

# 4<sup>th</sup> Global ARO Network Workshop

Global Clinical Research: Integrating Quality from the Beginning

## PROGRAM & ABSTRACTS

Date/Time

June 20<sup>th</sup>, Thursday, 2019

Venue

Paris Marriott Opera Ambassador Hotel

Organizer



**ARO Council**  
Academic Research Organization

Co-Organizer



大阪大学医学部附属病院  
Osaka University Hospital

**4th Global ARO Network Workshop**  
*"Global Clinical Research: Integrating Quality from the Beginning"*  
**June 20, 2019 ; Paris, France.**  
**Meeting Venue : Paris Marriott Opera Ambassador Hotel,**  
**16 boulevard Haussmann, Paris-France**

<b>1</b>	<b>Opening Remarks</b>	<b>8:30-8:40</b>
	<b>Norihiro Sato</b> Japan ARO Council/Hokkaido University	JAPAN P.04

<b>2</b>	<b>Session 1 : Global Clinical Research Networks, Consortia and Strategies</b>	<b>8:40-9:55</b>
	<b>Chair : Christian Ohmann</b> European Clinical Research Infrastructure Network (ECRIN)	GERMANY
	Grand Design of Global ARO Network	
<b>1</b>	<b>Akira Myoui</b> Japan ARO Council/Osaka University	JAPAN P.07
	Global Research Experience in a National Clinical Research Network	
<b>2</b>	<b>Heiko von der Leyen</b> Hannover Medical School, Hannover Clinical Trial Center	GERMANY P.09
	Rare Cancer ReGISTry NETwork in Asia	
<b>3</b>	<b>Toshirou Nishida</b> National Cancer Center Hospital	JAPAN P.11
	Wearables and Sensors in Clinical Trials	
<b>4</b>	<b>Samuel Volchenbom</b> University of Chicago	UNITED STATES OF AMERICA P.13

<b>Break</b>	<b>9:55-10:10</b>
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<b>3</b>	<b>Session 2 : Data Management and Standards for Global Clinical Research</b>	<b>10:10-12:30</b>
	<b>Chairs : Norihiro Sato</b> Japan ARO Council/Hokkaido University	JAPAN
	<b>: Rebecca Kush</b> Learning Health Community, Elligo Health Research and Catalysis	UNITED STATES OF AMERICA
<b>1</b>	<b>Christian Ohmann</b> European Clinical Research Infrastructure Network (ECRIN)	GERMANY P.17
	Development of ECRIN Data Center Certification Programme	
<b>2</b>	<b>Itadaki Yamaguchi</b> Translational Research Center for Medical Innovation (TRI)	JAPAN P.19
	Development of the Data Quality Control System based on the Requirements for Certification of ECRIN Data Centres	
<b>3</b>	<b>Masato Shiren</b> Osaka University	JAPAN P.21
	CDISC Standards Implementation in Japanese Academia	
<b>4</b>	<b>Seung-Hwan Lee</b> Seoul National University Hospital	KOREA P.23
	SNUH's Efforts to Improve the Quality of Data Management	
<b>5</b>	<b>Ueng-Cheng Yang</b> National Yang-Ming University	TAIWAN P.25
	An Attempt to Implement ECRIN and CDISC Standards by using Electronic System	
<b>6</b>	<b>Xuanhui Ng</b> Singapore Clinical Research Institute (SCRI)	SINGAPORE P.27
	Standards for Academic Research	
<b>7</b>	<b>Michael Kurilla</b> National Center for Advancing Translational Sciences National Institutes of Health	UNITED STATES OF AMERICA P.29
	Standards and Data Strategies for Global Regulated Research, from Protocol through Analysis	
<b>8</b>	<b>Rebecca Kush</b> Learning Health Community, Elligo Health Research and Catalysis	UNITED STATES OF AMERICA P.31
	Learning Health and a System of Accelerated Research (SOAR)	

<b>Lunch Break</b>	<b>12:30-13:30</b>
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*Opening*

*Remarks*

**Norihiro Sato**

Japan ARO Council / Hokkaido University



# Opening Remarks



## Norihiro Sato

JAPAN ARO Council / Hokkaido University Hospital



Japan

### Profile

#### Present Post:

Deputy Director, Hokkaido University Hospital (in charge of research)

Director / Professor, Clinical Research and Medical Innovation Center, Hokkaido University Hospital

#### Career Summary:

March 1985 Graduated from Hokkaido University School of Medicine

April 1985 Joined Second Department of Medicine, Hokkaido University School of Medicine (majored in Hematology)

October 1995 Research Section Chief, Hokkaido Red Cross Blood Center

November 2002 Deputy General Manager / Instructor, Division of Transfusion Medicine, Hokkaido University Hospital

July 2009 Director / Professor, Translational Research and Clinical Trial Center, Hokkaido University Hospital

April 2010 Professor, Department of Translational Research Management, Hokkaido University Graduate School of Medicine (another post)

April 2016 Deputy Director, Hokkaido University Hospital (in charge of research)

Director, Clinical Research and Medical Innovation Center, Hokkaido University Hospital

#### Degree:

25 March 1996 M.D., Ph.D. (Hokkaido University), No. 4905

#### Affiliated Academic Society:

Science Council of Japan (Member), ARO Council (Chairman of the board of Directors), Japan Society of Clinical Trials and Research (Trustee), Society for Regulatory Science of Medical Products (Trustee), The Japanese Society of Clinical Pharmacology and Therapeutics (Representatives, Special Advising Doctor), Society for Clinical Trials (SCT), etc.



# *Session 1*

*Global Clinical Research*

*Networks, Consortia and*

*Strategies*

**Chair: Christian Ohmann**

European Clinical Research Infrastructure Network (ECRIN)

# Grand Design of Global ARO Network



## Akira Myoui

JAPAN ARO Council / Osaka University



Japan

### ■Profile

Clinical Professor, the Director of the Medical Center for Translational Research (MTR), Department of Medical Innovation, Osaka University Hospital / Vice Chairman, ARO Council, Japan

He graduated from Osaka University Medical School in 1986 and finished PhD course in 1993. He worked on musculoskeletal tumors, bone cell biology, bone substitute materials and bone tissue engineering at the Department of Orthopedics, Osaka University until 2006, and then he joined MTR and started to work on the promotion of clinical translation of excellent basic biomedical discoveries from Osaka University and other academic sectors.

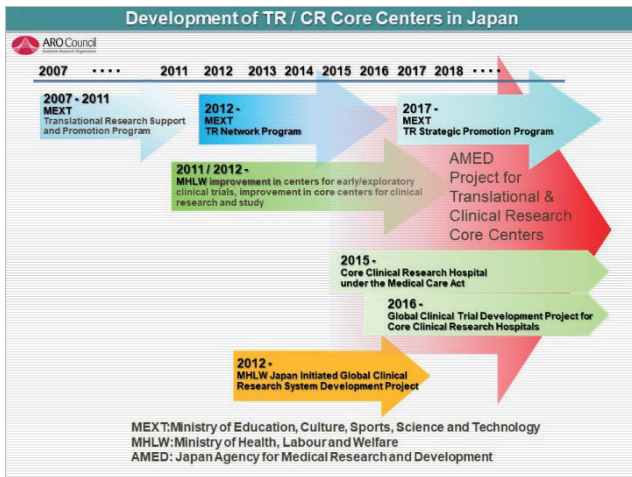
In 2015, he was awarded Economy, Trade and Industry Minister's Prize for the contributors in Industry-Academia-Public Collaboration through the development of functional artificial bone.

### ■Abstract

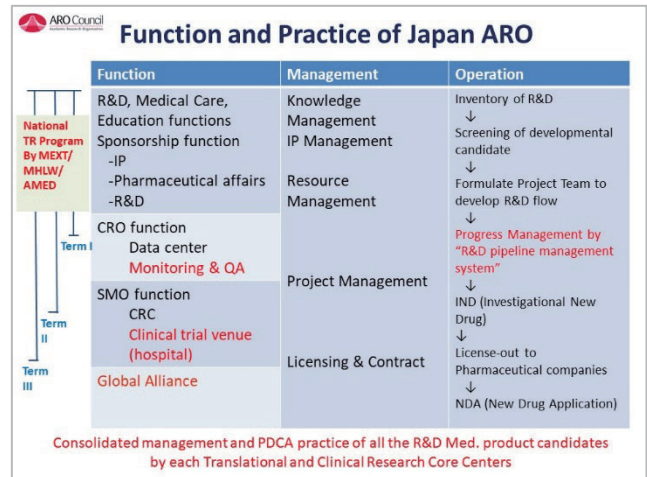
To promote the construction of robust infrastructure for medical innovation, Japanese government started several programs to facilitate the establishment of translational research / clinical research core centers and their network from 2007. In such programs, investigator-initiated trials for the purpose of new drug application and commercialization based on the discoveries of academic research discoveries have been strongly encouraged. In addition to funding for the institutions, research grants for those commercialization projects are provided as well. In consequence, as of the end of 2018FY, more than 50 innovative medical products originated from academia have been approved by the regulatory authority and launched to market by medical industries, indicating that such academia-driven R&D is very effective. ARO Council was established in 2015 as a general incorporated association consists of most major universities, core hospitals and a foundation, all of which are actively engaged in TR / CR. ARO council has been networking with AROs in other Asian countries as well as ECRIN and NCATS, while participating in the CRIGH's world-wide network. Thus, an infrastructure for global networking has been established. The important objectives of the global ARO network include the awareness of the difference in regulation and infrastructure, standardization, harmonization, and building mutual support. In parallel, initiation of global trial is important for stepping into the next-stage practical network. Its ultimate goal is to improve outcomes and overcome diseases simultaneously throughout the world.



