Responsibilities of Investigators for Clinical Trials from Consent to Safety Reporting

Young-Hak Kim, MD, PhD

Department of Medicine, Asan Medical Center,
University of Ulsan College of Medicine, Seoul, Korea

Responsibilities of Investigators

GUIDELINE FOR GOOD CLINICAL PRACTICE

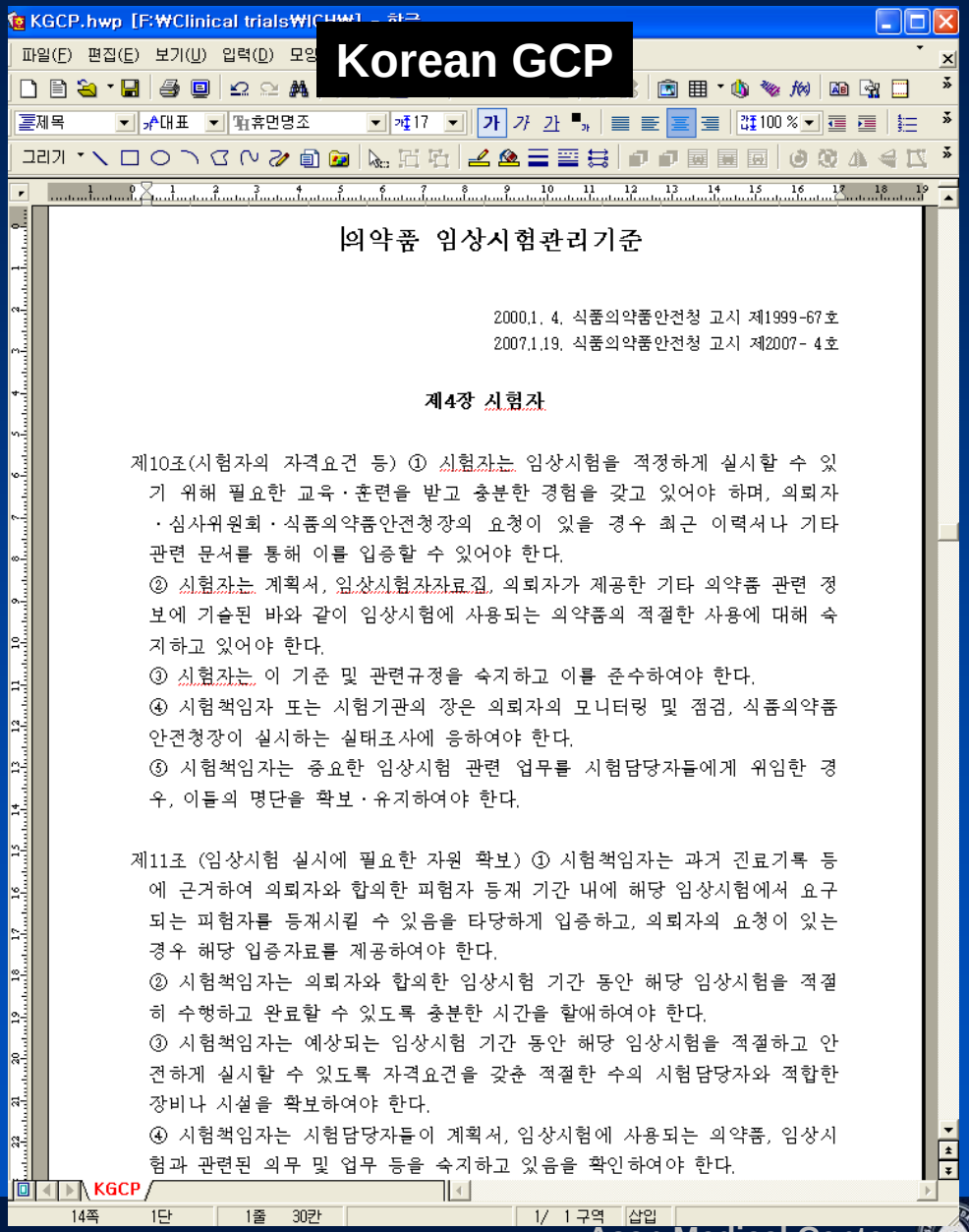
ICH Harmonised Tripartite Guideline

Having reached *Step 4* of the ICH Process at the ICH Steering Committee meeting on 1 May 1996, this guideline is recommended for adoption to the three regulatory parties to ICH

(This document includes the Post Step 4 corrections agreed by the Steering Committee on 10 June 1996)

