

Persevering effort by the dedicated people striving for the noble cause of saving lives. Protection of the rights, safety and welfare of study participants, the utmost importance. Respect for the contribution of heroic people volunteering to participate in clinical studies. Dedication to developing the most efficient and flawless system and delivering the highest quality data through innovative convergence technologies.

Min Soo Park, MD, PhD

Director of Medical Science Research Affairs & President of University-Industry Foundation



SEVERANCE HOSPITAL CLINICAL TRIALS CENTER

CONTENTS

- 05 MISSION & VISION
- 06 HISTORY
- 07 DIRECTOR'S GREETINGS
- 08 THE FEATURES OF CLINICAL RESEARCH AT SEVERANCE HOSPITAL Leading / Trust / Excellence / Safety / Efficiency

CHALLENGE

THE

- 40 REVIEWS
- 42 CONTACT





2014

2006. 02

Opened Severance Hospital Clinical Trials Center.

2008. 05

Designated as a Pfizer Center of Research Excellence Site.

2008. 09

Designated as a Pfizer Training Center for PK/PD Modeling and Simulation.

2008. 11

Selected as a Korea research-driven hospital.

2009

2009. 02

Opened the Clinical Trials Center for Medical Devices.

2009.05

Opened a specialized leading project –
Severance Integrative Research Institute for
Cerebral & Cardiovascular Diseases (SIRIC).

2009. 0

Reorganized the Clinical Trials Center (newly set up the Institutional Official Office for Clinical Research and the Human Research Protection Center).

2009.09

Designated as a bioequivalence study institution by the Korea Food & Drug Administration (KFDA).

2009. 12

Built and opened the USP 797 compliant aseptic drug preparation room at the Clinical Trials Pharmacy.

2010.04

Designated as a Bristol-Myers Squibb, OCE (Oncology Center of Excellence).

2010.06

Accredited for the Human Research Protection Program (HRPP) by AAHRPP.

2010.07

Selected as a Center of Excellence by Korea National Enterprise for Clinical Trials (KoNECT).

2011.05

Opened the e-IRB System.

2011.07

Initiated the u-CTMS Project.

2011.10

Established the Integrated Genomic Research Center for Metabolic Regulation.

2012.09

Designated as a Sanofi-Aventis Premier Site.

2012. 12

Established the Medical Science Research Affairs, Yonsei University Health System (Branch)

2013. 03

Opened the Avison BioMedical Research Center (ABMRC).

2013. 10

Reorganized the Clinical Trials Centeraffiliated departments (General Medicine Department, Cancer Medicine Department, and Medical Devices Department).

2013. 10

Published the "60 Seconds with CTC"

(Monthly Clinical Trials Center Newsletter).

2013. 11

Designated as a Global Center of Excellence for Clinical Trials by the Ministry of Health and Welfare.

2014. 02

Achieved A grade center for institution evaluation and proper classification center of excellent internal audit system by the Korea's Ministry of Food and Drug Safety.

2014.06

Selected as a pilot institution to operate the Human Research Protection Program and clinical trials by the Korea's Ministry of Food and Drug Safety.

Signed an agreement to operate the IRB for a Global Center of Excellence for Clinical Trials (IRB mutual recognition system, Yonsei University Health System-The Catholic University of Korea, Seoul St. Mary's Hospital-Inha University

2014. 12

Developed and initiated the e-CASE (e-CRF system).

2015.04

Published a clinical research guide book for Clinical Research Coordinators (CRCs).

2015.09

Opened a Yonsei University Health System (Sinchon-Gangnam) IRB Review Sharing System. 2016

2016. 01

Opened an integrated homepage of Global Center of Excellence for Clinical Trials (SCI-C).

2016.09

Opened a web-based interactive contract review system.

2016. 11

Opened a clinical research education management system (http://credu.yuhs.ac).

HISTORY OF CLINICAL RESEARCH
INFRASTRUCTURE IN SEVERANCE HOSPITAL

66

Welcome to Severance Hospital Clinical Trials Center

99

Severance Hospital Clinical Trials Center (CTC) was designated as a Regional Clinical Trials Center by the Ministry of Health and Welfare in 2006. Since then, CTC has strived to improve the quality of domestic clinical trials and to achieve global competition of the clinical trials field. As a result of their efforts to improve quality, CTC has been fully accredited by the Association for Accreditation of Human Research Protection Program (AAHRPP), and by Joint Commission International (JCI) for HRP. The designation of CTC as a global center of excellence for clinical trials by the Ministry of Health and Welfare in 2013 laid the foundation for the growth of a global clinical trials center.

CTC has recently established an IT-based system called u-CTMS (ubiquitous-Clinical Trials Management System), for more efficient and higher quality operations of clinical trials. Also, operating the CRMS (Clinical Research Management System) and the e-IRB system permit an easy access to the center support services. In addition, CTC provides the best service for clinical trials based on the accurate data provided by the development of e-CASE (e-CRF system with Accuracy, Safety, Efficacy), e-CRF system, linking with the Severance Hospital's OCS/EMR system, the first in Korea. From patient-oriented early phase clinical trials to late phase clinical trials for various diseases led by internationally recognized researchers, the high performing Severance Hospital Clinical Trials Center will do its best to provide a better treatment and full support for the development of new drugs and new medical devices.



Director, Severance Hospital Clinical Trials Center **Joong Bae Ahn**





Welcome to Severance Hospital Clinical Trials Center

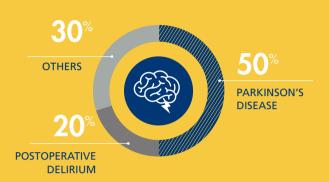
Severance Hospital Clinical Trials Center (CTC) was designated as a Regional Clinical Trials Center by the Ministry of Health and Welfare in 2006. Since then, CTC has strived to improve the quality of domestic clinical trials and to achieve global competition of the clinical trials field. As a result of their efforts to improve quality,

99



Professor of Neurology Phil Hyu Lee, Severance Hospital

Expertise: Parkinson's disease and movement disorder, Dementia, Stem cell





"Brain Neurology has not been yet pioneered by the medical world, and there is no proper therapy or drug for degenerative brain disease such as Alzheimer's or Parkinson's diseases, being classified as intractable diseases. With the support of Severance Hospital Clinical Trials Center, I have identified the neuroprotective effects of mesenchymal stem cells in the Parkinsonian syndrome for the first time in the world. I have also received impressive and satisfactory one-stop service for stem cell trials."



RESEARCH-DRIVEN SEVERANCE HOSPITAL, LEAD THE FUTURE HEALTHCARE INDUSTRY

The Severance Hospital Research and Development (R&D), the leader of the industrialization of medicine in Korea, strives to secure industrial competitiveness by selecting seven key research areas for the vitalization of academic-hospital-industry joint research, providing an environment to introduce, apply, and develop the results of each research area to clinical settings, laying the ground for the research planning and funding of each area, and business development.