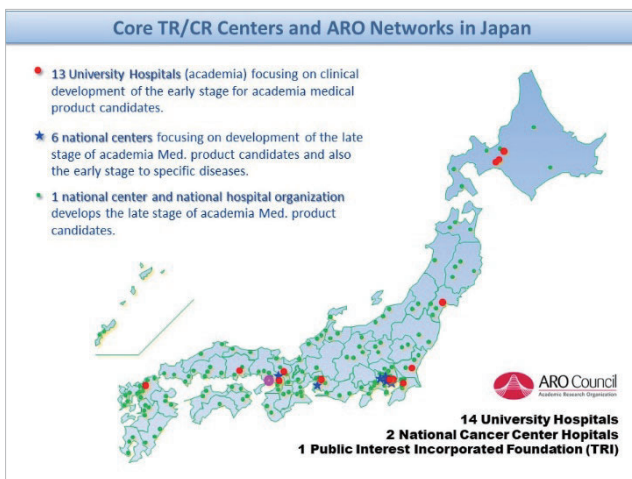
# Key Slides



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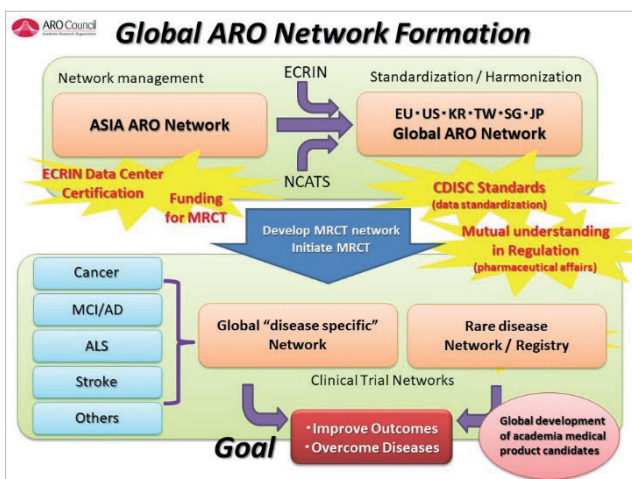


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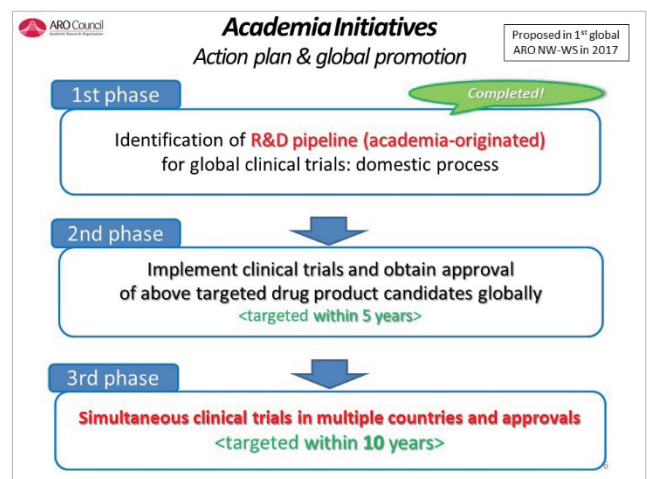
### List of Approved products originated from academic sector (FY2007~2018)

Medical drug / Regenerative medicine	Medical devices / In vitro diagnostic
Hokkaido Organization for TR (ATRO): Autologous MSC for Spinal Cord Injury, Autologous cultured epidermis (new indication)	Navigation system for endoscopic surgery, Gold marker and introducer, Motion tracking device for X-ray therapy, Motion tracking proton beam therapy system, Cone beam CT extension function, Jroflowmeter, Resin material for dental cutting manufacturing, Fetal heart rate monitor, CV5 Spinal System
Tohoku University: Prednisolone sodium succinate for injection, Indocyanine green for injection	Medical cannula and body fluid drain tube, Functional test oximeter, Medical X-ray device and medical X-ray tube
Gunma University: Indocyanine green for injection	Medical cannula and body fluid drain tube, Bio-sensing physical motion assist and rehabilitation device
Tsukuba University: Indocyanine green for injection	TAM light
Chiba University: Indocyanine green for injection	Single-use extracorporeal ventricular assist device
The University of Tokyo: Landiolol hydrochloride	Knottless-OK Suture PP line "Kashime", Autotaxin test kit
Keio University: Rituximab (new indication to ITP)	Spectroscopic imaging endoscope system, Oxygen saturation imaging system
National Center for Child Health and Development: Fentanyl citrate (new indication for children), Rituximab (new indication for children), Autologous cultured epidermis (new indication for children)	Shunt for fetal pleural effusion, Radiofrequency ablation for TRAP sequence
Nagoya University: Leuporelin acetate for injection (new indication)	NIU device injection needle, External fixator, Robotic surgery assist system, UV therapy device
Kyoto University: Leptin, Laserphyrin, Pertuzumab (new indication)	PD laser, PDI probe, Contact lens, Titanium bone substitute, Artificial skin, Da Vinci Surgical System (new indications), RF-ID tag
Osaka University: Autologous myoblast sheet, Siroimus gel, HGF plasmid	Custom-made osteotomy guide, Custom-made bone synthesis plate, Full thickness suture device for endoscopic surgery
Okayama University: Thermoregulator system	HDGS scope system for urinary tract
Kyusyu University: Multiphase auto-injector for contrast medium, Eye for ophthalmic surgery	Biodegradable bone substitute

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# Global Research Experience in a national Clinical Research Network



## Heiko von der Leyen

Hannover Medical School / Hannover Clinical Trial Center



Germany

### ■ Profile

Prof. Heiko von der Leyen, MD, is the head of the coordination center for clinical studies at Hannover Medical School (HCTC-KKS). He was co-founder and managing director of Hannover Clinical Trial Center GmbH (HCTC) which was founded in 2005 as an academic Contract Research Organization (CRO) dedicated to provide clinical trial management services and early product development support. HCTC GmbH recently was incorporated into Hannover Medical School. HCTC combines the clinical expertise and academic leadership of Hannover Medical School, a premier German university hospital and teaching institution, with the full-service operational capabilities of a contract research organisation (including project management, regulatory affairs, clinical monitoring, data management). Prof. von der Leyen was trained in Pharmacology, Internal Medicine, and Cardiology at University of Hamburg and Hannover Medical School. After 3 years of research at Stanford's Falk Cardiovascular Research Center with focus on cardiovascular gene therapy he was appointed as junior faculty member at the Division of Cardiovascular Medicine of Stanford University from 1995 to 1996. From 1998 to 2005 Prof. von der Leyen served on several top management positions in the biotechnology industry with focus on the clinical development of advanced therapy medicinal products (tissue engineering, gene therapy, DNA medicine). Prof. von der Leyen is currently the speaker of the board of the network of academic clinical research organizations in Germany (KKS-Network) and a member of the network committee of ECRIN-ERIC, a European clinical trial infrastructure organization.

### ■ Abstract

In my presentation I will give an example of an international academic trial and its challenges. A constantly growing European clinical research management infrastructure allows the conduct of such international trials. The German Coordination Centers for Clinical Research (KKS) and their network (KKS-N) provide the different layers of expertise for successfully conducting clinical trials. Furthermore, the European network ECRIN-ERIC connects the different national coordination centers to enable international collaboration.

## Key Slides

### 4th Global ARO Network Workshop

Global Clinical Research: Integrating Quality from the Beginning

#### Global Research Experience in a national Clinical Research Network

Prof. Dr. Heiko von der Leyen  
Hannover Clinical Trial Center  
Coordination Center for Clinical Trials  
HCTC-KKS  
Hannover Medical School




HCTC  
HANNOVER CLINICAL TRIAL CENTER GMBH

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### What do we need to successfully conduct an international academic trial?