TABLE OF CONTENTS

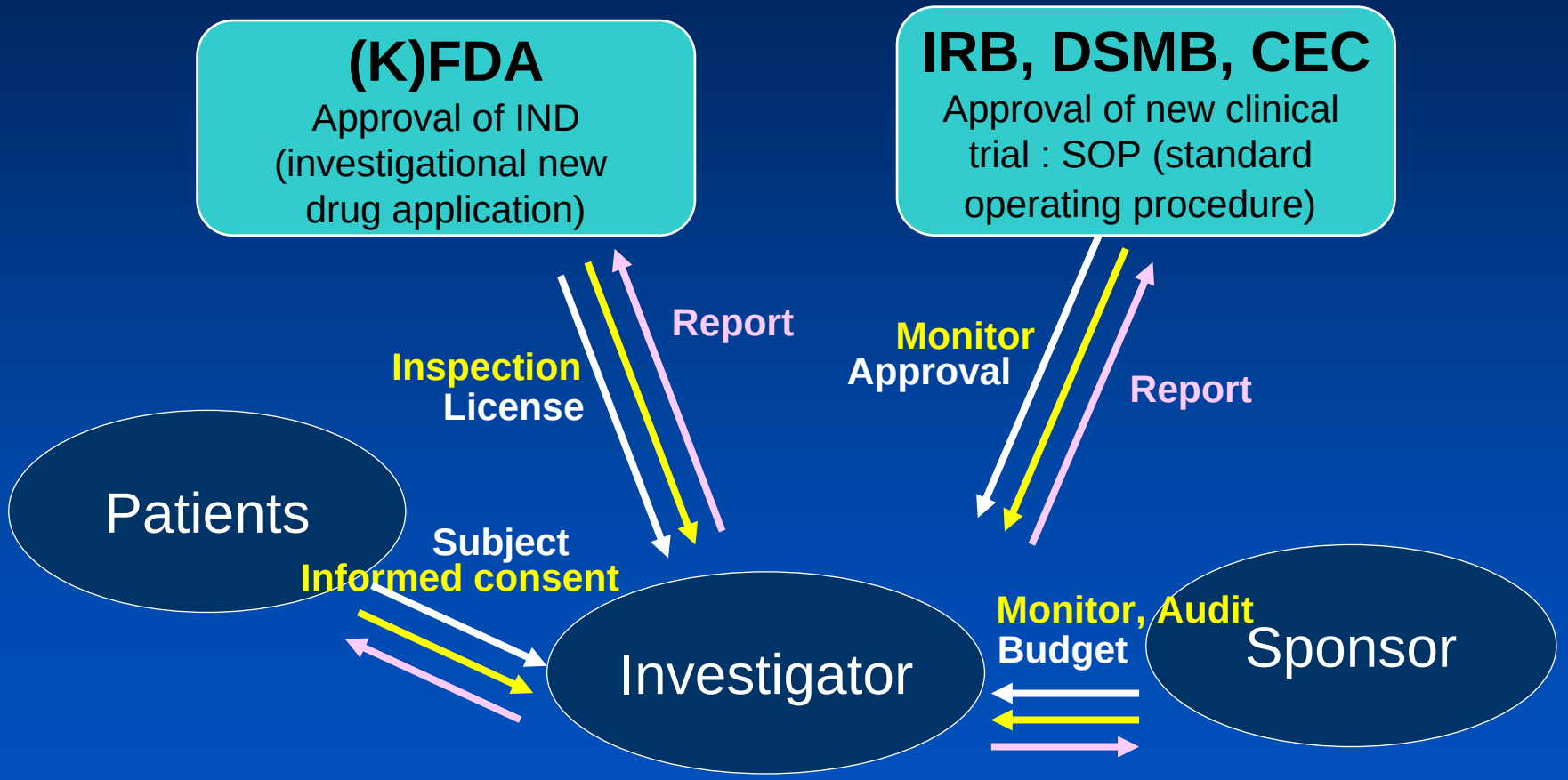
Korean GCP



Investigator's Responsibility

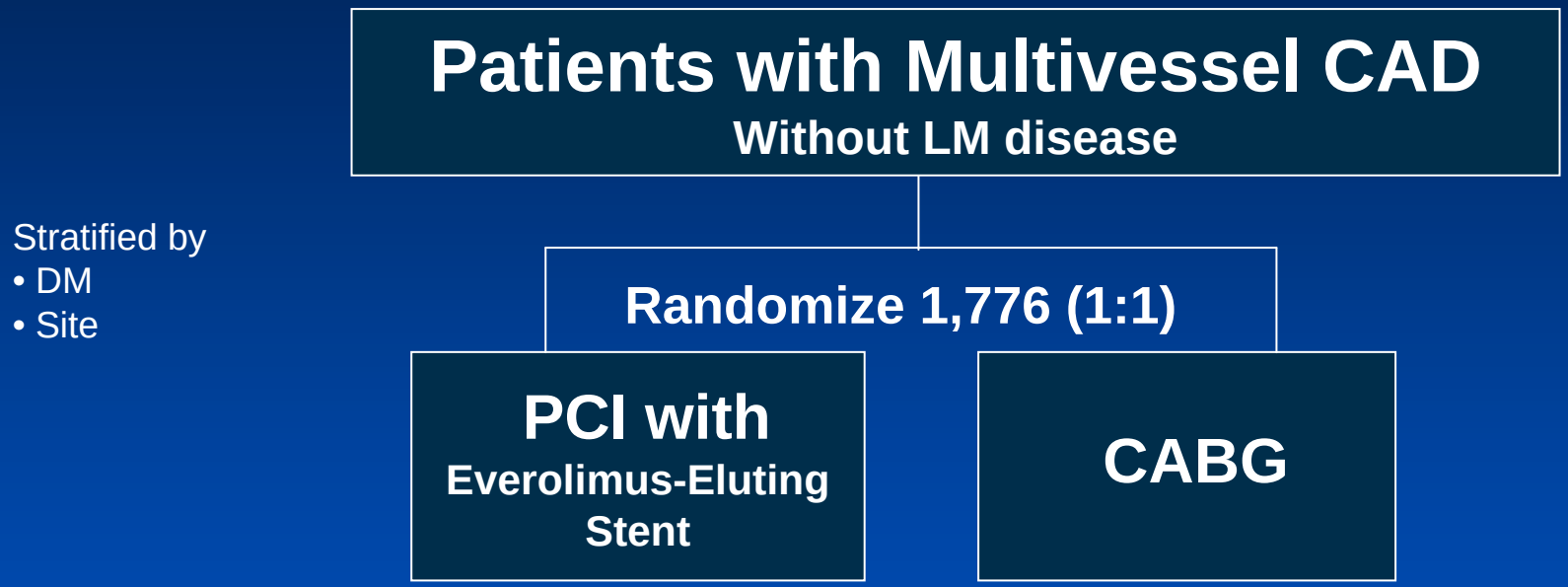
The investigator is responsible for insuring that an investigation is conducted according to the signed agreement, the investigational plan and applicable regulations for protecting the rights, safety and welfare of human subjects in the studies she/he conducts *(21 CFR 320-60, 21 CRF parts 50 and 56, 21 CFR 812-100, ISO 14155, ICH E6)*

Investigator :
A Core in the Process of Clinical Trial



Example
My Role in the BEST Trial

Randomized Comparison of Coronary Artery Bypass Surgery and Everolimus-Eluting Stent Implantation in the Treatment of Patients with Multivessel Coronary Artery Disease



- **PRIMARY Endpoint: mean 2-year clinical MACE (all death, MI, clinically-driven TVR)**
- **SECONDARY Endpoints: 2, 5 and 10-year MACE, MACCE, others**