Severance, leading the industrialization of healthcare

Designated as an organization for research and development to foster a Korea research-driven hospital under the Ministry of Health and Welfare, Severance Hospital is contributing to global healthcare industrialization. A Korea research-driven hospital means a future-oriented hospital, creating industrial values by developing new medical devices, new medical technologies and new drugs away from being a medical treatment-focused clinical hospital and further leading the healthcare industrialization.

CTC is at the center of the industrialization of medicine. Since its designation as a Regional Clinical Trials Center, CTC has been working hard on improving the level of clinical trials in Korea. As a result, it was designated as a global center of excellence for clinical trials by the Ministry of Health and Welfare in 2013, and is striving to achieve global clinical research capability.

Current status of Severance Hospital for clinical research (as of 2015)

Clinical Investigators	522
Hospital Beds	2,268
Inpatients	731,631
Outpatients	2,228,192
IRB Panels	7
IRB Members	109
Approved Clinical researches by IRB	1,311
Dedicated Beds for Ph1 Clinical Trials	55

Severance Hospital Research Facilities

Clinical Trials Center (CTC): CTC has Korea's largest clinical research exclusive space with over 3,000m² with 55 beds dedicated to research. Accurate data collection and examination can be provided by the clinical research specialized professional staff and equipment, and the efficient facilities layout maximizes the effective operation of clinical research.

Avison BioMedical Research Center (ABMRC): This state-of-the-art research center built on February 2013 includes the Korea's largest animal unit, a space to validate the development of medical devices, operating rooms, electrophysiological rooms, histopathological rooms, FACS, ultracentrifugal rooms, imaging center, radiation laboratory, and has the most advanced research equipment including BAS and NGS analysis devices.

Clinical Trials Center for Medical Devices (MDCTC): This center is responsible for the clinical trials of medical devices and related services, and shares their facilities with the Clinical Trials Center, making it possible to carry out clinical trials for drugs and medical devices in parallel and in a broader context.

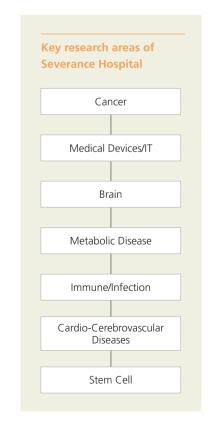
Medical Technology & Quality Evaluation Center: This center evaluates the medical safety of diagnostic and therapeutic medical equipment, medicine and medical supplies, medical materials and surrounding appliances used in daily life in terms of their direct/indirect impact to the human body. It has been officially designated as a medical devices testing organization by the Ministry of Food and Drug Safety (MFDS) and it has more than 26 types of the latest research devices including constant temp & humidity chamber.

Cardiovascular Products Evaluation Center (CPEC): With the network and system established for the validation of the research results of cardiovascular diseases obtained from individual institutions at home and abroad, this center provides services for the discovery and validation of domestic/international basic research results along with integrated consulting services.

Cell Therapy Center: With a lot of research technologies accumulated in cell therapy, this center has a wealth of clinical experience in stem cell transplants, cord blood transplants and cell transplants of heart disease patients. The Cell Therapy Center equipped with GMP facilities, a first for hospitals in Korea, plans to produce and provide quality-assured cell therapy products.



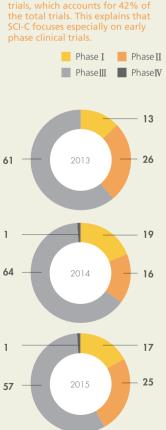




SCI-C National Performance About 50% of clinical trials performed in Korea, that is, 930 trials from the 1,935 trials approved by the Ministry of Food and Drug Safety (MFDS) between 2013 and 2015. SCI-C S.KOREA 652 2013 2014 2015

Early vs. Late Phase of **Clinical Trials**

118 early phase clinical trials (Phase I, Phase II) were conducted based on 2015 standards for SIT clinical the total trials. This explains that SCI-C focuses especially on early



Global Center of Excellence for Clinical Trials, SCI-C

Our innovative model of integrated CTCs (SCI-C*) provides solutions to the identified obstacles and inefficiency inherent in the conventional system of clinical development. Integration of resources such as investigators, patients, research staff, and experts and sharing of knowledge and experiences maximize productivity and increase the chances of clinical trial success.

SCI-C Focused Area and Performance

Area I: Early Phase Clinical Trial Operation SCI-C initiated about 50% of total clinical trials approved by MFDS (former KFDA) for last 3 consecutive years, we focused on early phase clinical trials and performed about 40% of all phases clinical trials within the consortium (e.g., 17%, phase 1; 25%, phase 2 in year 2015. Refer to the graph). Moreover, two third of global phase 2 clinical trials have been conducted annually, thereby demonstrating that SCI-C has worldwidely recognized sites at the level of scientific excellence as well as operational excellence by global pharmaceutical and biotech companies

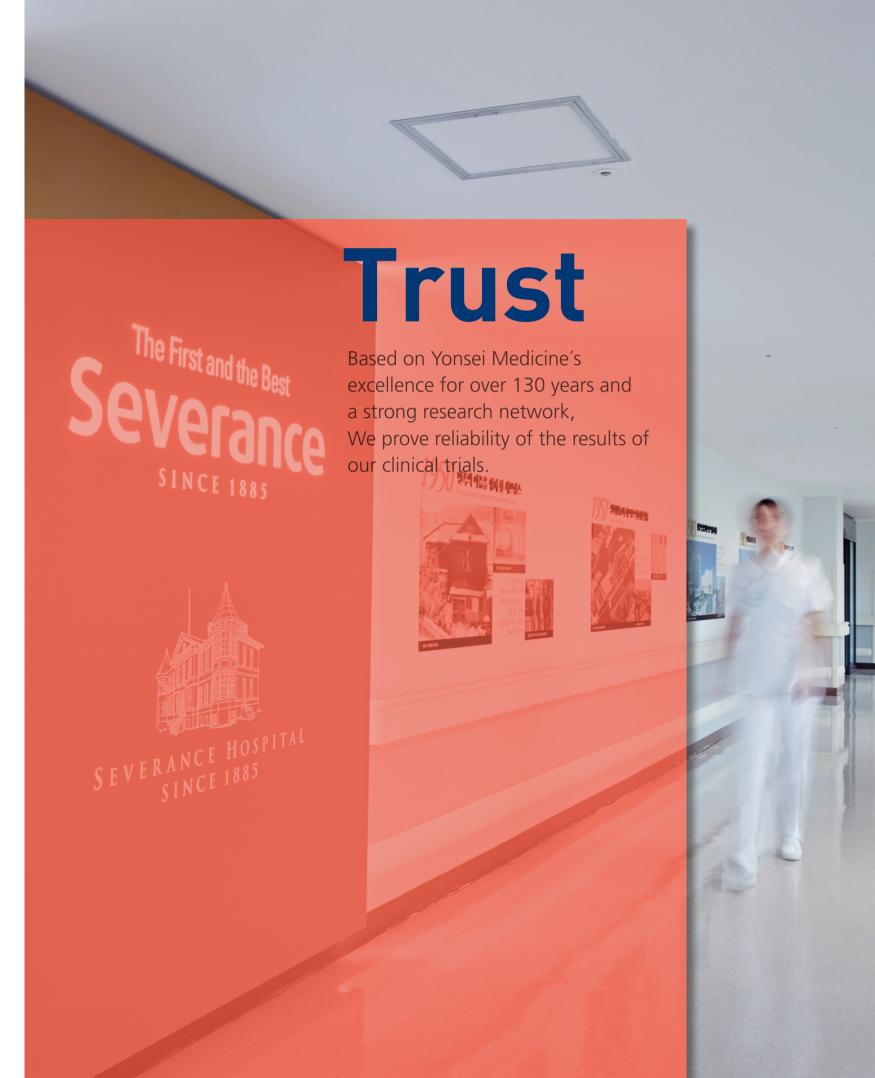
Area II: R&D Collaborative Platform for Drug Development SALT (Strategic Advisory Leadership Team) is organized to perform professional consultations on issues starting from preclinical stage to early phase clinical development. In addition, SCI-C will provide clinical indication-specific disease characteristics, diagnosis, medication pattern information, and clinical laboratory results from about 10 million de-identified patients' health records: thereby target market profile can be given as supplementary information along with consulting on clinical development plan.