- Good idea ☺
- Study protocol and budget
- **Versatile EDC system**
- **Experienced team**
  - „certified“ KKS
- **International partners**
  - **Academic Research Organization(s)**
  - ECRIN
  - ICN

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### HCTC –KKS: academic „CRO“

**Studies and projects in preparation**  
Central contact point for discussion and planning of clinical trial projects  
Support for compilation of proposals for grant applications

**Clinical research projects**  
Project development  
Regulatory Affairs

- Clinical Trial Application (CTA), medical writing
- Legal representative/authorized agent

Operational management

- Project management, monitoring, site management

Data Management

- MARVIN (Xclinical, München): eCRF/EDC, GAMP 5-validated, GCP-compliant

**Sponsor representative (IITs of Hannover Medical School)**

- Responsible for conduct and/or supervision of sponsor tasks

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### KKS-Network: 2005 - 2019

- 23 academic clinical trial units in Germany
- Membership requires external audit
- Organised in a network
- Share experience
- Develop and share tools
- Solve problems arising from conduct of trials
- Use challenges for improvement
- Training



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### ECRIN distributed organization, core team & EuCos national partners, distributed vs. central services

National partners providing distributed services and selected based on national coverage

Expert hubs providing central services and selected based on their specific expertise

- regulatory / ethics
- site monitoring
- vigilance
- data management



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### Regulation EU 536/14: change in paradigm

The new EU Clinical Trial Regulation will facilitate international academic clinical research:

- Regulatory harmonization: one submission - competent authorities and ethics committees
- Fixed timelines
- Clear cost structure
- Option for Co-Sponsor
- Option for low interventional trial
- Transparency
- Improved collaboration and information sharing

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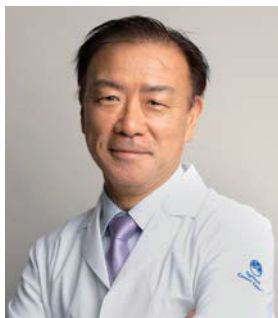
20 June 2019 ARO Paris

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# Rare Cancer ReGISTry NETwork in Asia



## Toshirou Nishida

National Cancer Center Hospital



Japan

### ■Profile

After graduate from Osaka University Graduate School of Medicine, T. Nishida had residency of general surgery in Osaka University Hospital and postdoctoral fellowship in Tufts University, Boston.

He is a surgical oncologist whose expertise area is gastrointestinal cancer, including gastric cancer and GIST. In the clinical practice, he works as a surgeon of the Department of Gastric Surgery of NCCH. He is conducting several clinical studies and some basic as well as translational researches investigating the underlying molecular mechanisms of gastrointestinal cancer with human samples. His research interests include elucidation of molecular mechanisms of carcinogenesis and cancer cell progression, and development of targeting therapy for sarcomas as well as gastrointestinal cancer. He has published more than 200 original reports in the major journals including Nat. Genet, Science, PNAS, Lancet, JCO and Gastroenterology and more than 30 review papers.

At the same time, he devotes considerable effort to manage and organize the hospital as the director of the National Cancer Center Hospital.

### ■Abstract

Patients with rare cancer defined as its incidence less than 60/million/year has several challenges including delay in diagnosis and lack of treatment. Although international clinical trials are common in sponsor-initiated trials (SIT) in these days, they are infrequent in academic- and investigator-initiated trials (IIT), especially in Asia. International academic network and collaboration in IITs are required for medical development for rare cancer and pediatric cancer in which pharmaceutical companies may have little interest. Our National Cancer Center Hospital is recently designated as Core Clinical Research Hospital, Global Clinical Trials Core Center, and Central Organization for Rare Cancer in Japan. To clarify clinical, pathological, and genetic features of rare cancer and to facilitate medical development in rare cancer, we are conducting the Masterkey project consisting of the registry study and sub-studies with basket and umbrella trials. In the sub-study part, several biomarker-based IITs or SITs are conducting and planned. The project is collaborated with several academic institutes, pharmaceutical companies and with Rare Cancers Japan, a patient advocacy group. Asia may have little ethnic difference, Asia-specific cancer and short distance, which may facilitate collaboration in clinical studies as well as Asian registry network. However, international collaboration in Asia may have challenges in different regulations, different health insurance system, different requirements for compensation/indemnity, lack of research funder, and different languages. Thus, we are constructing Asian disease-specific registry network in addition to the above-mentioned project. This disease-specific registry consist from retrospective as well as prospective registry studies of GIST and NET in Japan, Korea, Taiwan and China.

Key Slides

### Rare Cancer ReGISTry NETwork in Asia

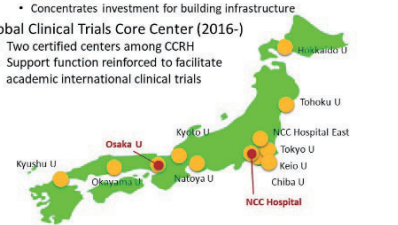


National Cancer Center Hospital, Tokyo  
Toshirou Nishida, Kenichi Nakamura, Kan Yonemori

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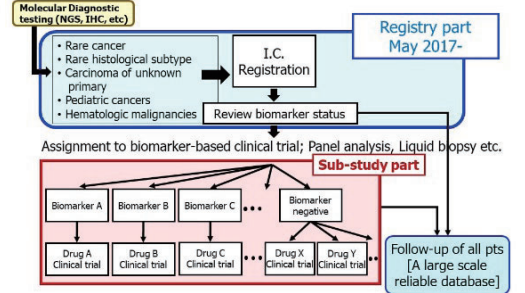
### Core Clinical Research Hospital & Global Clinical Trials Core Center

- Core Clinical Research Hospitals (CCRH)
  - Japanese Government has certified 12 CCRH (since 2015)
    - Hospitals with sufficient support function for investigator-initiated clinical trials
    - Concentrates investment for building infrastructure
- Global Clinical Trials Core Center (2016-)
  - Two certified centers among CCRH
  - Support function reinforced to facilitate academic international clinical trials



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### Development of Medicine: MASTER KEY Project



**Molecular Diagnostic testing (NGS, IHC, etc)**

- Rare cancer
- Rare histological subtype
- Carcinoma of unknown primary
- Pediatric cancers
- Hematologic malignancies

I.C. Registration

Review biomarker status

Registry part May 2017-

Assignment to biomarker-based clinical trial; Panel analysis, Liquid biopsy etc.

**Sub-study part**



- Biomarker A → Drug A Clinical trial
- Biomarker B → Drug B Clinical trial
- Biomarker C → Drug C Clinical trial
- ... Biomarker X → Drug X Clinical trial
- ... Biomarker Y → Drug Y Clinical trial
- ... Biomarker negative → Drug Y Clinical trial

Follow-up of all pts [A large scale reliable database]

3

### MASTER KEY: Collaboration among academia, industries and patients

Participating industries	
Astellas Pharma	
Eisai	
Ono Pharmaceutical	
Kyorin Pharmaceutical	
Daichi Sankyo	
Taiho Pharmaceutical	
Takeda Pharmaceutical	
Chugai Pharmaceutical	
Novartis Pharma	
Pfizer	
Ignyta	
... 2-3 more to participate in 2019	

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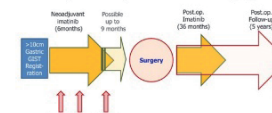
### Backgrounds of Asian Collaboration in GIST & NET

#### Asian GIST Guidelines (Japan, Taiwan, Korea, China)

Asian Consensus Guidelines for the Diagnosis and Management of Gastrointestinal Stromal Tumor

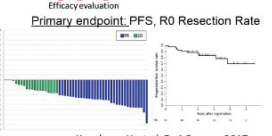
#### Collaboration Study between Japan and Korea

Phase II study of neoadjuvant imatinib in large gastric GIST



Efficacy evaluation

Primary endpoint: PFS, R0 Resection Rate




Kurokawa Y, et al. Br J Cancer. 2017

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### Asian Registry Network in GIST & NET

- 1st ReGISTry Network Meeting** April 8<sup>th</sup> 2017, Osaka, Japan
  - To share registry studies and regulations in each countries
- 2nd ReGISTry Network Meeting** March 7<sup>th</sup> 2018, Tokyo, Japan
  - To discuss on a new protocol of GIST registry and a method of data sharing
- 3rd ReGISTry Network Meeting** March 1<sup>st</sup> 2019, Numazu, Japan
  - To finalize the retrospective protocol and logistics of registry study in GIST



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# Wearables and Sensors in Clinical Trials



## Samuel Volchenbom

The University of Chicago



United States of America

### ■ Profile

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Dr. Volchenbom is an associate professor of pediatrics and the associate chief research informatics officer for the biological sciences division at the University of Chicago. He is the Dean of Masters Programs and directs a program in health sciences informatics for the division. His clinical specialty is pediatric hematology / oncology, caring for children with cancer and diseases of the blood. In addition to his clinical practice, he directs the University of Chicago's Pediatric Cancer Data Commons, a research group dedicated to liberating and democratizing data for pediatric malignancies. He participates in and leads various data governance initiatives throughout the University and medical center. He is the director of the Informatics Core for the Clinical and Translational Science Award (CTSA). Since 2015, he has been the faculty director for the Masters in Biomedical Informatics at the Graham School at the University of Chicago.