PI: Seung-Jung Park, MD, PhD

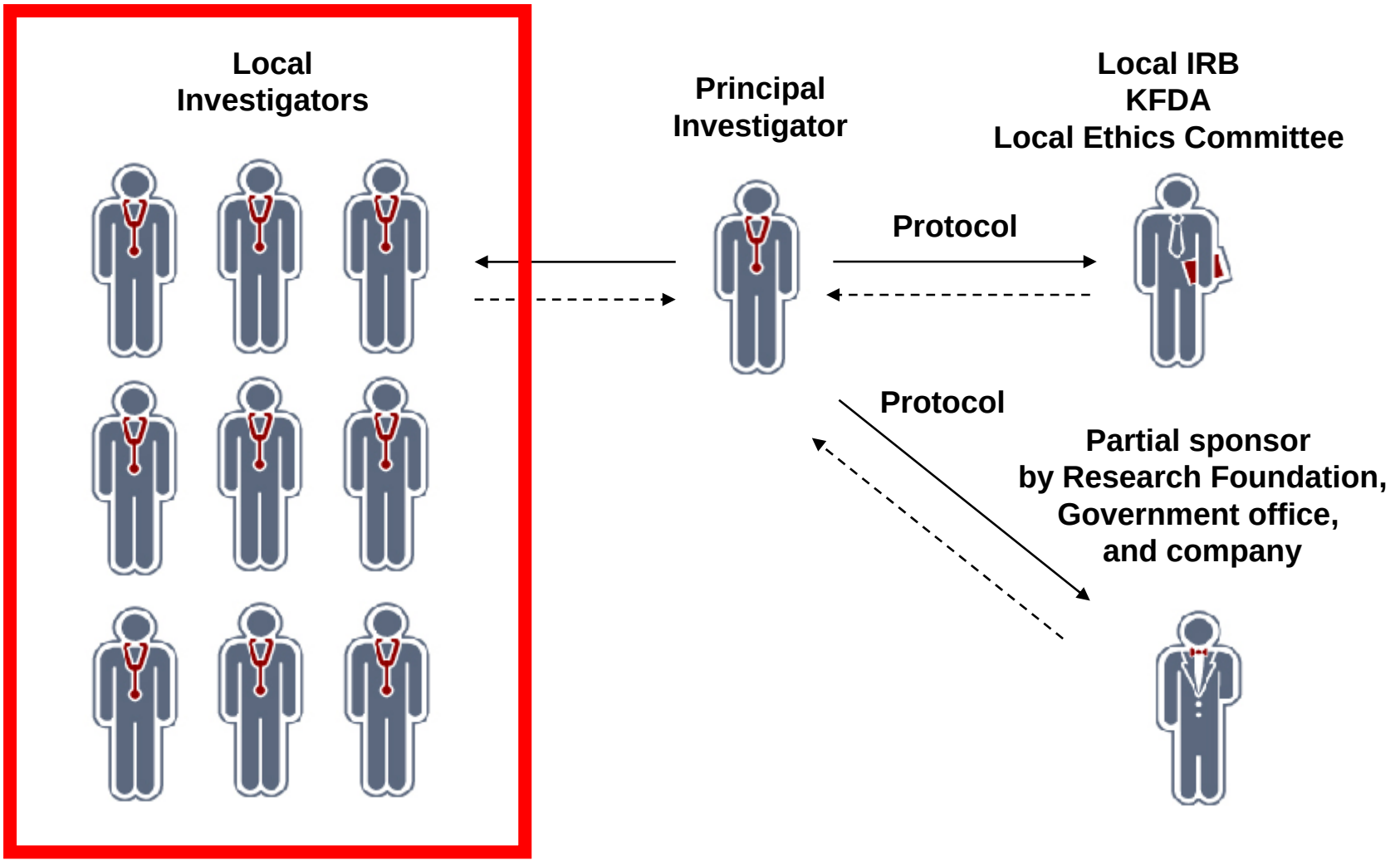
Organization

- **Sponsor**
  - CardioVascular Research Foundation (CVRF), Seoul
- **Funding :** CVRF, Abbott Corp
- **PI:** Seung-Jung Park, MD, PhD
- **Executive Committee**
- **Steering Committee**
- **Data Safety Monitoring Board**
- **Clinical Event Committee**
- **Angiographic Core Lab :**
- **Data Management :**

CVRF

- **Thallium Study Core Lab :** Asan Medical Center
- **Sites:** Korea, China, Malaysia, Hong Kong, Taiwan

Process of the BEST Trial
Study Initiation



Before Initiation
Qualification

- The investigator must have qualifications recognized within his/her country of practice and be competent in the field of study as evidenced by **a written curriculum vitae**
- Be competent and experienced in research or receive scientific support from an **experienced colleague**
- Have **good knowledge of and experience** in the field of study defined by the protocol
- Have the **necessary resources** to participate in and take full responsibility for the proper conduct of the study
- Is not listed on the debarment list

Before Initiation
Investigational Product

- The investigator must have a knowledge of the properties, effects and side effects of the **investigational product**
- Must be familiar with the **pre-study data**, as described by the sponsor in the investigator's brochure, and
- Must be satisfied that the **possible advantage** to be gained from the study justifies any **discomfort or risks** involved for the participant

