Regulatory Inspection and Quality Improvement of Korean IRBs

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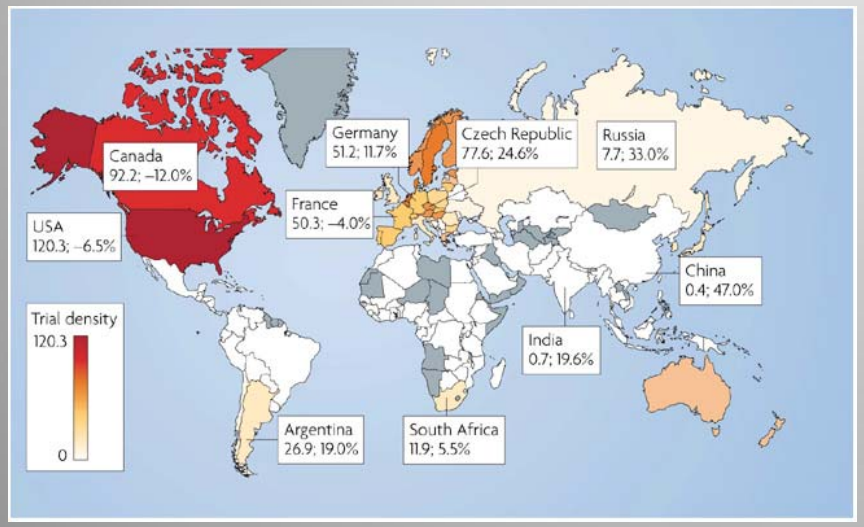
Trends in the globalization of clinical trials