Area III: Business Development & Marketing To identify research resources available in the university hospital and subsequently to introduce more reliable process of collaboration with industrial partners for new drug development, SCI-C organized and reinforced the dedicated team, the so-called the consortium secretariat which mainly focuses on business development & marketing through BIO international conference and other domestic partnering meetings.

SCI-C Network and Capacity

SCIC

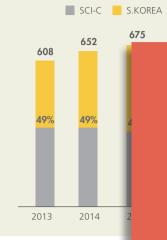
Number of Beds in all hospitals	5,909 beds
Clinical Pharmacology Unit	177 dedicated beds
Number of In- and Out-Patients	more than 7.0 million patients per year
Staff Involved in Clinical Trials	1,545 clinical investigators
Number of Clinical Trials	1,100 sponsored contract per year
Operational Structure	10 subcommittees under three divisions (Clinical Operation, Research Infrastructure, Business Development & Marketing)



^{*} SCI-C: Severance Hospitals, the Catholic Univ. of Korea Seoul St. Mary's Hospital, Inha Univ. Hospital-Consortium

SCI-C National Performance

About 50% of clinical trials performed in Korea, that is, 930 trials from the 1,935 trials approved by the Ministry of Food and Drug Safety (MFDS) between 2013 and 2015.



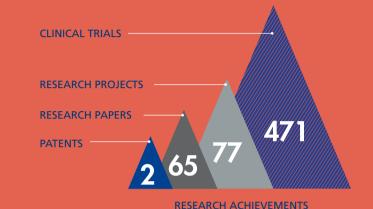
Global Center of Excellence for Clinical Trials, SCI-C

Our innovative model of integrated CTCs (SCI-C*) provides solutions to the identified obstacles and inefficiency inherent in the conventional system of clinical development. Integration of resources such as investigators, patients, research staff, and experts and sharing of knowledge and experiences maximize productivity and increase the chances of clinical trial success.



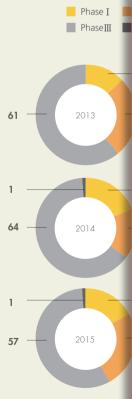
Professor in Oncology Joo Hyuk Sohn, Severance Hospital

Research areas: Chemotherapy for breast cancer, Clinical trials and gene therapy



Early vs. Late Phase of Clinical Trials

I , Phase II) were conducted on 2015 standards for SIT of trials, which accounts for 4 the total trials. This explain SCI-C focuses especially on phase clinical trials.



"Clinical research are not the result of an individual investigators but of many. An organic collaboration between medical departments based on respect to each other is essential to quickly produce the results of clinical trials. I am confident that Severance Hospital is the best among the large hospitals in Korea in terms of such collaboration between internal medicine and surgery divisions. As a result of this collaboration, the number of patients enrolled is higher than other hospitals. That's why so many sponsors trust and select Severance

Hospital."



GIVING FAITH IN MEDICAL TREATMENT AND RESEARCHES AS THE FIRST AND THE BEST PRACTICES

Severance Hospital was founded in 1885 and is Korea's first modern hospital. With the cooperation of the Korean government, two Americans, businessman and philanthropist Louis H. Severance and medical missionary Dr. Horace N. Allen launched what is now Korea's most globally advanced hospital. Severance's success stems from the explicit expectations that come from being Korea's first and the best. We have made our mark on medical history as a role model and a leader to other prominent health care institutions. We stand at the center of Korea's rapidly developing medical field. As Asia's leading hospital, Severance continually pursues and shapes the vision of medicine to serve patients from all over the world.

Severance Hospital has treaded the first routes aiming to be the best

1985	Established Korea's first western-style hospital (Gwanghyewon renamed to Chejungwon)		
1904	Established Korea's first general hospital (Severance Hospital)		
1969	Built Korea's first cancer center (Yonsei Cancer Center)		
1975	Created Korea's first pediatric surgery		
1993	Proclaimed Korea's first 'Patient's Bill of Rights'		
2001	Succeeded in Korea's first artificial heart transplant		
2003	Opened Korea's first clinic for early diagnosis of liver cancer		
2005	Performed Korea's first Da Vinci robotic surgery		
2006	Opened Korea's first University hospital retina center		
2006	Introduced Korea's first liver fibrosis scan laboratory		
2007	Obtained Korea's first JCI (Joint Commission International) accreditation		
2009	Established Korea's first Yonsei liver disease specimen bank		
2009	Introduced Korea's first radiation cancer therapeutic apparatus, '3rd generation Tomotherapy'		
2011	Presented World's first robotic surgery guidelines		
2011	Succeeded in Asia's first 3D endoscopic sinus surgery		
2012	Obtained Korea's first ISO 27001 certification for hospital information security management system (integrated certification)		
2013	Introduced Korea's first professional medical sign language interpretation services in general hospital		
2013	Performed World's first 10,000 robotic surgery cases		
2014	Introduced Asia's first advanced sample tracking system for biopsy		
2014	Performed Korea's first 100 lung transplants		
2015	Succeeded in Korea's first pulmonary heart valve replacement without surgery		
2016	Introduced Korea's first cancer therapeutic apparatus, heavy ion accelerator		

Reliable protection programs for patients and subjects

JCI accreditation is a process that assesses a hospital's performance on whether a patient receives the best medical services in a safe environment based on international standards.

Since its first JCI accreditation in Korea in 2007, Severance Hospital has been internationally accredited for patient safety over the last 10 years up to the 4th reaccreditation in 2016. This is the world's first case for a hospital having more than 2,000 beds to achieve such JCI accreditation.