### ■ Abstract

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Clinical trials are plagued by manual and inefficient data collection methods. Patient-reported outcomes are still collected via antiquated surveys that require a high level of recall and compliance. The costs of these methods are enormous, as the decision to advance drug development often relies on these faulty measures. The use of wearables and sensors to support real world data collection for clinical trials has the potential to revolutionize this process. Many manual and outdated clinical outcomes assessment (eCOA) measures may be replaced by data collection from wearables and sensors. A case study at the University of Chicago will be used to illustrate the potential for incorporating these methods into study. Over 250 patients with inflammatory bowel disease (Crohn's and ulcerative colitis) were given a wearable (Fitbit) and a mobile application (Litmus Health, Inc.), both of which were used to collect passive and active data (patient-reported outcomes). The initial results of the study demonstrate for the first time the use of passive biosensor data to predict elevated biomarkers of inflammation in IBD. Of course, the use of wearables and sensors for clinical trials poses challenges, including accuracy, compliance, worries about equivalence and data provenance, and privacy and security considerations. These issues, along with a review of the global landscape of the industry's approach to using wearables and sensors in trials will be discussed.

## Key Slides

### Wearables and sensors in clinical trials

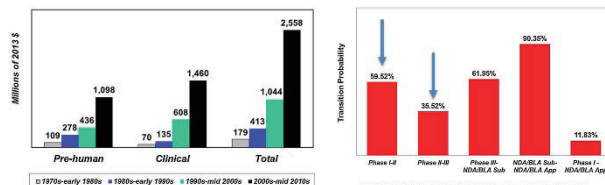
#### Objectives

- **Understand** the landscape of consumer wearables, sensors, and devices in clinical trials
- **Appreciate** the caveats and opportunities of leveraging these devices for data collection as part of a clinical trial
- **Learn** why data standardization for wearables and sensors are key to acceptance and usage

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### Bad data lead to waste in clinical trials



\$2.5B to develop a new drug

Making go/no-go decisions

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J.A. DiMasi et al. / Journal of Health Economics 47 (2016) 20-33 21

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### Opportunities for using wearables in clinical trials

- More realistic, real-world patient-centric outcome measures
- Better safety monitoring and side-effect profiling
- Patient engagement and increased retention
- Lower variability = fewer subjects = better, faster, cheaper
- Reduced costs by decreasing need for clinic visits
- Objective + subjective criteria = better QoL measures

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The Growing Availability of Wearable Devices: A Perspective on Current Applications in Clinical Trials  
Niklas Morlok, David Bleichman, May 27, 2016, Applied Clinical Trials

3

### Wearables and sensors for COAs

mHealth data type	Clinical outcomes assessments (COAs)		non-COA
	Patient/caregiver-reported outcome (PRO)	Clinician-reported outcome (ClinRO) (requires HCP)	Performance outcome (PerO) (requires HCP) Biomarker or surrogate endpoint
Patient/caregiver-reported data	Mobile device questionnaire	Photo uploaded by patient	
Task-based measures	PRO support? (e.g., med adherence)		Six minute walk test? Smartphone memory test
Active sensor data	PRO support? HR + feeling faint		Smart-phone based spirometer? Home blood glucose
Passive sensor data	PRO confirmation? PSCl + sleep		Data mining to document fitness? HR, steps, sleep

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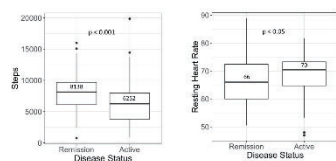
Chen S, Laine A, and Volkerboum SL. Use of Wearable, Mobile, and Sensor Technology in Cancer Clinical Trials. JCO Clinical Oncol Informatics. June 2018.

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### University of Chicago IBD study

189 Patients Enrolled  
123 Patients with 330 disease activity assessments  
59 Patients with 142 disease activity assessments with biosensor data in the preceding week

- 54 CRP
- 22 FCP
- 58 clinical assessments
- 23 colonoscopies



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Sossenheimer PH. Wearable Devices Can Predict Disease Activity in Inflammatory Bowel Disease Patients. Digestive Diseases Week (DDW). 2019. San Jose, CA.

5

### Bringing it all together

- Wearables, sensors, and smartphones are transforming the clinical trials industry
- Concerns are valid but surmountable
- Keys to success are **standardized data collection** and **normalization** with appropriate attention to **privacy** and **security**

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# Memo

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# *Session 2*

## *Data Management and Standards for Global Clinical Research*

**Chair: Rebecca Kush**

Learning Health Community, Elligo Health Research and Catalysis

**Chair: Norihiro Sato**

Chairman of ARO Council/Hokkaido University

# Development of ECRIN Data Centre Certification Programme



## Christian Ohmann

European Clinical Research Infrastructure Network (ECRIN)



Germany

### ■ Profile

**Christian Ohmann** has a graduation in mathematics (PhD), an interim examination in medicine and a habilitation in the field of “Theoretical Surgery”. He was the head of the Coordination Centre for Clinical Trials (KKS) at the Medical Faculty of the Heinrich-Heine-University Duesseldorf, Germany (1999-2014) and is now retired. He is currently the German representative and Chair of the Network Committee and chair of the Independent Certification Board. of ECRIN. In addition, he provides consultancy services for ECRIN in several EU H2020-funded projects. He has major competence and experience in the field of clinical research/clinical trials as well as clinical research informatics and data management.

### ■ Abstract

After a pilot phase (EU FP7 project ECRIN-IA, 2011), the ECRIN data centre certification programme was implemented in 2015. Aim of the programme is to provide a clear interpretation of regulatory and good practice requirements for academic CTUs and to confirm the ability of CTUs to provide compliant, effective and efficient data management services for clinical trials. Major components of the programme are the standards (currently version 4.0 from April 2018, publicly available at <https://zenodo.org/record/1240941#.XOlP2ZV7ncs>), an Independent Certification Board, auditors, a scientific secretary and system development and maintenance. Following a yearly call, so far 36 external audits have been performed and 12 centres in 5 countries have been certified. In addition, auditors training and a joint ECRIN/CDISC training initiative have been performed in 2019. Evaluation of the programme (Ohmann et al, Contemp Clin Trials Commun. 2017;5:153) revealed that the standards are detailed pragmatic statements of good practice tailored at academic CTUs and with national impact (e.g. Switzerland, Germany, France, Japan), certification increases the quality of DM services, programme participation rewards through the sharing of latest technical developments and training on DM and auditors receive advanced training with DM, creating potential for lead expert role in a country. Globalisation of the programme has recently been started (e.g. Japan, South-Korea).

# Key Slides

### ECRIN data centre certification programme Aim\*

- To audit individual units against the standards, to confirm their ability to provide compliant, effective and efficient data management services for controlled clinical trials, and for ECRIN-supported multi-national trials in particular
- To provide a clear interpretation of regulatory and good practice requirements, in the particular context of non-commercial trials units in Europe, and so act as a practical guide to establishing and managing high-quality data management services.



\*Ohmann et al., *Contemp Clin Trials Commun*, 2017 Mar; 5: 153

1

### ECRIN data centre certification programme Requirements for Certification, Version 4.0\*

**General Standards (4)**

GE01 Centre Staff training and support (4)

**IT Standards (41)**


IT01 Management of IT Infrastructure (9)  
 IT02 Logical Security (7)  
 IT03 Logical Access (7)  
 IT04 Business Continuity (6)  
 IT05 General System Validation (9)  
 IT06 Local Software Development (3)

**Data Management Standards (61)**

DM01 Data Management Planning (1)  
 DM02 CDMAAs - Design, Development and Validation (8)  
 DM03 CDMAAs - Change management (7)  
 DM04 Site Management, Training & Support (9)  
 DM05 Data Entry and Processing (7)  
 DM06 Managing Data Quality (12)  
 DM07 Managing Data Transfers (5)  
 DM08 Delivery and Coding of Data for Analysis (8)  
 DM09: Long Term Data Storage (4)

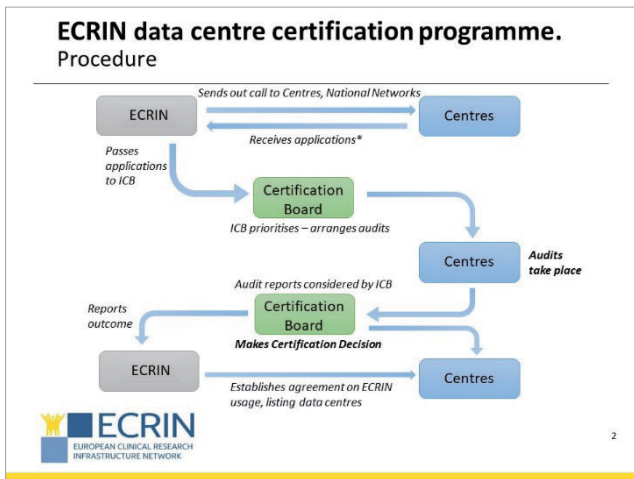
**Optional Standards (9)**

ST01: Treatment Allocation standards (9)



\*https://zenodo.org/record/1240941#.X0lhmJV7ncs

2




3

### ECRIN data centre certification programme. Status of the programme

- 36 external audits performed
- 16 auditors (7 new)
- 12 centres certified (2015-2019)

Certification per country	Number
Germany	5
Italy	3
France	2
Portugal	1
Japan (pilot)	1



Certification per attempt	Number
Certified at 1st attempt	4
Certified on CAPA	5
Certified after re-audit	3