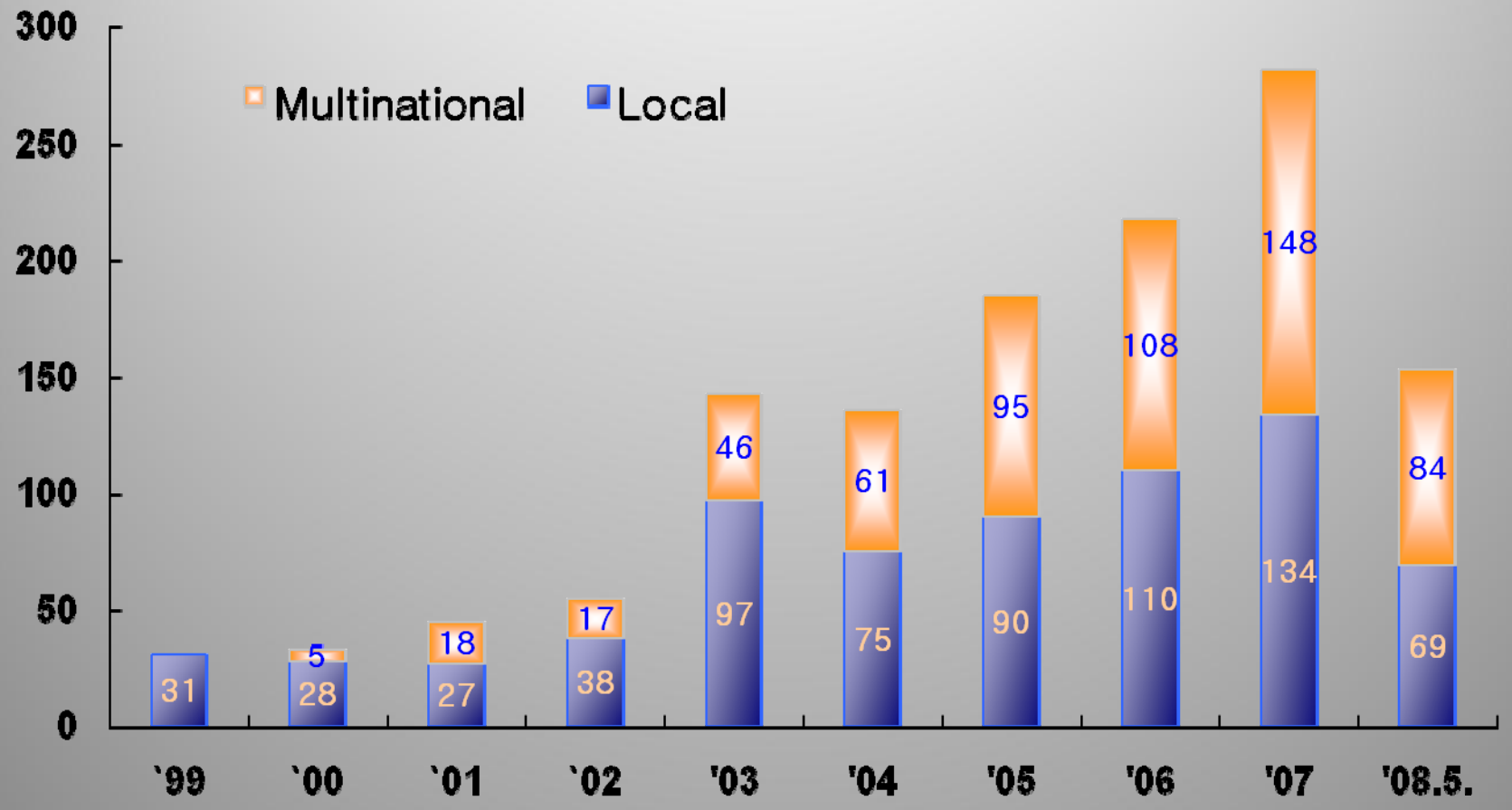
Nature Review 7:13-14, 2008



Rank	Country	Number of sites	Share (%)	ARAGR (%)	Trial capacity	Trial density
1	United States	36,281	48.7	-6.5↓	43.7	120.3
2	Germany	4,214	5.7	11.7↑	10.9	51.2
3	France	3,226	4.3	-4.0↓	9.6	50.3
4	Canada	3,032	4.1	-12.0↓	8.6	92.2
5	Spain	2,076	2.8	14.9↑	6.8	46.4
6	Italy	2,039	2.7	8.1↑	6.7	34.6
7	Japan	2,002	2.7	10.3↑	33.4	15.7
8	United Kingdom	1,753	2.4	-9.9↓	7.6	29.1
9	Netherlands	1,394	1.9	2.1↑	6.8	85.0
10	Poland*	1,176	1.6	17.2↑	5.3	30.9
11	Australia	1,131	1.5	8.1↑	5.4	54.4
12	Russia*	1,084	1.5	33.0↑	5.8	7.7
13	Belgium	986	1.3	-9.4↓	5.2	94.8
14	Czech Republic*	799	1.1	24.6↑	4.5	77.6
15	Argentina*	757	1.0	26.9↑	4.8	19.0
16	India*	757	1.0	19.6↑	5.8	0.7
17	Brazil*	754	1.0	16.0↑	5.1	4.0
18	Sweden	739	1.0	-8.6↓	5.1	81.0
19	Mexico*	683	0.9	22.1↑	4.0	6.2
20	Hungary*	622	0.8	22.2↑	4.1	62.5
21	South Africa*	553	0.7	5.5↑	4.3	11.9
22	Austria	540	0.7	9.6↑	3.8	65.1
23	China*	533	0.7	47.0↑	5.3	0.4
24	Denmark	492	0.7	9.2↑	4.4	90.3
25	South Korea*	466	0.6	17.9↑	3.4	9.5

*Countries in emerging regions. ARAGR, average relative annual growth rate. Trial capacity is the number of sites in the country involved in large trials (20 or more sites) divided by the number of large trials in the country. Trial density is the number of recruiting sites on April 12th 2007 divided by the country population in millions.