In addition to health care, Severance Hospital proves excellent safety to subjects in the research area. Severance Hospital has passed JCI Human Research Programs (HRP), accrediting patient safety for clinical research programs, and has been fully accredited by the Association for Accreditation of Human Research Protection Program (AAHRPP). AAHRPP assesses if a site and Institutional Review Board (IRB) performs ethical research for the rights and welfare protection of subjects by reviewing documents and onspot investigation, and it grants certification to organizations that meet its standards.

As such, Severance Hospital is constantly trying its best to protect the rights and welfare of clinical trials participants.

Research competitiveness for shaping a better future

Selected as a Korea research-driven hospital in 2013 and believing that its success is dependent on research capability, Severance Hospital has focused on basic and clinical research support in a bid to become a world's leading hospital. As a result, we are designated as a Korea research-driven hospital again in 2016 and continue to achieve excellent research outcomes.

Since the establishment of Medical Science Research Affairs of Yonsei University Health System in charge of overall works related to the hospital such as intellectual property rights and technology commercialization, intellectual property rights and technology transfer has grown. The number of intellectual property rights application and registration rose to 314 in 2015 from 162 in 2012, while the number of technology transfer contracts also increased to 11 in 2015 from 6 in 2012. In 2015, Severance Hospital signed a technology transfer contract worth KRW 20 billion with ATGen Co., Ltd. and was selected as a leading Health TLO (Technology Licensing Office) member.

We are also trying to build an integrated platform for convergence research through three steps: laying a foundation for a Korea research-driven hospital (2013~2015), strengthening capabilities to become a Korea research-driven hospital (2016~2019), and emerging to become a Korea research-driven hospital.







Severance Hospital JCI 4th reaccreditation



AAHRPP Full Accreditation



Severance Hospital
No.1 in National Customer
Satisfaction



Global Management Award for five consecutive years



i-severance App Award Korea



2011 Korea Medical Award Attracting Foreign Patients

Academy-Industry-institute joint R&D network

For research industrialization, Severance Hospital is actively engaged in joint R&D efforts with leading overseas research institutes, global universities, pharmaceutical companies, and medical devices manufacturers, and in network-based R&BD activities such as the exchange of human resources, preclinical trials, and clinical trials.



Severance Hospital is reinforcing its research and industrialization capabilities through the cooperation in industry-university-institute joint research and the establishment of convergence research infrastructure with a focus on attracting R&D research at home and abroad and expanding technical partnerships.

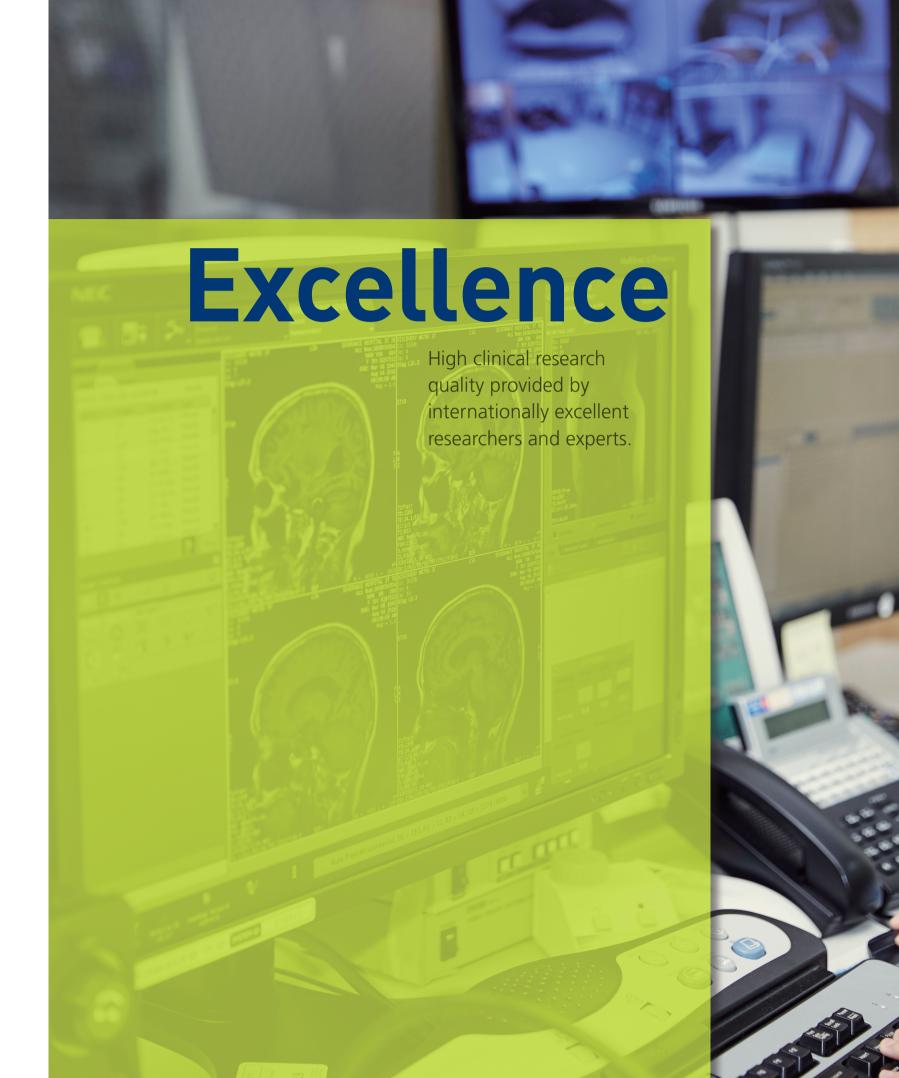
Recognized as a reliable hospital by hospital evaluation and A grade (Excellent) institution

A growing interest of the public in patient safety and quality medical services, the hospital evaluation system led by the government was shifted to a 'certification system' based on voluntary participation by medical institutions in 2010. Severance Hospital was certified as an acute care hospital by the Korea Institute for Healthcare Association (KOIHA), representing its excellence in the quality of medical services.

In case of clinical trials, local Institution was uniformly examined in the past, but now they are evaluated through differentiated follow-up management on institution's facilities and equipment, the presence of excellent manpower and related guidelines, and the compliance to the guidelines. As a result, institutions are graded to three levels: Excellent (A), Moderate (B), and Insufficient (C). Severance Hospital received Grade A to be locally and internationally recognized for its excellence in clinical research.







Academy-Industry-institute joint R&D network

For research industrialization, Severance Hospital is actively engaged in joint R&D efforts with leading overseas research institutes, global universities, pharmaceutical companies, and medical devices manufacturers, and in network-based R&BD activities such as the exchange of human resources, preclinical trials, and clinical trials.

Severance Hospital is reinforcing its research and industrialization capabilities through the cooperation in industry-university-institute joint research and the establishment of convergence research infrastructure with a focus on attracting R&D research at home and abroad and expanding technical partnerships.