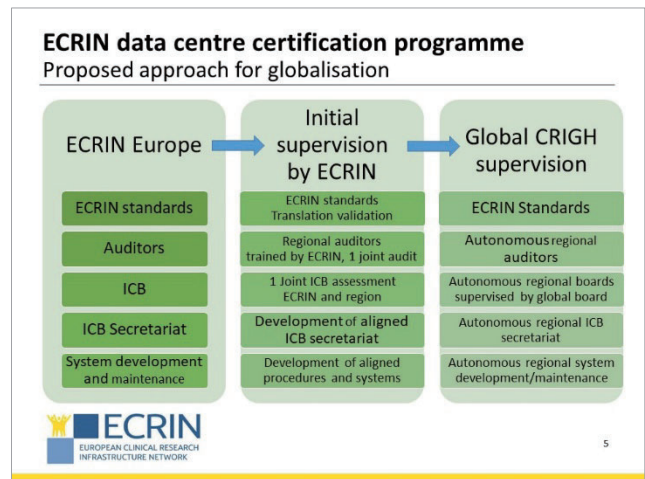
4

### ECRIN data centre certification programme Evaluation of the programme

- ECRIN standards detailed pragmatic statements of good practice tailored at academic CTUs, national impact (e.g. Switzerland, Germany, France, Japan)
- Certification increases the quality of DM services
- Programme participation rewards through the sharing of latest technical developments and training on DM
- Auditors receive advanced training with DM, creating potential for lead expert role in a country
- Challenge is more involvement of certified data centres in ECRIN-supported trials

5



6

# Development of the Data Quality Control System based on the Requirements for Certification of ECRIN Data Centres



**Itadaki Yamaguchi**

**Translational Research Center for Medical Innovation (TRI)**



Japan

## ■Profile

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Itadaki Yamaguchi, PhD, is the Group leader of Division of Corporate Planning at Translational Research Center for Medical Innovation (TRI).

Prior to joining the TRI, he was engaged in non-clinical study under GLP/GMP as study director. At TRI, he has experience as an auditor and works on translational research promotion and supports academia's research and development.

## ■Abstract

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TRI was established in 2003 by the Ministry of Education, Culture, Sports, Science and Technology (MEXT) and Kobe City. It is the first academic data center and statistical analysis center in Japan. We provide comprehensive clinical trial management services for studies of all phases from research planning to data analysis. Our vision is to improve the prognoses of those suffering from intractable diseases. We have given consultation services and support to develop many medical product candidates. We have had to over 670 research consultations and have given supports for approximately 400 clinical studies, of which over 270 papers have been published as of in March 2019. We are also conducting global clinical trials and have extensive experience as a data center.

In order to further promote global collaborative studies and to improve the quality as a data center, we have developed a data quality control system based on the ECRIN data centre certification. TRI is the first data center in Asia who has been audited by ECRIN, and it acquired the certification in 2019.

Thus, we are able to harmonize with Europe AROs. As a future perspective, we hope to conduct multicenter trials with European countries and Global.

# Key Slides

### Introduction of TRI - Support Clinical Trials & Medical R&D

➤ **Only one open Data Center for academia**

Provide comprehensive clinical trial management services for studies of all phases from research planning to data analysis.

R&D Strategy	Clinical trial
<ol style="list-style-type: none"> <li>R&amp;D policy                             <ul style="list-style-type: none"> <li>Market &amp; competitive analysis</li> <li>Competitive Research</li> <li>R&amp;D scheme · R&amp;D truck</li> </ul> </li> <li>Patent strategy                             <ul style="list-style-type: none"> <li>Patent consultation</li> <li>Patent research support</li> </ul> </li> <li>Non-clinical                             <ul style="list-style-type: none"> <li>Efficacy · Safety · Pilot production</li> </ul> </li> <li>Search for possible corporation (Liaison)</li> <li>ARO establishment support</li> </ol>	<ol style="list-style-type: none"> <li>First-in-man trial strategy and regulations</li> <li>Starting clinical trials and its management</li> <li>Data Management</li> <li>Medical statistics</li> <li>Information systems development</li> <li>Plan, start-up, support of global clinical trials</li> <li>Monitoring, Audit</li> </ol>

1

### Schematic Presentation: TRI Mission and Activities

We can accelerate this cycle dynamically through *global data sharing*

**Disease-specific Registry - complete enrollment**

**Cure and Overcome All Diseases**

**Big Data AI assisted**

**Standardization & Harmonization REQUIRED!**

2

### Summary of TRI Achievement

**[Number of Consultation]**

- Total: 675 product candidate (seeds) (Apr. 2009 - Mar. 2019)
- Application in FY 2018: 101 seeds

**[Number of Supported projects] (2003 - Apr. 2019)**

- Protocols: 403
- Published or accepted papers: 275
- Total citation number: 4953

Database: Web of science, as of April 17, 2019

3

### TRI Achievement

TRI aims for disease control and healthy life extension. With past activities, some diseases, especially the major diseases that cause long-term care, can be overcome. In the future, we will strongly promote digital health innovation and contribute to the extension of the healthy life span.

**2003年 TRI Establishment**

**15th anniversary**

**Feedback to citizens**

**Vocal cords: TITANBRIDGE, December 15, 2017, approval (The first approval in SAKIGAKE Designation System!)**

**Nerve, Spinal cord: Stenirac, December 28, 2018, condition and time-limited approval**

4

### ECRIN Data Centre Certification program

The ECRIN Independent Certification Board certifies that: **Translational Research Center for Medical Innovation (TRI)** is authorized for Research Research and Innovation of data (RRI) - 13-4 Innovative Research Center - since April 2018/2019.

ECRIN Data Centre Certification program

Reference: ECRIN Data Management Standards, Version 4.1, dated January 2018

5

### Future Scope for Global Vision

Network management: ECRIN(EU), Asia ARO Network, Taiwan-Japan ARO Workshop since 2015, NCATS(US), Global ARO Network.

Global development of academia medical product candidates

CDISC Standards

Global "Disease-specific" Consortium

Cancer, MCI/AD, ALS, Stroke, Others

Clinical Trial Network

Goal: Improve Outcomes · Overcome Diseases

6

# CDISC Standards Implementation in Japanese Academia



**Masato Shiren**

**Osaka University**



Japan

## ■Profile

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Masato Shiren is the group leader of subject allocation group in the Data Coordinating Center at Osaka University Hospital.

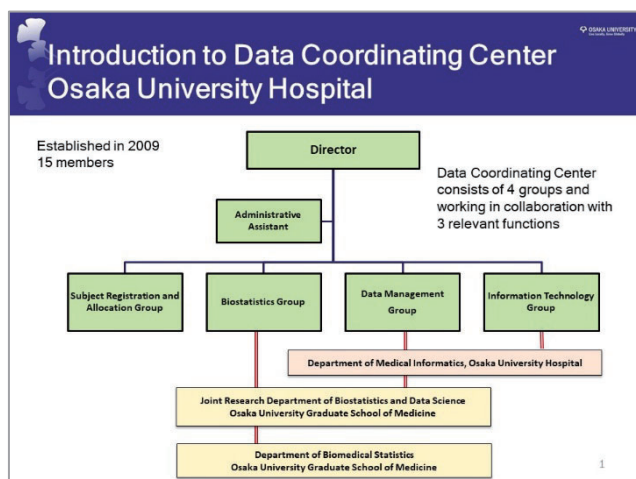
Prior to joining the Osaka University Hospital, he worked for Japanese subsidiary of German company Boehringer Ingelheim and was in charge of Clinical On-site Monitoring, Drug Safety Operations, Clinical Data Management and Quality Management of Clinical Trials.

## ■Abstract

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CDISC Standards are required for NDA submissions to FDA and PMDA and has been implemented in Pharmaceutical industries and CROs within a relatively short period of time since it is regulatory requirements and there is no other way. On the other hand, how about the situation of CDISC implementation in Japanese Academia? Today, I would like to talk about what Japanese ARO data center is doing on a daily basis and PMDA requirements briefly in order to promote better understanding about the local environment and explain about the current situation of CDISC implementation in Japanese AROs based on the survey results conducted by ARO council.