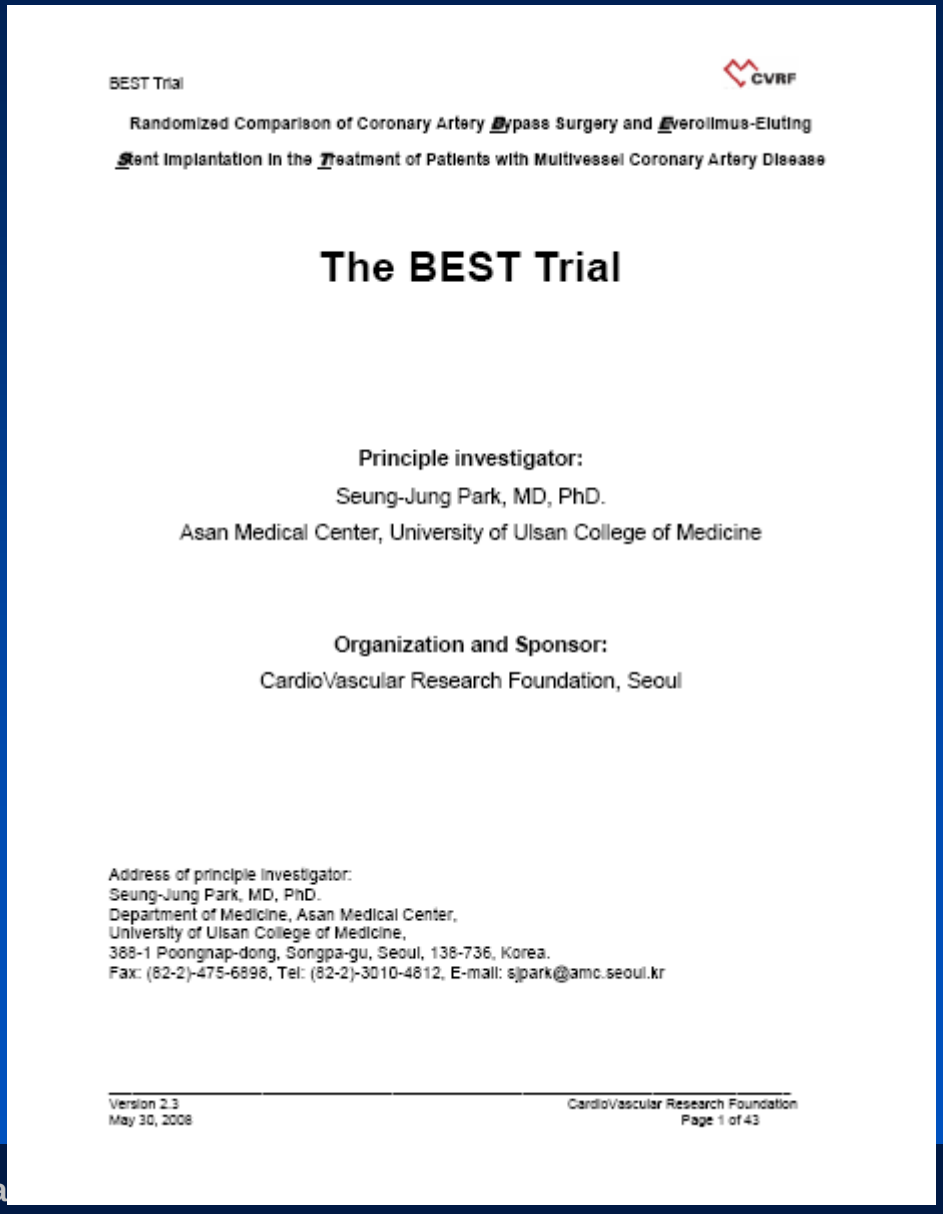
Before Initiation
Protocol

- The investigator must have a good **knowledge of the protocol**, protocol related documents and the requirements of the local participant code of rights and privacy legislation
- The protocol and related documents should be approved and signed by the **principal investigator** and a representative of the sponsor
- A budget in the form of a **written contract** should be established and documented in the investigator's information package for each study

Before Initiation
Protocol

- **Data ownership** should be stated clearly in the protocol or contract
- The **protocol related documents** should clearly describe a process for resolving problems concerning any investigator who has failed to adhere to any aspect of the agreement contained within the protocol

BEST Trial
Investigator's Brochure



BEST Trial

CVRF

Randomized Comparison of Coronary Artery Bypass Surgery and Everolimus-Eluting Stent Implantation In the Treatment of Patients with Multivessel Coronary Artery Disease

The BEST Trial

Principle investigator:

Seung-Jung Park, MD, PhD.

Asan Medical Center, University of Ulsan College of Medicine

Organization and Sponsor:

CardioVascular Research Foundation, Seoul

Address of principle investigator:
Seung-Jung Park, MD, PhD.
Department of Medicine, Asan Medical Center,
University of Ulsan College of Medicine,
388-1 Poongnap-dong, Songpa-gu, Seoul, 138-736, Korea.
Fax: (82-2)-475-6898, Tel: (82-2)-3010-4812, E-mail: sjpark@amc.seoul.kr

Before Initiation
Facilities and Staff

- The **safety of the participants** in a study should be of the highest concern
- The study site must have the **necessary facilities**, including emergency equipment and appropriate medical, paramedical and clerical staff to support the study

BEST Trial

Questionnaire for Feasibility Test

CVRF

Site Recruitment Questionnaire

Part A: Contact Information (Please complete or correct)

Investigator					
First Name			Last Name		
Mailing Address					
Phone		Fax		e-mail	

Part B: Ethics Committee

B.1. Which type of IRB or Ethic committee do you use at your Clinical Site able to use a Central Ethics Committee?	☐ Central IRB	☐ Local IRB
B2. If No (your site cannot use a Central Ethics Committee), how often does the local IRB at your clinical site meet?	☐ Once per week ☐ Twice a month ☐ Once per month ☐ Other (specify:)	
B3.How many weeks are typically required to receive IRB approval following the IRB meeting?	☐ One week ☐ Two weeks ☐ Three weeks ☐ Other _____	

CVRF

Part C: Center Feasibility

C. 1. Do you have previous **experience of clinical trials** (in this indication)?	☐ Yes	☐ No
C. 2. Do you have **clinical research staff resources** at your site to support conduct of this study?	☐ Yes	☐ No
a) If yes, please specify the position of the staff:	☐ Physicians ☐ Study Coordinators ☐ Research Nurses ☐ Other research staff (specify:)	
b) Please provide the contact information of the clinical research staff : Name: Phone No: Fax No: Email:		
C. 3. Do you have experience of using **electronic case reports forms?(e-CRF)**	☐ Yes	☐ No
If yes, please provide the contact in formation of the best person in this regard: Name: Phone No: Fax No: Email:		

Please return this questionnaire by e-mail to Jay Jang (jay0025@amc.seoul.kr)

Thank you for taking the time to complete this questionnaire.