Status of Clinical Trials



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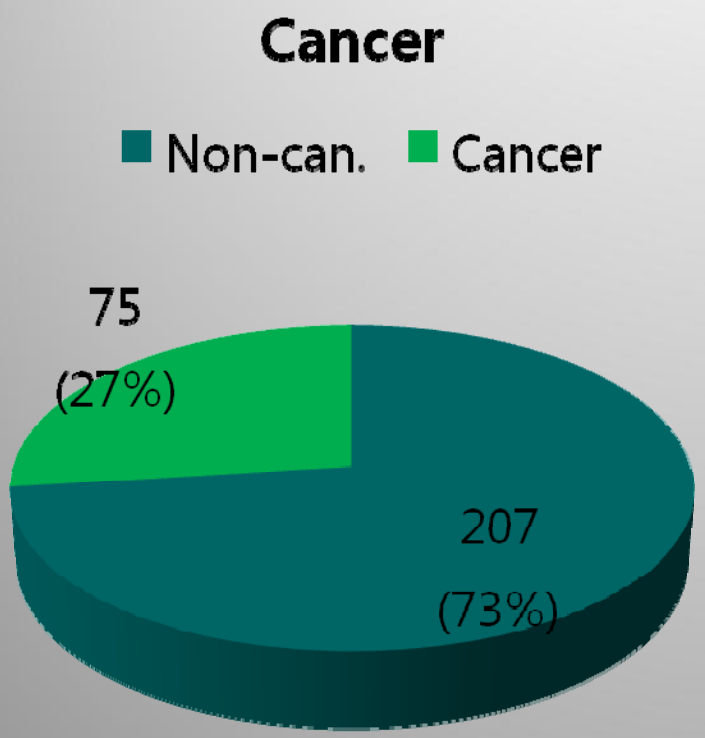
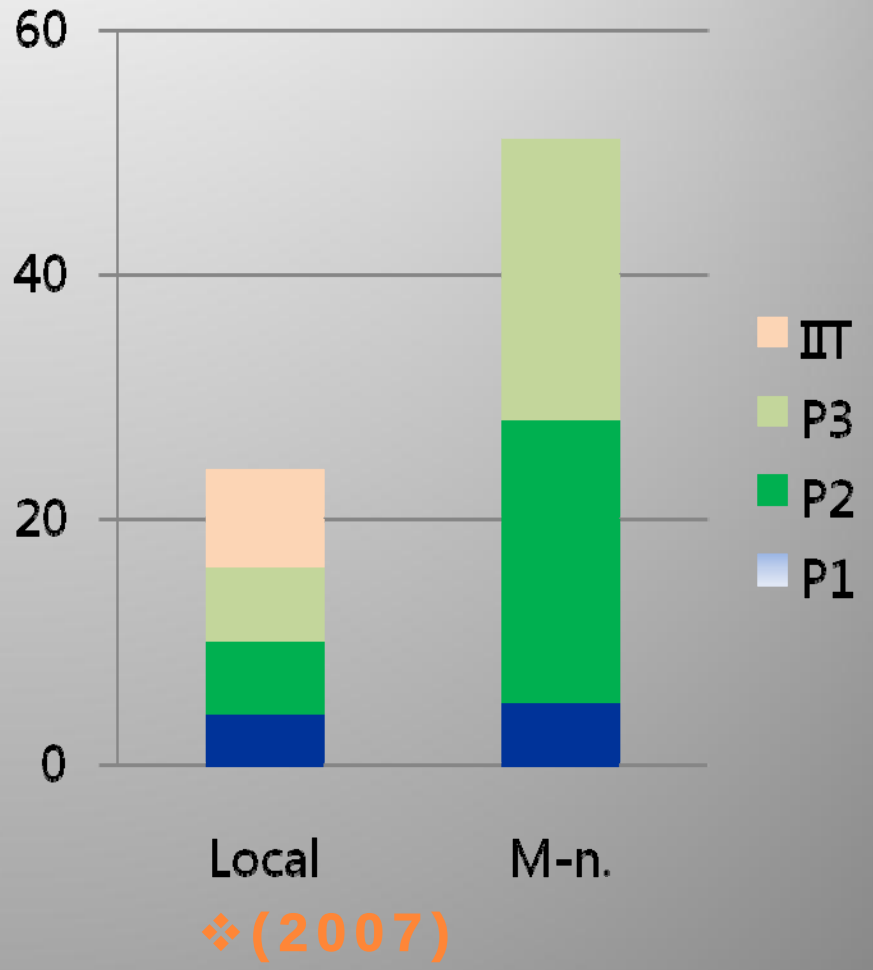
Status of Clinical Trials





❖(2007)

Regulations for Clinical Trials

- Pharmaceutical Affairs Law

- Enforcement regulation of Pharmaceutical Affairs Law
  - *Guidance for GCP*
  - *Guidance for INDs*
  - *Guidance for Accredited Clinical Institutes*