## Key Slides



1

### Regulatory Requirements of CDISC Standards in Japan

PMDA Requirements of CDISC Standards in Japan

- ✓ From April 2020 onward, PMDA will require sponsors to submit CDISC compliant electronic datasets and e-CTD for regulatory submission
- ✓ PMDA only requires CDISC Standards for regulatory submission of new drugs
- ✓ "Medical Devices" and "Regenerative Medicines" are outside the scope of PMDA's CDISC regulations
- ✓ PMDA required CDISC Standards are as follows:
  - SDTM
  - ADaM
  - Define-XML
  - Analysis Results Metadata (ARM for Define-XML)

2

2

### Situation of CDISC implementation in Japanese Academia : ARO Council Japan

ARO Council Japan consists of following 16 AROs:

- Hokkaido Organization for Translational Research
- Tohoku University
- The University of Tokyo
- Nagoya University
- Kyoto University
- Osaka University
- Foundation for Biomedical Research and Innovation at Kobe
- Kyushu University
- Gunma University
- Chiba University
- National Cancer Center Japan
- Keio University
- Okayama University
- National Center for Child Health and Development
- National Hospital Organization Nagoya Medical Center
- University of Tsukuba

And CDISC workgroup of ARO council conducted a survey in order to grasp the situation of CDISC implementation in 2017 and 2018

3

3

### Situation of CDISC implementation in Japanese Academia : 2017 Survey Results

Sites *	No. of NDAs**	No. of finished trials	No. of on-going trials (including preparing)	CDISC Standards Compliance
A	8	0	4	No
B	6	8	3	No
C	4	1	6	No
D	4	0	5	No
E	4	0	3	No
F	3	0	3	No
G	2	0	4	No
H	2	0	2	Yes
I	1	0	1	Almost Yes
Total	34	9	31	-

\*: 9 of 16 AROs \*\*Anticipated No. of NDAs to PMDA after 2020

4

4

### Situation of CDISC implementation in Japanese Academia : 2018 Survey Results

Sites *	No. of NDAs**	No. of finished trials	No. of on-going trials (including preparing)	CDISC Standards Compliance
A	12	9	7	Yes (3) No (13)
B	11	1	12	Yes (3) No (10)
C	8	0	12	Yes (2) No (10)
D	7	3	4	No
E	5	0	5	No
F	4	0	4	No
G	4	2	3	Yes (2) No (3)
H	4	1	3	Yes
I	4	1	3	No
J	4	1	3	Yes (2) No (2)
K	2	0	2	Yes
L	1	0	1	No
Total	66	18	59	-

\*: 12 of 16 AROs \*\*Anticipated No. of NDAs to PMDA after 2020

5

5

### Summary

1. In terms of CDISC implementation in Japanese academia, there are some progress between 2017 and 2018 based on the survey results
2. Some obstacles still remain if academia intends to implement company-level, perfect CDISC which can pass PMDA's CDISC conformance check
3. Another possibility is taking step by step approach and start from what we can do now e.g. "CDISC like" for moving forward standardization. It's better than nothing
4. Japanese academia should continuously work toward enhancing CDISC implementation in order to gain accessibility, interoperability, re-usability of research data and advantage to dealing with big data

6

6

# SNUH's Efforts to Improve the Quality of Data Management



## SeungHwan Lee

Seoul National University Hospital



Korea

### ■Profile

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Dr. SeungHwan Lee is currently a Clinical Associate Professor of Department of Clinical Pharmacology and Therapeutics and the Head of Quality Improvement Office of Clinical Trials Center in Seoul National University Hospital (SNUH).

After graduating from Seoul National University College of Medicine, he completed internship at SNUH and went on to be trained in the clinical pharmacology residency program at SNU/SNUH. He received his Ph.D. from this university in 2012, and has been involved in many clinical pharmacology research projects since training.

He is interested in various topics related to early phase clinical trials, PK-PD modeling & clinical trial simulation, and individualized pharmacotherapy. Recently, Dr. Lee has been participating in more than twenty clinical research projects annually, as principal investigator or co-investigator. He is also giving many consultations regarding clinical drug development.

### ■Abstract

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Seoul National University Hospital (SNUH) is one of the largest Academic Research Organization in Korea. SNUH has its own data management function and is constantly striving to improve its quality. As a part of the efforts, SNUH has applied for ECRIN data center certification. For the certification, the criteria for certification (Requirements for Certification of ECRIN Data Centres version 3.1 and version 4.0) was translated into Korean and all data managers were trained about the standards. In addition, SOPs and IT infrastructures related data management were revised to meet the requirements, so the current data management process of all clinical studies have been conducted in compliance with the standards. The audit for certification by ECRIN is scheduled for January 2020. SNUH have also been tried to implement CDISC, but it faces many obstacles in terms of technology, institution and regulation. However, SNUH will make various efforts to overcome these difficulties and apply CDISC within a few years.



# Key Slides

## SNUH's Efforts to Improve the Quality of Data Management

**SeungHwan Lee, M.D., Ph.D.**  
Head, Quality Improvement Office, Clinical Trials Center & Associate Professor, Department of Clinical Pharmacology and Therapeutics, Seoul National University Hospital

**SNUH** 서울대학교병원 임상시험센터

1

## Role of SNUH in Clinical Trials

	SNUH		CRO
	CTC	MRCC	
1. Project management	O	X	O
2. Researcher meeting	O	X	O
3. Protocol/CRF development	O	O	O
4. IRB/KFDA Submission	O	X	O
5. Randomization	X	O	O
6. Monitoring	△	X	O
7. Audit	O	O	△
8. Data management	X	O	O
9. Statistical analysis/Statistical Report	O	O	O
10. Clinical Study Report	O	X	O

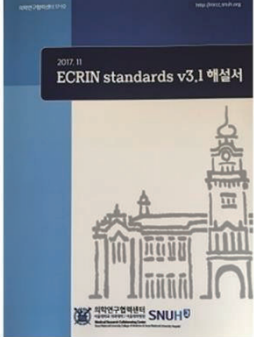
\*CTC: Clinical Trials Center  
\*MRCC: Medical Research Collaborating Center

**SNUH** 서울대학교병원 임상시험센터

2

## ECRIN data center certification

- Translation of ECRIN standards
  - Version 3.1 & Version 4



**1. Introduction and Background**

이 문서는 ECRIN 표준의 소개와 ECRIN 표준의 필요성, ECRIN 표준의 목적, ECRIN 표준의 적용 범위, ECRIN 표준의 개발 과정, ECRIN 표준의 검증 과정, ECRIN 표준의 배포 과정, ECRIN 표준의 유지 보수 과정, ECRIN 표준의 폐기 과정, ECRIN 표준의 저작권, ECRIN 표준의 라이선스, ECRIN 표준의 기타 사항을 설명합니다.

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3

## ECRIN data center certification

- Revision of SOPs
  - Mapping of SOPs of MRCC and CTC to ECRIN standard
  - Comparison
  - Review real working process
  - Revision of SOPs in accordance with ECRIN standard

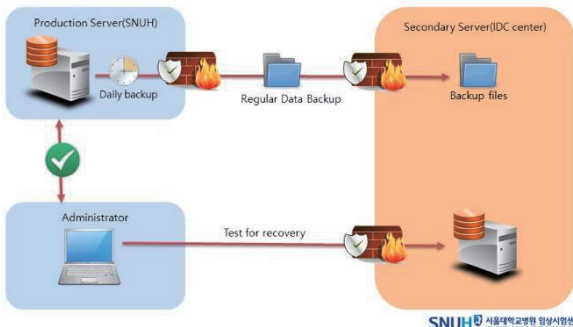
ECRIN standard v4.0	MRCC/CTC SOP
GE01: Centre Staff training and support	SNUH_MRCC/TRM 0010 Staff Training SNUH_MRCC/TRM 0030 New Staff Training : Data Manager
GE01.01: Policies for training:	MRCC TRM0010 Staff Training MRCC TRM0030 New Staff Training : Data Manager MRCC TRM0040 Education of SOPs
GE01.02: Documentation of training	MRCC TRM0050 Management of Education Record
GE01.03: Managing training requirements	MRCC TRM0010 Staff Training
GE01.04: Managing concerns – alternative pathways	SNUH_MRCC/COCK 0010 Study Coordination

**SNUH** 서울대학교병원 임상시험센터

4

## ECRIN data center certification

- Upgrade infrastructure
  - Build secondary server outside of hospital

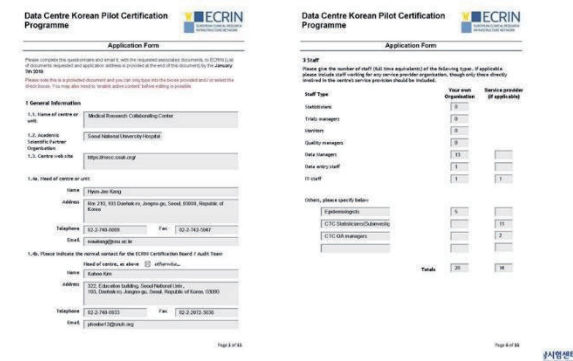


**SNUH** 서울대학교병원 임상시험센터

5

## ECRIN data center certification

- Applied for ECRIN data center certification in January 2019



**SNUH** 서울대학교병원 임상시험센터

6

# An Attempt to Implement ECRIN and CDISC Standards by using Electronic System



**Ueng-Cheng Yang**

**National Yang-Ming University**



Taiwan

## ■Profile

Dr. Ueng-Cheng Yang was graduated from Dept. of Agricultural Chemistry at National Taiwan University. He then got his Ph.D. degree from Dept. of Molecular Biology at Princeton University. After he completed his postdoctoral training in Dept. of Chemistry at Yale University, he moved back to the National Yang-Ming University in Taiwan.

Dr. Yang established the Bioinformatics Program in year 2002 and the Institute of Biomedical Informatics in year 2007 at National Yang-Ming University. Both programs are the first such programs in Taiwan. He has been the vice-president of the Asian-Pacific Bioinformatics Network and the officer of the Bioinformatics Society of Taiwan. He was the Director of the Information and Communication Center, the Institute of Biomedical Informatics. He is now the Director of the Center for Systems and Synthetic Biology at National Yang-Ming University.