We are very much looking forward to collaborating with you on this exciting protocol.

Before Initiation
Study Participants

- The principal investigator (PI) is responsible for ensuring the selection of participants for the study and should have access to an adequate number of individuals who could fulfill the entry criteria
- The investigator is responsible for ensuring that an adequate information package is available for use in the process of **seeking informed consent to participate in the study** (IRB/MEC approved documents)

Before Initiation
Study Participants

- Once consent to participate in the study has been obtained, **a copy of the signed consent** form and a source document identifying the study and recording the dates of participation should be placed in the participant's medical record
- The investigator must ensure that participants are provided with high quality medical care during and after the study, including care to the participants should they suffer an adverse event and be withdrawn from the study

During the Study
Adherence to the Protocol

- The PI is responsible for ensuring that **the protocol and appendices** are strictly followed
- The investigator must not omit, delete, or add any procedures to those detailed in the protocol nor can the investigator make any changes to the investigational product use, or the product
- **Written approval** of any protocol amendments from the IRB / ethics committee must be received prior to the investigator instituting any changes to the protocol

During the Study
Handling of investigational products

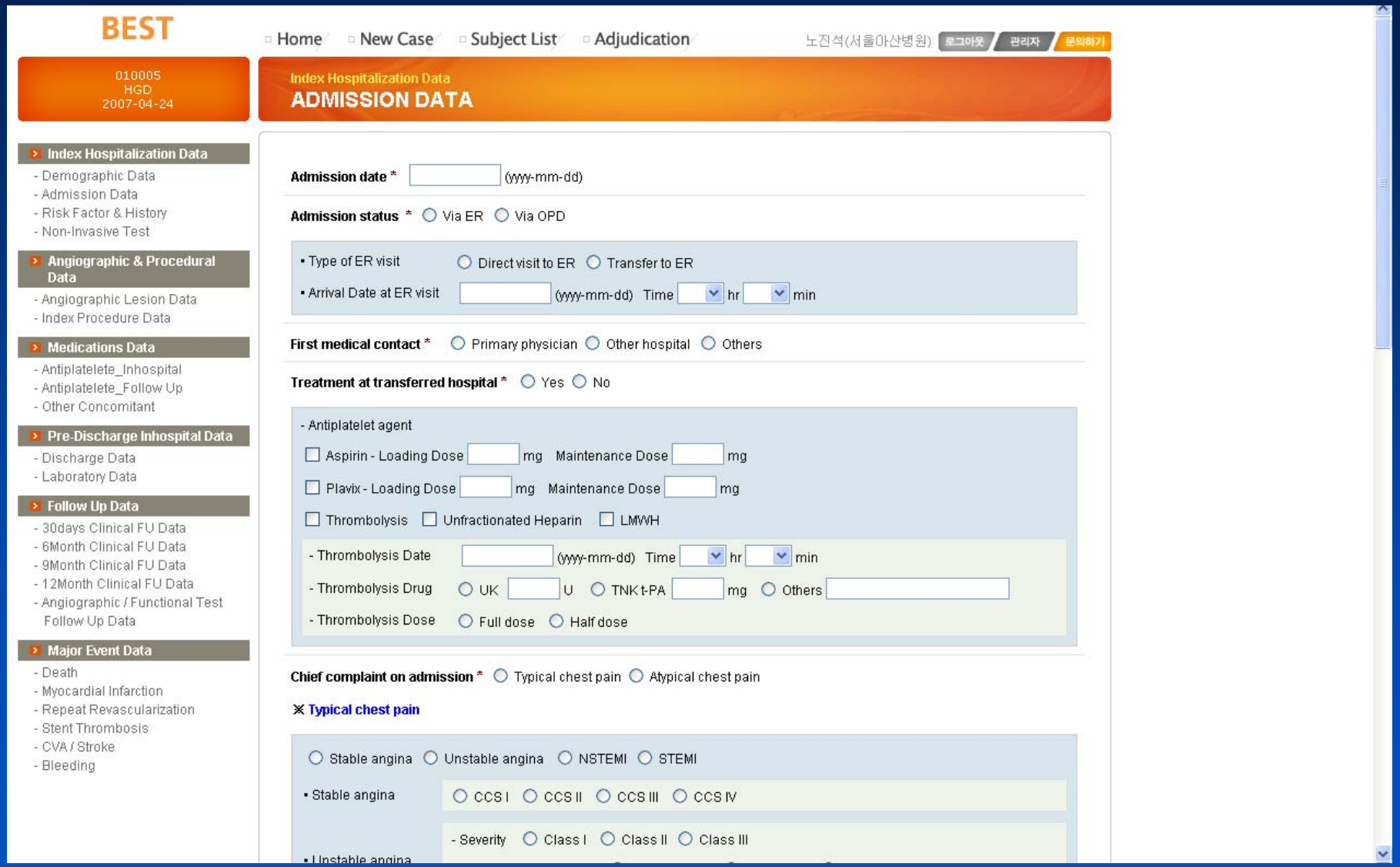
- Responsible for
  - the safe handling, storage and use of the **investigational product(s)**
  - the safe handling, storage and use of the reference product(s) and placebo used in the study, and
  - the keeping of records