History of KGCP

- Established as of December 28, 1987
- Enforced since October 1, 1995
- Revised as of January 4, 2000

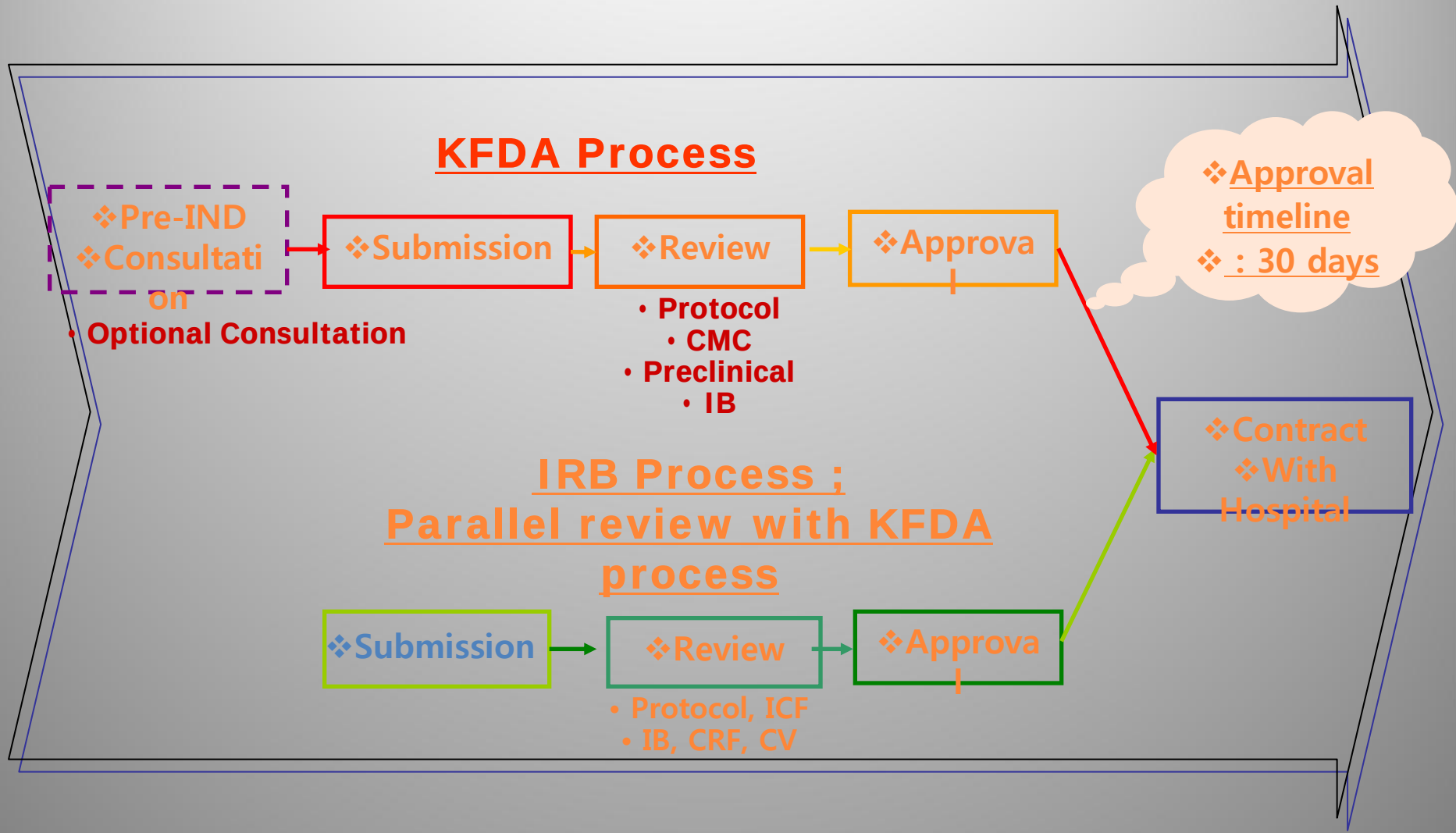
- Harmonize with ICH guideline E6
- Protect the rights and safety of subjects
- Clarify the responsibility of investigator
- Reinforce the function of IRB

Essential Elements in Clinical Trials

❖*defined in the Enforcement regulation of Pharmaceutical Affairs Law*

- Protocol approved by KFDA
- Only at the accredited clinical sites
- Qualified investigator
- Protect the right and safety of subjects
- Informed consent before enrolling subjects

❖IND Process



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Accredited Clinical Institutes

❖*Guidance of Accredited Clinical Institutes*

- Purpose
  - to ensure the quality and integrity of data
- Number of *Accredited Clinical Institutes*

  : 124 training hospitals (2008.8.)