## ■Abstract

The Taiwan Clinical Trial Consortium (TCTC) provides a single contact window for 12 therapeutic areas. TCTC provides an internet service provider (ISP)-like data management service to the consortium of a specific therapeutic area. Moreover, fourteen hospitals have harmonized their application forms and workflows and are using the same protocol tracking and management system (PTMS). Thus, submitting a protocol for multi-centered trial are efficient and easy. Five of these hospitals are certified by AAHRPP. The consortium members may use the clinical study information system (CSIS) to collect clinical information. CSIS supports the ODM (operational data model) format of CDISC. Therefore, public eCRFs from molecular data model can be imported and be used in CSIS readily. Moreover, CSIS has question libraries, so a user may easily create not only the annotated CRF (aCRF), but also the CDISC-compliant eCRFs. Even though such system is available, the most important thing is to follow the standard operating procedures (SOP) to run the trial. ECRIN provides a pathway through Europe to conduct multinational trials. Thus, it is important for the clinical trial centers be certified by ECRIN standards. Instead of using the traditional paper-based quality management system, Taiwan attempts to establish an electronic quality management system for ECRIN certification. The process and operations mapping part are almost done and can be implemented by using a business process management (BPM) software to control the workflows based on the existing SOPs. Naïve users, who are not familiar with the SOPs, may simply follow the workflow to avoid violating the SOPs. The sign-off process is archived and the changes are recorded in the audit trail. Thus, not only the documents, but also the supporting evidences can be easily retrieved during the certification process.

# Key Slides



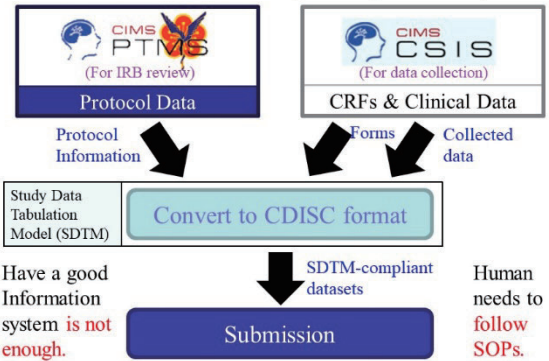
**An attempt to implement ECRIN and CDISC standards by using electronic system**

Ueng-Cheng Yang  
National Yang-Ming University,  
Taiwan. [cims@ym.edu.tw](mailto:cims@ym.edu.tw)

The 4<sup>th</sup> global ARO workshop,  
June 20, 2019

1

Merging protocol data and trial data for the submission to the regulatory authority



2

1

2

**Preparing ECRIN certification by using IT tools**

- Using “Redmine” to keep track of the preparation of ECRIN certification process
  - It is easy to make a plan, but it is difficult to see the **progress of every jobs.**
- Using “PTMS” to keep track of the training records
  - The protocol tracking and management system (PTMS) stores the **evidence of training** for all applicants.
- Using “business process management” tool to keep track of the sign-off processes
  - It is easy to establish a set of SOPs. However, it is **difficult to follow the SOPs** exactly when you have **multiple trials.**

3

**The advantage of establishing an eQMS for ECRIN standards**

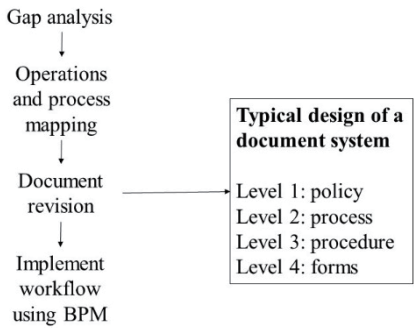
- A process will be executed based on the standard operating procedure (SOP)
- A naïve user may follow the workflow without remembering the details of a SOP
- Simple quality control can be implemented to discover input errors
- Signoff records are automatically archived
- Electronic form records can be searched
- Has audit trail for changes

4

3

4

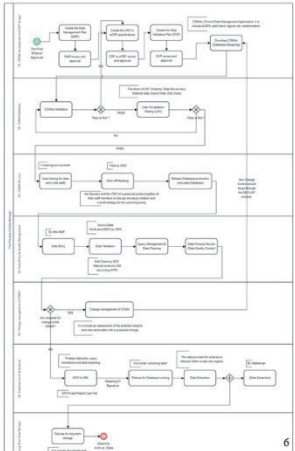
**Preparation for the ECRIN certification**



5

**High level processes of a trial**

- CDMA development and CRF design
- CDMA validation
- CDMA go live
- Data entry and quality management
- Change management of CDMA
- Database lock and analysis
- Long term data storage



6

5

6

# Standards for Academic Research



## Xuanhui Ng

Singapore Clinical Research Institute (SCRI)



Singapore

### ■ Profile

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Ng Xuanhui serves as Head of Data Management at the Singapore Clinical Research Institute (SCRI), and provides leadership to a team of data management professionals in supporting clinical research efforts in Singapore.

Coupled with her Certified Clinical Data Manager (CCDM) title from the Society for Clinical Data Management (SCDM), Ms Ng's years of extensive expertise help in ensuring clinical research data is accurate, reliable, and in accordance with protocol requirements and regulatory standards.

She is passionate about using healthcare research to improve the lives of people, and is driven by doing meaningful academic research work. As an advocate for providing structured training opportunities, Ms Ng actively encourages her associates to get accredited in order to stay relevant in the healthcare industry.

### ■ Abstract

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Amidst the plethora of global standards that the scientific community currently employs as best practices in clinical research, we shine a light on clinical research standards, specifically for academic research organisations (AROs).

In this workshop, the four approaches of acquiring and maintaining a set of standards for AROs will be explored in greater detail.

It is worth noting that during this development of a system of standards, we must set the tone right from the start. Standards should be adaptable in nature without compromising efficiency in existing processes.

With the ARO network, delegates are able to capitalise on this platform to share their views and support one another in adopting respectable standards. A well-planned implementation programme is equally essential in helping research institutions achieve these goals.

AROs should also continuously encourage like-minded supporters to join in the implementation of global standards. This will allow them to keep up to speed with any changes to the clinical research scene.

In conclusion, the ARO network plays a crucial role in shaping the future of academic research. Only by ensuring the harmonisation and acceptance of appropriate clinical research standards, will we be able to improve efficiencies and benefit patients and our society.

## Key Slides

# Standards for Academic Research

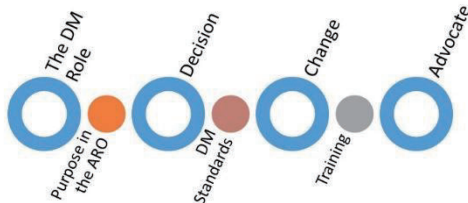
Ng Xuanhui  
Head, Data Management

ADVANCING CLINICAL RESEARCH FOR OUR NATION • IN SEARCH OF BETTER VALUE TREATMENTS FOR OUR PATIENTS




1

## How do we get there?



ADVANCING CLINICAL RESEARCH FOR OUR NATION • IN SEARCH OF BETTER VALUE TREATMENTS FOR OUR PATIENTS




2

## The Data Management Role

Part 1

- **Function:**
  - **Academic**
    - Apply appropriate standards for academic research while still meeting basic requirements from the clinical research industry
  - **Core Capabilities**
    - Appreciate the best industry practices
    - Acquire unique standards for academic research
  - **Infrastructure**
    - Use appropriate systems for academic research

ADVANCING CLINICAL RESEARCH FOR OUR NATION • IN SEARCH OF BETTER VALUE TREATMENTS FOR OUR PATIENTS



3

## 7 Steps to Decide Standards

Part 2



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4

## Training & Accreditation

Part 3



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5

## Be An Advocate

Part 4

- **Why is it important to advocate our standards?**
  - Encourage others to keep up with the trends
  - Easier to collaborate with global partners
  - Higher efficiency in research execution
  - Being relevant in clinical research

ADVANCING CLINICAL RESEARCH FOR OUR NATION • IN SEARCH OF BETTER VALUE TREATMENTS FOR OUR PATIENTS



6

# Standards and Data Strategies for Global Regulated Research, from Protocol through Analysis



## Michael Kurilla

National Center for Advancing Translational Sciences,  
National Institutes of Health



United States of America

### ■ Profile

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Michael Kurilla is the director of the Division of Clinical Innovation at NCATS. In this capacity, he oversees the Clinical and Translational Science Awards (CTSA) Program, which supports innovative solutions to advance the efficiency, quality and impact of translational science, with the ultimate goal of getting more treatments to more patients more quickly. Prior to joining NCATS, Kurilla served as the director of the Office of Biodefense Research Resources and Translational Research within the National Institute of Allergy and Infectious Diseases (NIAID), where he focused on translational efforts toward infectious disease product development, including vaccines, therapeutics and diagnostics, with emphasis on biodefense and emerging infectious disease threats. Prior to joining NIAID in 2003, Kurilla was an associate director for infectious diseases at Wyeth. He also worked in antimicrobials at DuPont and on clinical microbiology and molecular pathology at the University of Virginia Health Sciences Center.