During the Study
Data Management

- The PI is responsible for the collection, quality, recording, maintenance and retrieval of **source data** arising from the clinical study
- Each CRF case book (and selected pages) must be signed and dated by the investigator, or designated person, then stored securely
- The investigator should make the data available to the sponsor on a timely basis
- The investigator must be available for **agreed visits** by the monitor during the study and also cooperate in the data editing, quality control and audit

BEST Trial

Electronic Data Capturing

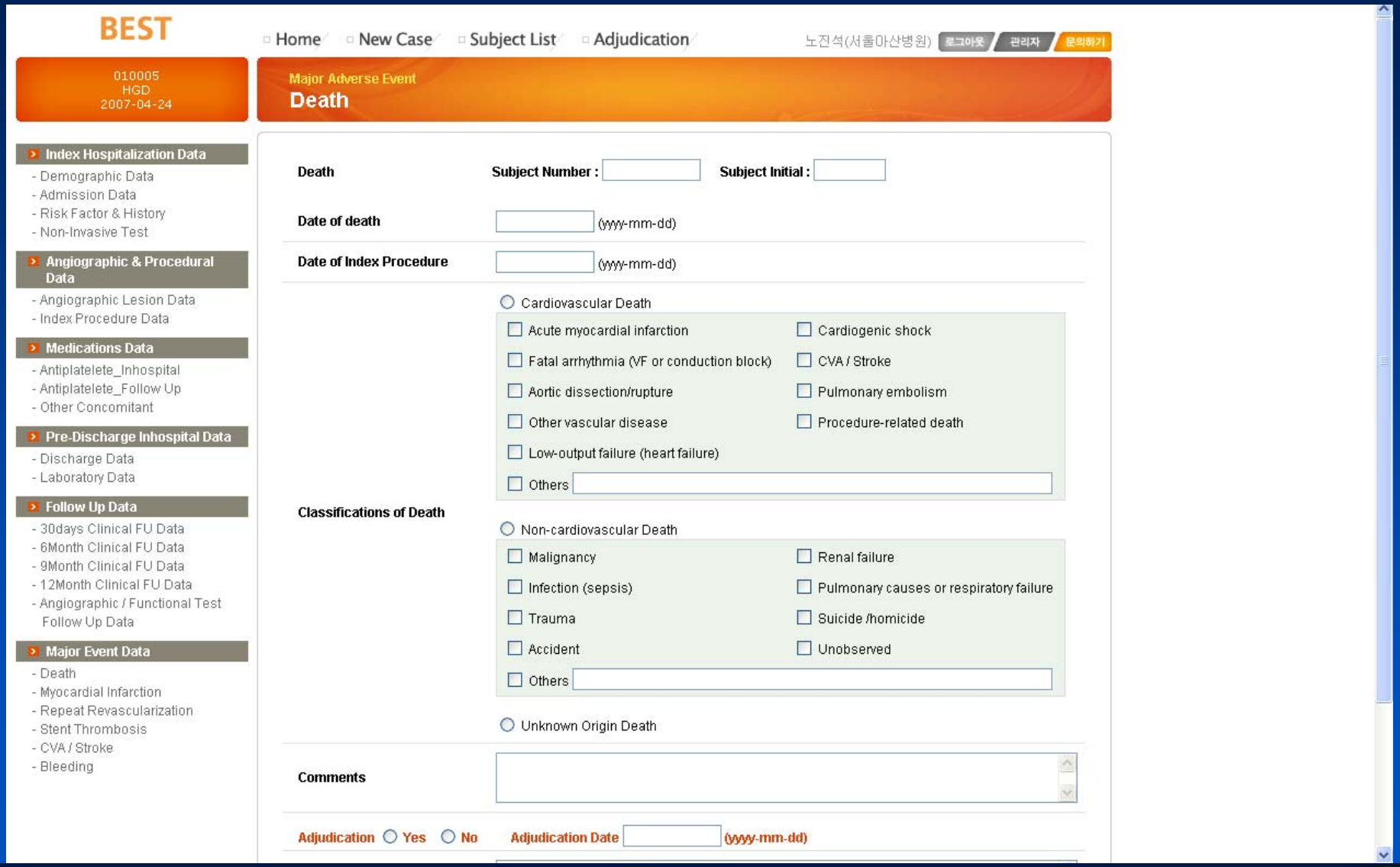


During the Study
Safety Issues

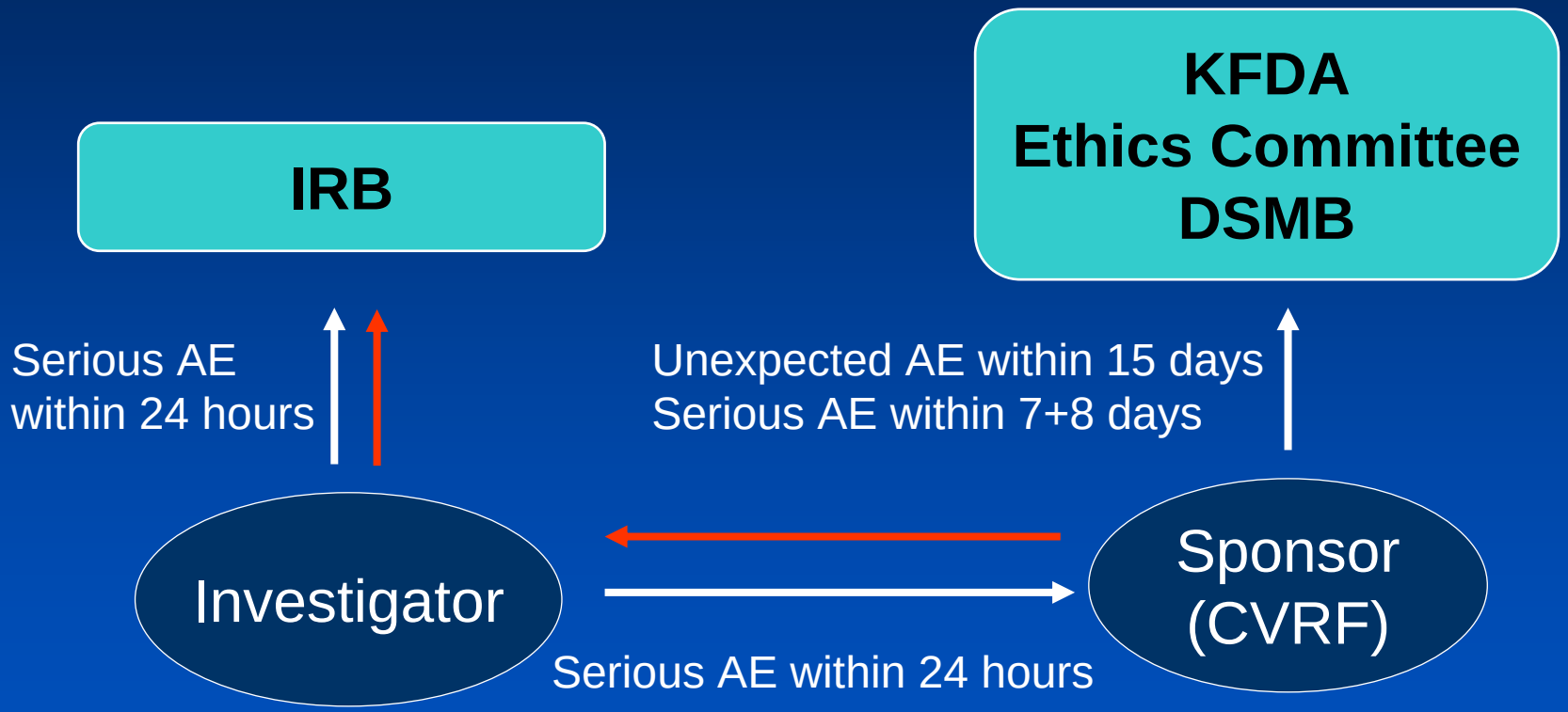
- Decisions and actions relevant to the clinical management and safety of the participant in acute situations are the responsibility of the investigator.
- The investigator must also know the requirements for reporting serious adverse events to the IRB / ethics committee and to the regulatory authority

BEST Trial

Reporting of SAE



Reporting of Adverse Event by Investigators



During the Study
Progress Report

- The investigator is obliged to **submit progress reports** as required by the sponsor, the regulatory authority and/or the relevant IRB / Medical Ethics Committee (MEC)
- These reports should contain information on how the study is progressing (including safety updates at the time of the report), the number of participants included in relation to the number expected, the number of dropouts and withdrawals

After the Study

- After the study has ended the investigator is obliged to **notify** the study participants, IRB/MEC and, if required, regulatory authorities that the study has finished
- Following completion of the study **all source documents** should be available to the sponsor to review the CRFs for accuracy, completeness and legibility as well as use in independent adjudication of adverse events

Responsibility of Investigators

- We appreciate your tremendous contributions to our study….