What are necessary to be accredited?

- Appropriate facilities and equipments
- Pool of personnel to support the clinical study
- Activities of IRB
- Education program of GCP
- Structures and activities to manage the clinical study

KFDA's New Inspections Program

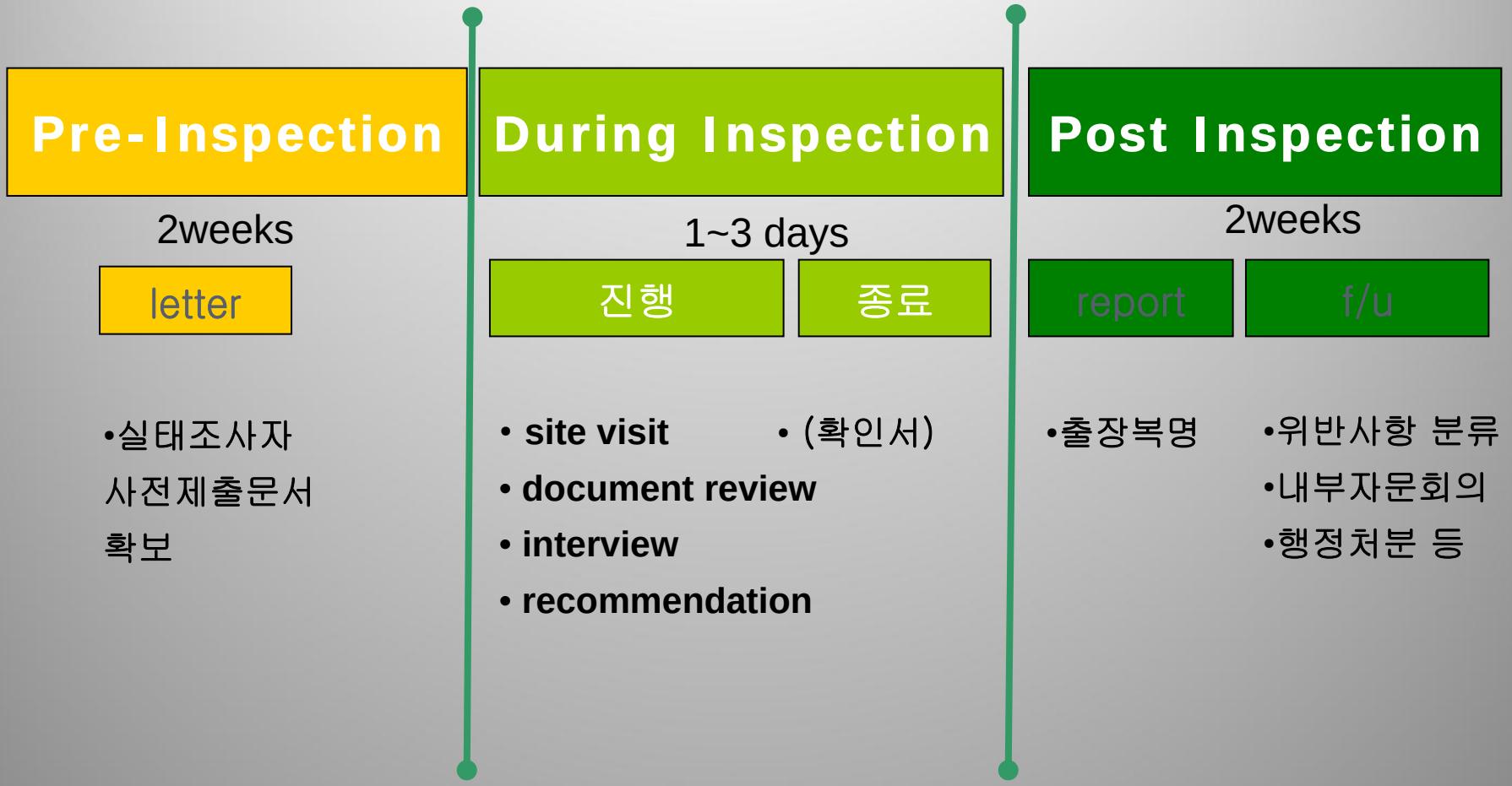
- Begins in 2007
- Check-list for Inspection to facilities
- Categories
  - Routine : every other year
  - Directed : protocol-based, for-cause
- Based on
  - Annual report, safety report
  - Notification on the completion of clinical trial