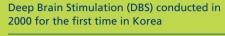






Professor Of Neurosurgery Jin Woo Chang, **Severance Hospital**

Expertise: Stereotactic and functional neurosurgery, Gamma knife surgery, Hyperhidrosis







"Stereotactic and functional neurosurgery is closely related to brain science, which has been rapidly developing from the 20th century. I have opened the possibility of a new medication to the Blood Brain Barrier (BBB), impeding the influx of drugs from blood to brain for brain diseases such as dementia and Parkinson's disease, and I am now in the process of subsequent studies including ultrasound brain surgery. Other enthusiastic researchers are gaining competence in their own areas, too. The performance and capabilities of leading research professors will be a key factor in selecting an institution."



THE BEST CLINICAL RESEARCH FROM BEGINNING TO END

A variety of clinical studies can be conducted by Severance Hospital's each department is carried out through the Clinical Trials Center. From patient-oriented early phase clinical trials to late phase clinical trials for various diseases by internationally recognized researchers, Severance Hospital Clinical Trials Center

is trying its best to perform fast, accurate and high quality research.

Severance Hospital Research Resources (searched by Y-HRN* for the period of 2011-Dec. 1st, 2016)

Researchers

1,137

Research papers

37,579

atents

1,645

Research project

21,669

Clinical trials

12,587

*Yonsei Health Research Network, Y-HRN

Consulting and statistical analysis by specialized clinical research professionals

The Clinical Trials Center provides researchers and sponsors with clinical study design, target number of subjects, definition of target groups and statistical analysis methods randomization to clinical studies. The center also provides statistical analyses for presenting and reporting accurate evidence-based study results. CTC is able to provide high quality and professional statistical services through a MOU with the Department of Statistics of Yonsei University's College of Medicine.

Quality control of staff for the best clinical research

Quality control of research staff participating in clinical research is more important than anything to improve the research's efficiency, reliability and ethical aspects. Experienced and trained Clinical Research Coordinators (CRCs) of the Severance Hospital Clinical Trials Center recruit, manage, and educate subjects considering their rights and safety; and help researchers and clients with carrying out high quality research in a convenient environment. Know-how accumulated from over 10 years' experience and close cooperation between researchers and CRCs increase the adherence of a protocol and the quality of clinical research data.

Severance Hospital as a Global Center of Excellence in Clinical Trials is striving for training professional manpower through continuing training and seminars, etc., and it has a number of certificates related to clinical trials such as CCRP (Certified Clinical Research Professional), CCRC (Certified Clinical Research Coordinator), QCRC (Qualified Clinical Research Coordinator) and QCRP (Qualified Clinical Research Pharmacist).

The first step of individualized clinical trials, Optimal advisory team

SALT (Strategic Advisory Leadership Team) is organized to perform professional consultations on issues starting from drug discovery through late stage of clinical development and to post-approval medical affairs in a multidisciplinary approach. To meet the needs of clients, whichever stage their drug development is in, we can provide a tailored solution through experts in drug discovery, non-clinical & pre-clinical development, clinical development, biomarkers including bioimaging, pharmacometrics, pharmacogenomics, bio-statisitics, regulatory affairs, and intellectual property & technical transfer. SALT tries to give advices on optimal strategies and planning for the areas of unmet needs and for the most efficient and effective drug development.

SALT uses a research network system (Y-HRN) within Severance Hospital to organize a team by searching for optimal specialists efficiently and identifying the number of patients that have a specific disease, which allows a swift determination of the possibility of clinical research.

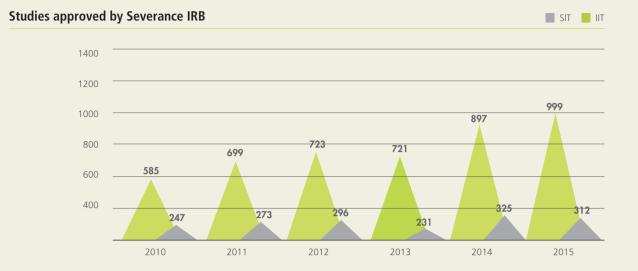




CLINICAL INVESTIGATORS (2013~2015)

Departments	Number of PI's	Number of Studies	Departments	Number of PI's	Number of Studies
Oncology	52	305	Allergy and Immunology	2	40
Gastroenterology	40	286	Hepatobiliary Pancreas Surgery	11	39
Cardiology	37	255	Rheumatology	9	38
Anesthesiology and Pain Medicine	24	188	Clinical Trials Center	4	36
Ophthalmology	21	175	Cardiovascular Surgery	2	31
Pedicatircs	22	162	Nuclear Medicine	3	28
Endocrinology and Metabolism	15	113	Colorectal Surgery	9	27
Urology	21	111	Organ Transplantation	4	25
hematology	23	103	Family Medicine	10	24
Neurology	9	91	Infectious Diseases	6	23
Dermatology	13	77	Nephrology	4	22
Pathology	12	76	Plastic Surgery	4	22
Gastrointestinal Surgery	9	73	Pediatric Oncology	2	22
ENT	13	72	Thyroid Surgery	3	21
Obstetrics and Gynecology	24	70	Chest Surgery	6	18
Radiology	7	66	Pediatric Surgery	2	4
Neurosurgery	12	58	Clinical Genetics	1	4
Pulmonology	17	55	Others	52	305
Laboratory Medicine	9	52	Tabl	F22	2200
Rehabilitation	6	43	Total	522	3208

Severance Hospital Clinical Trials Center Performance (2010~2015)



Studies approved by Phase



Studies approved by Investigational Site

	2010	2011	2012	2013	2014	2015
Phase I	21	31	26	22	34	34
Phase II	61	57	69	56	59	71
Phase III	86	84	128	95	143	137
Phase IV	60	44	57	42	41	39
Others	295	321	332	324	373	386
Bioequivalence	4	1	1	0	0	0
Medical Devices	11	37	35	33	46	70
Retrospective	258	357	344	353	487	538
PMS	36	40	33	27	39	36

Multi-center Multinational Single center

2014

1400 1200 1000 800 600 463 585 400 246 248 257 217 264 268 203 123

2012

2013

2011



Severance Hospital Clinical Trials Center Performance (2010~2015)

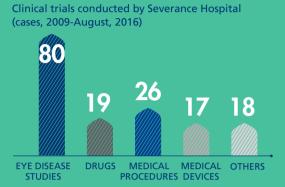
Studies approved by Severance IRB

1400

120

106

Professor of Ophthalmology,
Tae Im Kim, Severance Hospital
Expertise: Cataract, Cornea, External eye
disease, Vision correction surgery



Studies approv

2015201420132012

2010

2011

Studies approv

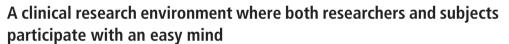
"The safety of subjects should be a top priority as clinical trials are performed to human beings. However, if a researcher is blinded by obtaining his or her research goal in a short period of time, he or she may overlook the safety to the subjects. Therefore, the rights and safety of subjects are protected during the entire period of and after the research by the supervision of the Institutional Review Board (IRB) for the clinical research plan and the entire process. Clinical ethics may refer to 'moral standards in my heart'. If researchers and clinical research organizations apply the three basic ethics of 'human respect', 'beneficence' and 'justice' to each condition of their research and subjects accordingly, the safety of subjects will be ensured as much as possible."