Kurilla received his M.D. and his Ph.D. in microbiology and immunology from Duke University. He was a postdoctoral research fellow at Harvard Medical School and completed a residency in pathology at Brigham and Women's Hospital. He received a B.S. in chemistry from the California Institute of Technology.

### ■ Research Topics

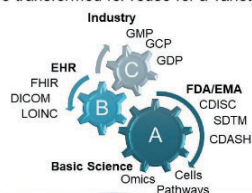
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Kurilla's research interests include all facets of translational science, especially innovative and novel interventional concepts requiring additional input from regulatory science to enable viable, robust developmental pathways.

## Key Slides

### Parallelism vs Translation

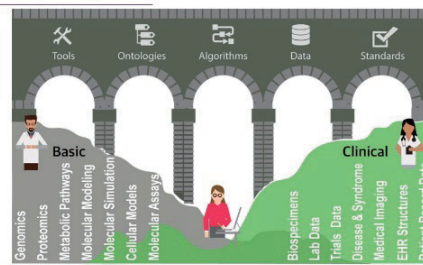
- We cannot regulate ourselves into a single data standard
- But, Smart Data can be transformed for reuse for a variety of purposes



1

### \*Chasm of Semantic Divide

- The sources of evidence will continue to expand.
- Scientific knowledge is growing logarithmically.
- Translation is the bridge between the scientific and the clinical communities

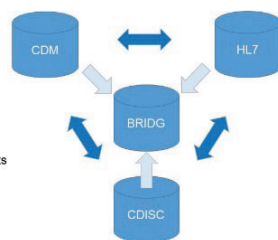


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### Smart Data Models

\*Four components to a smart data model:

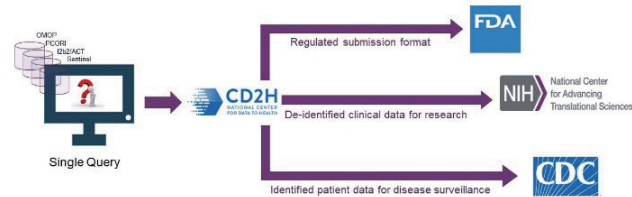
- Concept: defines what the model represents
- Structure: defines a valid syntactical model
- Ontology: defines the context
- Relationships: defines the relationship between components



3

### Real World Data: Common data model harmonization with \*FHIR

Collaboration with the NCATS, FDA, CDC, NCI



4

### All of the TIN multisite single IRBs utilize NCATS' SMART IRB Reliance Agreement

The screenshot shows the SMART IRB website. The page features the SMART IRB logo, navigation links (SMART IRB AGREEMENT, ONLINE RELIANCE SYSTEM, HARMONIZATION, RESOURCES, ABOUT US, SUPPORT), and a main heading "Supporting single IRB review Advancing collaborative research". Below this is a description of SMART IRB and an "Online Reliance System" section.

5

### Trial Innovation Network Innovating and Harmonizing – Contracts



TIN uses the FDP-CTSA Master Contract for NIH supported studies

Kirkakis, Olin & Transl Science, 2015; [www.ara4us.org](http://www.ara4us.org)

#### Roadblock

- Contract negotiations are the top reason for study delay.

#### Innovation and Harmonization

- The TIN is implementing the FDP-CTSA Master Contract.
  - Addresses Indemnification, Confidentiality, Publication, Intellectual Property
- Hopes to implement a harmonized contracting system across CTSA's
- Will collect metrics to determine if the FDP-CTSA decreases delays

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# Learning Health and a System of Accelerated Research (SOAR™)



## Rebecca Kush

Learning Health Community, Elligo Health Research and Catalysis



United States of America

### ■ Profile

Rebecca Daniels Kush is President of Catalysis.; Chief Innovation Officer for Elligo Health Research, and Fellow for Japan's TRI/Foundation for Biomedical Research and Innovation. She is also Founder and President Emeritus for CDISC. Dr. Kush has over 30 years of experience in clinical research and related data standards and technology to improve research and healthcare, including positions with academia, the U.S. National Institutes of Health, a global CRO and biopharmaceutical companies based in the U.S. and Japan. She was on the Board of HL7, participated in projects with IMI and CORBEL in Europe, and she is currently on the Board of the Learning Health Community and Associate Editor of the Learning Health Systems Journal. Dr. Kush earned her Doctorate in Physiology and Pharmacology from the University of California San Diego (UCSD) School of Medicine and Bachelor of Science degree in Biology and Chemistry from the University of New Mexico.

### ■ Abstract

Truly bridging health care and clinical research has been a dream since EHRs emerged in the 1980s. Efficiencies that can be gained through “bridges” that enable the use of health care data for research to inform patient care have been documented; however, such bridging has been inadequate to date. Incentives are misaligned when EHR vendors maintain data in proprietary formats; when vendors increase revenues through customization of EHRs by practice/customer or by treating patient data as an asset rather than acting as a trusted guardian; or when users focus on the requirements for billing rather than patient care in their feature sets. Clinical research is also an inefficient process and may not focus adequately on the patient.

In her keynote presentation at the Research & Clinical Health Care Collaborative in April 2018, Dr. Janet Woodcock, director of FDA/CDER, proposed five “bridge features” for bridging research with health care: 1) the patient and treating physician should be at the center; 2) research should be integrated into the workflow of patient care; 3) data must be robust by intent, not by quality control (QC); 4) consent and randomization should be integrated into a digital environment; 5) there should be “rapid knowledge turns.” Increasingly rapid knowledge turns are the underlying basis for learning health systems (LHSs) and the focus of the Learning Health Community, which has published consensus-based Core Values of a Learning Health System that are now endorsed by many organizations and becoming globally appreciated.



This presentation will describe activities and projects that are being conducted through the Learning Health Community and Elligo Health Research to move the needle toward more efficient clinical research and more rapid learning health cycles to better bridge research and healthcare. These efforts will include a System of Accelerated Research (SOAR™), which integrates the aforementioned ‘bridge’ features, standards and eSource from the start with a patient-focused approach.

## ■ Key Slides

**ONCE LOST NOW FOUND**

**Learning Health and a System of Accelerated Research (SOAR™)**

4th Global ARO Network Meeting  
20 June 2019, Paris, France  
Rebecca D. Kush, PhD

The journey to find the 97 percent of lost physicians and patients.

ELLIGO Health Research

1

**Learning Health Systems**

The Learning Health System will improve the health of individuals and populations.

The LHS will accomplish this by generating information and knowledge from data captured and updated over time – as an ongoing and natural by-product of contributions by individuals, care delivery systems, public health programs, and clinical research – and sharing and disseminating what is learned in timely and actionable forms that directly enable individuals, clinicians, and public health entities to separately and collaboratively make informed health decisions.

www.learninghealth.org

2

**Core Values and the LHC**

**Core Values of the Learning Health System**

1) Person Focused	2) Privacy
3) Inclusiveness	4) Transparency
5) Accessibility	6) Adaptability
7) Governance	8) Leadership
9) Scientific Integrity	10) Value

Endorsements of the LHS Core Values

3

**Learning Health Cycle**

Information from health care (private, aggregated) to enable research

**HEALTH CARE**

- Quality health care
- Informed decisions
- Personalized medicine
- Patient safety and privacy
- Public health
- Improved therapies
- Efficiency/reduced costs

**RESEARCH**

- Discovery of new therapies
- Understanding diseases
- Testing/comparing therapies
- Assessing efficacy
- Monitoring safety
- Understanding responses (genomics, biomarkers)
- Public health/quality evaluations
- Post-marketing surveillance

**INEFFICIENT -17-YEAR CYCLE**

Research findings to inform health care decisions

4

**"Bridge" Features to Better Link Research and Healthcare**

- The patient and physician are at the center
- Quality and standards-based data are integrated from the start
- Workflow is centered on the patient and health care provider
- Informed consent is integrated and the process simplified
- Learning health cycles are more rapid

Adapted from April 2018 Bridging Collaborative Keynote by Dr. Janet Woodcock, FDA

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**The System of Accelerated Research (SOAR™)**

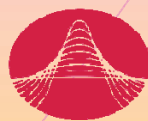
SOAR™ integrates 'bridge' features and transforms the research process

- Patient-centricity, retaining the patient-physician dyad
- Standards from the start, beginning with eSource at the research site
- Flexibility to follow site workflow for healthcare (and research)
- Electronic critical documents/master files, cloud-based
- Accelerates the cycle of learning from research
  - No re-entry of data (direct source) improves quality and speeds data flow
  - Real-time management information is a by-product of the system
  - CDISC CDASH and Protocol standards from the start enable rapid study set-up and enable SDTM generation with minimal mapping
  - Patients and physicians receive summary information
  - Enables transparency with appropriate security and privacy
  - Financial requirements are handled more rapidly
  - Complies with research and healthcare regulations

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大阪大学医学部附属病院  
Osaka University Hospital



**ARO Council**  
Academic Research Organization