Types of inspections

- Surveillance inspections
- Directed inspections

Surveillance inspections

- Period : every other year
- Oversee the entire *Accredited Clinical Institutes*
- Inspection teams – 2 or 3 investigators (included headquarters, field investigators)
- Examine to determine whether they conform to current KFDA regulations and IRB/institution's own written procedures



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- Procedures
  - Contact, schedule the site visit
  - Issue a notice of inspection
  - Interview to obtain information about the IRB's policies and procedures
  - IRB’s procedures and membership rosters are examined
  - IRB's performance is evaluated by tracking one or more studies

    - annual report, notification on the completion of clinical trial, IND safety reports

- During the inspection, review
  - Records of IRB membership
  - IRB procedures and guidelines
  - Minutes of IRB meetings for the past 3 year
  - Documents related to the studies given by the clinical investigator to the IRB
  - Documents related to the studies sent by the IRB to the clinical investigator
  - Any other materials about these studies

- After an inspection
  - Conduct an *exit interview with responsible institutional and IRB representatives*
  - Discuss the findings from the inspection
  - If deficiencies are found, issue a written Inspectional Observations to the most responsible IRB representative

- Following a written Inspectional Observations
  - *An informational letter*

    : that identifies deviations from statutes and regulations for which voluntary corrective action is sufficient. Occasionally, such letters request a response from the IRB.
  - *A Warning Letter*

    : that identifies serious deviations from applicable statutes and regulations. A Warning Letter generally requests prompt correction by the IRB and a formal written response to the Agency.

Directed inspections

- unscheduled inspections
  - focused on the IRB’s review of a specific clinical trial or trials.
  - result from a complaint, clinical investigator misconduct, or safety issues pertaining to a trial or site.

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defined in the Enforcement regulation of Pharmaceutical Affairs Law

Administrative penalties

위반사항	행정처분내용			
	1차	2차	3차	4차
식약청장이 지정하지 아니한 기관에서 임상시험실시	당해품목 임상시험업무정지 6월	당해품목 회수폐기		
피험자동의규정 미준수	당해품목 임상시험업무정지3월 및 임상시험책임자변경	당해품목 임상시험업무정지 6월 및 임상시험책임자변경	당해품목 임상시험업무정지 9월 및 임상시험책임자 변경	당해품목 회수폐기 및 임상시험실시기관지정취소
피험자보호규정 미준수	당해품목 임상시험업무정지3월 및 임상시험책임자변경	당해품목 임상시험업무정지6월 및 임상시험책임자변경		
기타 식약청장이 정한 임상시험관리기준 미준수	경고	당해품목임상시험업무정지1월	당해품목임상시험업무정지3월	당해품목임상시험업무정지6월
임상시험책임자가 임상시험실시기준 미준수	경고	임상시험배제 3월	임상시험배제 6월	임상시험배제 9월

Findings of Inspection 2007

Suggested corrective actions (1)

- For institutions

1.support IRB’s independence

2.provide archiving storage

3. properly manage trial drugs

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Suggested corrective actions (2)

- For IRBs

1.non-affiliated members' attendance

2.writing minutes

3. continuing review & its frequency

4. PI's reports to IRB

5. member training

Suggested corrective actions (3)

- For investigators

1.ICF signatures

2.CRF documentation

3. delegation/authorization documentation

4. prescription documentation

5. delay in SAE report

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Thank you for your attention.

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