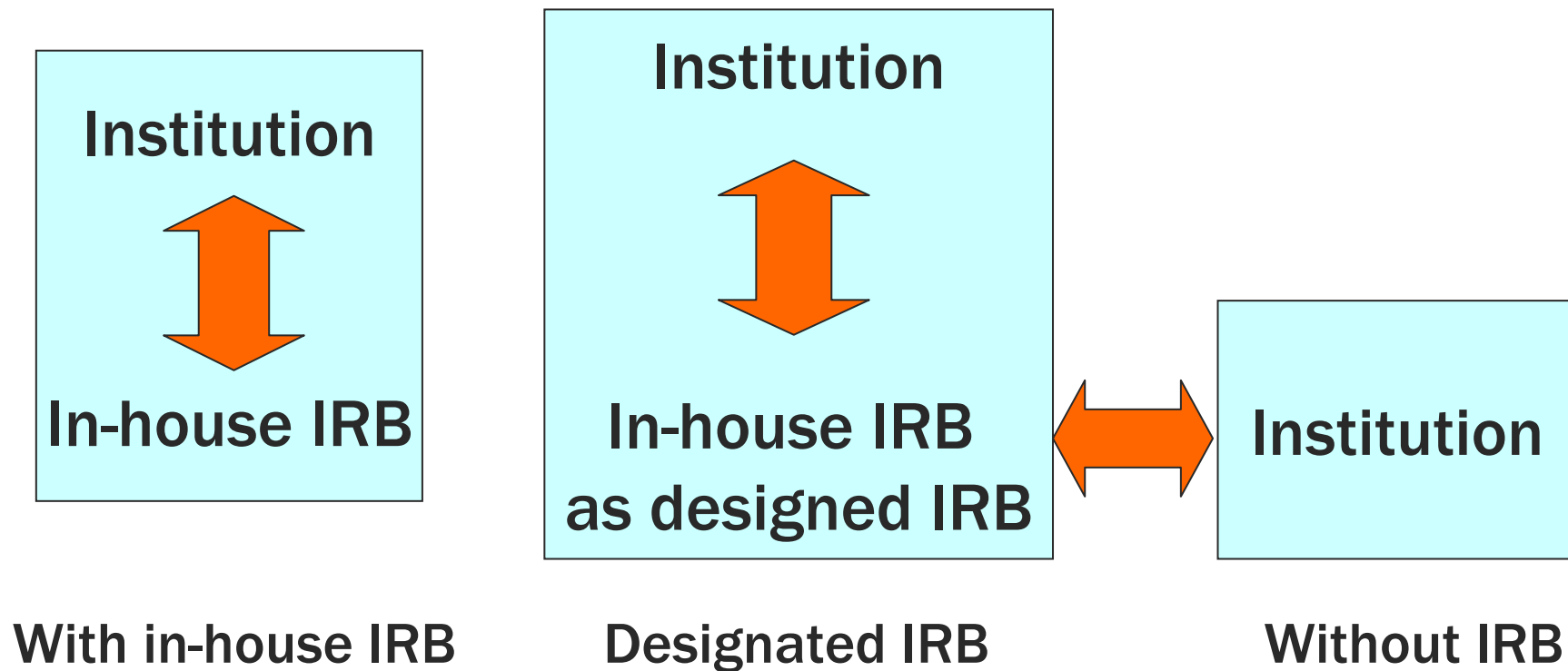


- Institutions have their IRB's.
- The IRB's supervised trials conducted outside the institutions as well as their institutions

Larger hospitals have IRB which is their in-house IRB as well as supervising other institutions' clinical trials.



# Managing Medical Institutions



This slide shows the three kind of IRB's the institutions have.

# Institutions Certified for Conducting Trials

(as of 1<sup>st</sup> May 2008)



**With IRB: 30**

**With Designated IRB: 13**

**Without IRB: 1**

※ Listed in

<http://kfda.go.kr> →

Device Headquarters →

Trials →

**Institutions Conducting Trials**

Korean FDA since two thousand seven, certified medical institutions for conducting FDA-approved clinical trials. As of first of May this year, there are forty-four. Among them, one institution does not have in-house IRB.



They are listed in the FDA homepage. The red circle indicates Asan Medical Center.

# Developing Trial Management & Support Systems

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- **“Working Group for Device Clinical Trials (since Jan 2007)”**
  - **Medical doctors, bioengineering scientist, government personnel**
  
  - ❖ **Supervising KFDA for policy development**
  - ❖ **Technical assistance to promote clinical trials**
  
  - **Technical assistance on**
    - **Running KFDA IRB’s**
    - **Developing educational center and program**
    - **Certifying institutions and managing IRB’s**
    - **Post-certification institutional management including Inspections**
    - **Developing protocols as well as R&D for clinical trials**

To develop systems for managing and support quality clinical trials, working group was formed last year with twenty members, which are medical doctors, biomedical engineering scientist, governmental personnel including myself. So many missions are prepared for the group as mentioned in the slide. To be frank, there are so just a few personnel for clinical trials in device headquarter of Korean FDA.

# **Developing Protocols & Institutional SOP's**

## ■ **Clinical protocols**

- ❖ **by product classes; by indications**
- ❖ **newly developed devices; devices invoking societal issues**
- ❖ **3 kinds/year; \$0.1 million for each by KFDA R&D projects since 2006**

## ■ **Institutional (conducting trials) Standard Operating Procedures (SOP)**

- ❖ **Developing and propagation**
- ❖ **Internationally harmonized SOP's**
- ❖ **KFDA R&D project in year 2007**

Recently, research project for developing disease-specific or device-specific prototypes of protocols are under way as well as developing institutional SOPs

# International Collaboration; Researches

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- **Collaborating with foreign centers**
  - ※ Training and exchange program with foreign centers since 2007
- **Participating in AHWP Clinical division**
  - ※ to be an important clinical trial center in Asia
- **Considering the possibility of bridging studies for imported products**
- **Developing scientific methodologies for clinical trials since year 2007**

In the future, international collaboration should be encouraged. Bridging studies for medical devices in this slide are unfamiliar concept. For approving foreign products, considering ethnicity might be possible for devices like the medicinal products. Several important research works relevant in device trials should be encouraged.

# Setting up the Infrastructure for Trials

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- **Specialized clinical trial centers and personnel**
  - Certification of institutions conducting trials
- **Developing clinical protocols and instructional SOP's**
  - Protocols by indications
  - Internationally harmonized institutional SOP's
- **International collaborations**
  - Foreign exchange and training program
  - Participation in the AHWP Clinical Division
- **Consolidation of relevant regulations and systems**

I should close the presentation summarizing the current status of device trials. In Korea, recent progress is achieved in setting up infrastructure, focusing certified medical institutions and educating trial personnel. Secondly, prototypes of clinical protocols and institutional SOPs have now been under development. However, it remains much to be done.

# Relevant Regulations on Device Trials

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- **Medical Devices Act**

- § 10(Approval of Clinical Protocols) (2004. 5. 30)

- **Regulations**

- § 12(Approval of Clinical Protocols) (2004. 5. 30)
- § 13(Good Clinical Practice) (2004. 5. 30)

- **Notice**

- Approving Trial Protocol for Medical Devices (2005. 7. 14)
- Good Clinical Practices for Medical Devices (2005. 7. 14)
- Certifying Institutions Conducting Device Trials (2006. 12. 14)
- Reviewing Technical Documents of Medical Devices – Safety and Efficacy
- Good Manufacturing Practices – Production, Importation, Quality Control