RELIABILITY IS INCREASED BY PROTECTING THE SAFETY OF SUBJECTS

Severance Hospital established, for the first time in Korea, the Human Research Protection Center (HPC) in 2008, which meets international standard, thereby being able to conduct research through human research protection programs and IRB in order for researchers to perform ethical and scientific research.



Severance Hospital has established HPC independently of clinical research, to which HRPP is effectively applied and implemented in order to understand and represent the position of subjects. This center continually supervises research to ensure that they are being carried out in compliance with relevant standards and regulations and that the protection of subjects is well in place. HPC provides subjects with counseling related to clinical research and it provides researchers with a variety of training programs including research ethics, bioethics and clinical research regulations.

In addition, HPC operates an ombudsman system, which allows everybody including subjects, legal representatives, researchers, IRB members, hospital staff and other personnel to make comments, suggestions or complaints regarding HRPP or IRB.

HPC always monitor, manages and handles all comments and responses regarding the Human Research Protection Program and the IRB review process.

Institutional Review Board for the safety and welfare of subjects

Severance Hospital Institutional Review Board (IRB) has been an independent and impartial review board since its establishment in 1994. IRB reviews protocol or protocol amendment, methods to obtain a written consent from a subject or information to be provided, and it continually checks them so as to protect the rights, safety and welfare of subjects, thereby determining the performance of all research in which human beings participate and monitoring





the research operation. IRB is compliant with the Pharmaceutical Affairs Act, Medical Devices Act, Bioethics and Safety Act, Good Clinical Practice (GCP), ICH-GCP and other bodies.

In addition, Severance Hospital is a leading organization in the safe use of drugs and medical devices by committing to monitor the safety of drugs and medical devices in order to fulfill 'patient safety' goal, one of the Severance Hospital operational objectives. As for drugs, Severance Hospital is one of the 27 designated regional drug safety centers by the Ministry of Food and Drug Safety (MFDS), Severance Hospital collects, reports and consult adverse events, and also provide related training and publicize reported drug adverse events. As for medical devices, accredited as one of the 20 medical device safety monitoring center in Korea by the MFDS, Severance Hospital identifies and reports adverse events related to medical devices on the market.

Severance Hospital carries out such activities to seek the safety of patients and health care providers taking drugs or using medical devices, and contributes to the improvement and development of domestic drugs and medical devices through communications with the medical industry.

Number of patient safety reports (serious adverse events: SAE)

SAE	2013	2014	2015
Expected	968	850	872
Unexpected	477	594	856
total	1,442	1,444	1,728

IRB Panels

7

IRB Members

115

IRB Review Schedule

Panel 1 Thursday 1st week
Panel 2 Monday 2nd week
Panel 3 Friday 3rd week
Panel 4 Friday 4th week
Panel 5 Tuesday 4th week
Panel 6 Friday 2nd week
Panel 7 Thursday 3rd week

Number of clinical trials and investigational products managed by the pharmacy* (2016. 9) 1341 529 IPs clinical trials * Based on the clinical trials for which

the CTC pharmacy was requested to

manage drugs for clinical trials

IT-based systematic management of investigational product (IP)

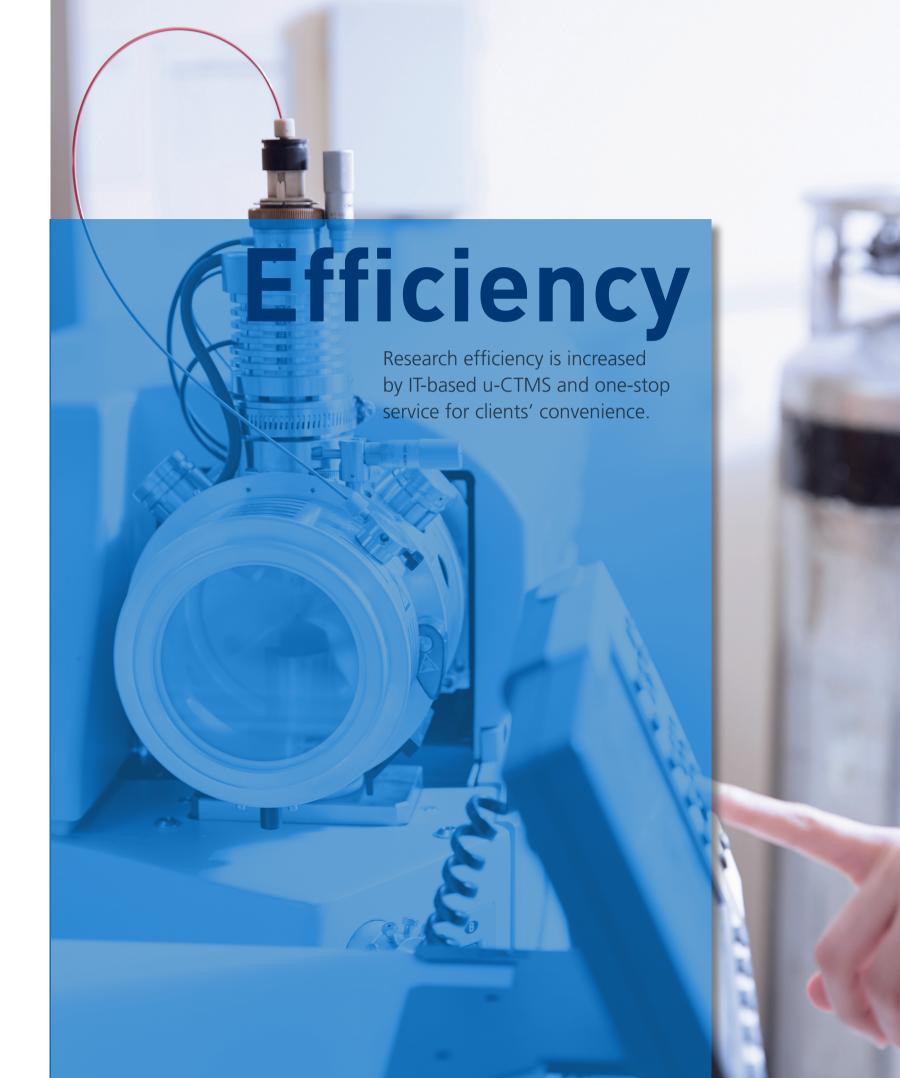
Severance Hospital operates a management system for the investigational products (IP) by developing computer programs and acquiring experience in clinical trials as part of the realization of the world's best clinical trials. Severance Hospital performs diverse tasks from consulting to overall IP management for clinical trials in accordance with the Pharmaceutical Affairs Act, GCP, IP management for clinical trials standards, center SOPs and others, increasing the quality of their clinical trials.

The Protocol and pharmacy manual of each clinical research are efficiently implemented on computer programs where the IP administration history of each subjects and detailed information can be checked. A responsible pharmacist uses computer system to systematically manage investigational products, for instance creating a IP codes, managing releases and receipts of drugs, reviewing prescriptions, preparing, checking and guiding the administration of IP for clinical trials.

As for the IP administration guide, which is directly linked to the IP compliance of a subject, the administration and dosage by an IP code is automatically printed out on a label along with the prescription. Severance Hospital is contributing to the increase of IP compliance using computer programs, which allow a subject to check on the label important information required for IP administration.







Number of clinical trials and investigational products managed by the pharmacy* (2016. 9)



* Based on the clinical trials fo the CTC pharmacy was requ manage drugs for clinical tria

IT-based systematic management of investigational product (IP)

Severance Hospital operates a management system for the investigational products (IP) by developing computer programs and acquiring experience in clinical trials as part of the realization of the world's best clinical trials. Severance Hospital performs diverse tasks from consulting to overall IP management for clinical trials in accordance with the Pharmaceutical

INTERVIEW

GlaxoSmithkline plc. (GSK), Vice President Yil Seop Lee

Expertise: Pediatrics, Clinical pharmacology, Pharmaceutical medicine

"When sponsor select the site, most of them take into account 'efficiency' for fast and quality results with the same time and cost. Hospitals, searching for a perfect therapy to cure diseases, and sponsors, trying to develop a better drug share the same objectives. When a clinical trials center reinforces investment for the efficient research performance, it would be mutually beneficial. I hope that sponsors, CROs (Contract Research Organizations) and hospitals closely cooperate with each other for delivering better treatments in the world."







Professor Choon Ok Kim Department of Clinical Pharmacology



HIGH RESEARCH EFFICIENCY USING ADVANCED MEDICAL INFORMATION SYSTEMS

Severance Hospital is the first ubiquitous hospital that has established the Severance Hospital integrated medical information system (u-SMART), Korea's first Web-based medical information system. IT-based research administrative services for clinical research are provided for an efficient management and fast operation of clinical research.



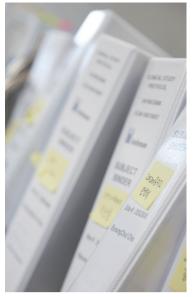
Severance Hospital has been working to improve the efficiency of patient treatment, research and hospital management by establishing a smart ubiquitous system 'u-SMART' since 2005. u-SMART is a web-based integrated medical services system including OCS (Ordering Communication System), PACS (Picture Archiving and Communication System), EMR (Electronic Medical Record), and ERP (Enterprise Resource Planning). They are used to provide the management, faculty, clients, and others with research data of Yonsei University Health System in real time, which suit the purpose of each user.

On the other hand, Severance Hospital operates ubiquitous-Clinical Trials Management System (u-CTMS) for the efficient and fast management of clinical research u-CTMS consists of the Clinical Research Management System (CRMS) for implementing administrative works, sample storage and venue reservation for clinical research, the e-IRB which is a computing system for all IRB review related processes, and the e-CASE (e-CRF system with Accuracy, Safety and Efficiency).

In addition, the Yonsei-Health Research Network (Y-HRN) was built to allow researchers to share information for the first time in Korea, making it possible to easily access all research data and resources of the Yonsei University Health System.

Severance Hospital also obtained the ISO 27001 certification (an international standard of information security controls enacted by ISO; International Organization for Standardization) in May 2015 in order to computerize medical data and gain international confidence in information security control.





One-stop service for successful clinical trials

A one-stop service has been established for the integrated management of the entire process of clinical researches from beginning to end. The one-stop service centralizes equipment, staffs and operating systems required for clinical researches into a single point of contact, allowing the integrated management of researches. It also serves as the point of contact for communication between sponsors and researchers, increasing the satisfaction and efficiency of researchers as they can consult and get advice at any time. Entering into a MOU between Clinical Trials Center and sponsors and providing feasibility assessment services help the hospital attract as many clinical research as possible.

Clinical Trial Center (CTC) has another core competence of being able to stably supply trained clinical research coordinators to meet the increasing demand for very diverse and patient-oriented clinical trials. To this end, CTC is working to secure well-trained manpower by designating a training organization for clinical research professionals to provide systematic training programs for its globally leading areas as well as professional and specialized areas.

Number of center tours classified according to purpose of visit (2013~2015)

Audit, inspection, PSV, Site Selection	16
Benchmarking	16
Feasibility Check	20
Site Tour	33

Percentage of research performed using e-CASE

IIT

60%

SI

40%

Number of tours for Clinical Trials Center (2013~2015)

local organizations

30 visits

global organizations

55 visits



e-CASE, easy and efficient clinical trial data management for researchers

e-CASE system (http://ecase.yuhs.ac) is a web-based e-Case Report Form (e-CRF) and data management system which is developed based on years of clinical trial experience. e-CASE saves the time and effort of researchers, and entry errors due to repeated data entry by the automatic linking feature between electronic medical records (EMR) and ordering communication system (OCS). It also supports fast and accurate statistical analysis by ensuring data reliability and increasing the efficiency of data management. e-CASE provides an integrated solution for researchers to manage clinical data easily and efficiently.

e-CASE Features

- Integrated data collection and management system
- Provide an integrated solution to effectively collect and manage the research data.
- Well qualified system management
- e-CASE system is validated according to SOPs and regulations.
- Direct interworking with OCS/EMR

Data from OCS/EMR is directly interwork to the eCRF, and this work minimize entry errors and save time when re-enter subject's data into the eCRF system.

User friendly CRF page creation and editing

Variety format of CRF templates are provided. User can utilize and easily create the CRF page considering the research specification.

• Data-export by CRF (Category), CRItem (Value), Subject

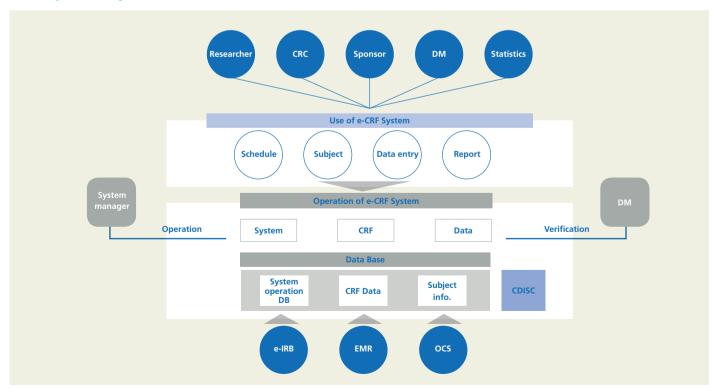
Entered data can be exported by Value, Subject and CRF domain, and can be edited by researcher as needed.

• Data accommodated in Severance DB secure system

To comply with regulations, security simulation has conducted regularly in

Severance Hospital IT department. Also dedicated server is managed for the safety and security of e-CASE system.

e-CASE system configuration



CTC support services

Research Process	Service Details					
Feasibility	Recommend feasible investigators and cooperate in PSV (site tour, feasibility check, EMR check list preparation, etc.)					
	(Site tour, leasibility Crieck, Elvin Crieck list preparation, etc.)					
Protocol development / consulting	Consultation of protocol development, Protocol development					
Budgeting	Estimate research costs and calculate CTC service cost					
Submission and Approval of MFDS/IRB	Respond to inquiries regarding researchers and sponsors					
Contract & CTC services agreement	Review and execute a contract Inform CTC services agreement process					
	V					
Initiation of clinical research	Issue/handle receipts regarding the payment of research cost, create CR code, create EMR ID, check the delivery of investigational products (IPs), and create IP code					
Conduction of clinical research	Pre-screening via CDRS (Clinical Data Retrieval System), Explain and support the use of CTC services (space and facilities) (use of outpatient clinics, phase 1 unit, specimen collection room, specimen storage, monitoring room, other equipment and facilities and others) Support a clinical pharmacy Support a clinical research coordinator upon request					
Monitoring/audit (on-going)	Explain the venue and equipment reservation for monitoring/audit by a sponsor Request cooperation from relevant departments					
	_					
Completion of clinical research	Provide coordination for the submission of a MFDS/IRB completion report					
	_					
Data Management	Support data entry, data analysis, data cleaning and DB lock					
Statistical analysis report Clinical study report	Support and consult statistics Develop or consult the clinical study report					
Inspection or audit (after completion)	Respond to the audit/inspection (reserve venue and request cooperation from relevant department)					
	_					
Document archiving	Explain how to request archiving and archive/manage documents					

Reviews for Severance Hospital Clinical Trials Center

CRC services

"I am conducting clinical research more efficiently and stably in a convenient environment thanks to the clinical research coordinator services. I'm really thankful for CTC's hard work and sincere support."

• Professor Park Eun Sook (Department of Rehabilitation Medicine)

External affairs services

"Thanks to the Director and everyone involved for their sincere support in regards to the Yonsei University Health System's collaboration."

• Part Leader Lee Yang-Jae (Medical Science Research Affairs)

Research coordination services

"I could not have completed many studies without CTC's help. I wish Severance Hospital CTC's tremendous success, and I wish CTC to become a great driving force in developing Severance Hospital's research competitiveness, too."

• Professor Park Sungha (Department of Internal Medicine)

e-CASE service

"e-CASE allows reliable data collection by automatically correcting errors that can be easily made in a multicenter study, and it is a researcher-friendly system, automatically exporting data."

Professor Park Mi-Suk (Department of Radiology)

IP management service

"Investigational product should be quickly and accurately accounted and administered to each subject. If you request it to the center pharmacy, you can rely on them entirely."

Professor Kim Choon Ok (Department of Clinical Pharmacology)

"I don't feel any inconvenience even carrying out several studies thanks to the systematic and well-controlled service including the computerized system established for calculating medicine costs and registering monitoring."

• Kang Da-In (CRA, Novonordisk)

"I always appreciate the great help from CTC that allows me perform research seamlessly with their kind and fast feedback along with detailed discussions concerning investigational products from beginning to end."

• Kim Min-Su (CRA, inVentiv Health Korea)

Contracting service

"It takes significantly shorter time for Severance Hospital from a contract review request to the completion of the review than other institutions. Also, the reason for the request is clear, so we can proceed with a research without unnecessary discussions. Therefore, Severance Hospital CTC is a preferred institution for discussions of a clinical research contract."

Jin Jeong-Won (Parexel Korea)

"After a contract review request, an email from CTC confirming its receipt arrives on the same day or the day after, which is very helpful for a contract client who doesn't have to check their reply separately. I have confidence in their prompt preparation for research initiation, kind responses and professional approaches."

• Kim Seon-Yeong (INC Research)

Specimen collecting services

"Precise implementation under the protocols, open communication with other researchers, kind response to subjects: It is the best specimen collection room for researchers."

Nurse Choi Jeong-Hee (Department of Endocrinology)

Subjects

"I was able to satisfactorily participate in the clinical trial thanks to the pleasant environment, well-balanced diet and always kind staff."

Age 29, healthy volunteer

"It was the best of the best. I didn't see any problem that needed to be corrected nor to be improved. I really had a great time thanks to the CRCs."

Age 28, healthy volunteer

"I have been fighting against lung cancer for 4 years now. Two years ago, on the recommendation of Professor Kim Hye Ryun, I started to take a target therapy that was in process of clinical trials. Fortunately, the new drug did a positive effect on me and my condition got better since then. My life is no different from ordinary people now. I am always grateful to Professor Kim Hye Ryun and the CRCs."

• Age 52, subject participated in lung cancer study

Contact

♠ http://ocr.yuhs.ac

Services	Tel	Email	
Center tour/Inquiry for homepage	+82 2-2228-0507	ctc_tour@yuhs.ac	
Consultation for the use of center service (request for study, feasibility, etc.)	+82 2-2228-0558	ctcqi@yuhs.ac	
Contract	+82 2-2228-0502,0506	contractctc@yuhs.ac	
CR code application	+82 2-2228-0504	ctc_fund@yuhs.ac	
Data management and statistics	+82 2-2228-0480	ctcdm@yuhs.ac	
Documents archiving	+82 2-2228-0502	ctc_docs@yuhs.ac	
e-CASE	+82 2-2228-0472	ctcdm@yuhs.ac	
Education	+82 2-2228-0556	ctcqi@yuhs.ac	
EMR ID	+82 2-2228-0470	dm0704@yuhs.ac	
External audit and inspection	+82 2-2228-0557	ctcqi@yuhs.ac	
Investigational product management	+82 2-2228-0511~7	ctc_pharm@yuhs.ac	
Research budget	+82 2-2228-0503,0504	ctc_fund@yuhs.ac	
Service cost for research	+82 2-2228-0559,0460	sevctc@yuhs.ac	
Venue reservation (conference room, monitoring room)	+82 2-2228-0500	iactr@yuhs.ac	
Inquire for IRB	+82 2-2228-0430~2	irb@yuhs.ac	
Human Research Protection Center (HPC)	+82 2-2228-0430	hpc@yuhs.ac	

CLINICAL TRIALS CENTER

Yonsei-ro, Seodamun-gu, Seoul 03722, Korea
Tel +82 2-2228-0500 Fax +82 2-392-0668 Homepage http://ocr.yuhs.ac

CLINICAL TRIALS CENTER

SEVERANCE HOSPITAL YONSEI UNIVERSITY COLLEGE OF MEDICINE