4th Global ARO Network Workshop

Global Clinical Research: Integrating Quality from the Beginning

PROGRAM & ABSTRACTS

Date/Time	June 20th, 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

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

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

	Break		**9:55-10:10**

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

	Lunch Break		**12:30-13:30**

Opening Remarks

Norihiro Sato

Japan ARO Council / Hokkaido University

Memo

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.

Memo

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

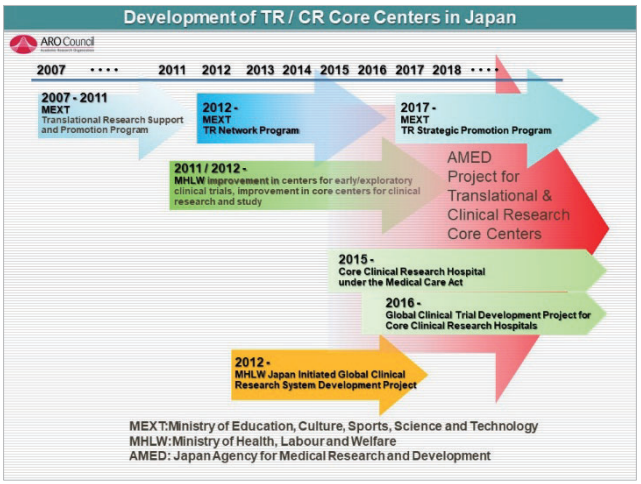
He graduated from Osaka University Medical School in 1986 and finished PhD course in 1993. He worked on musculoskeletal tumors, bone cell biology, bone substitute materials and bone tissue engineering at the Department of Orthopedics, Osaka University until 2006, and then he joined MTR and started to 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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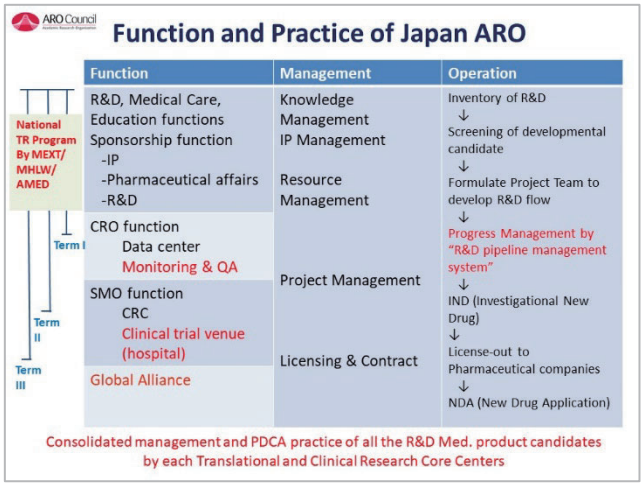

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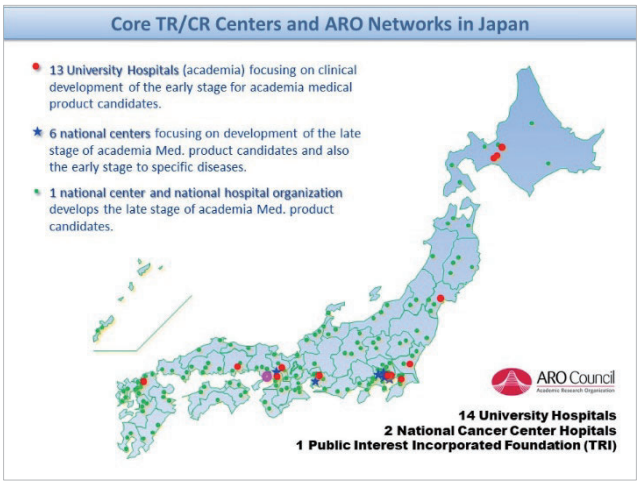

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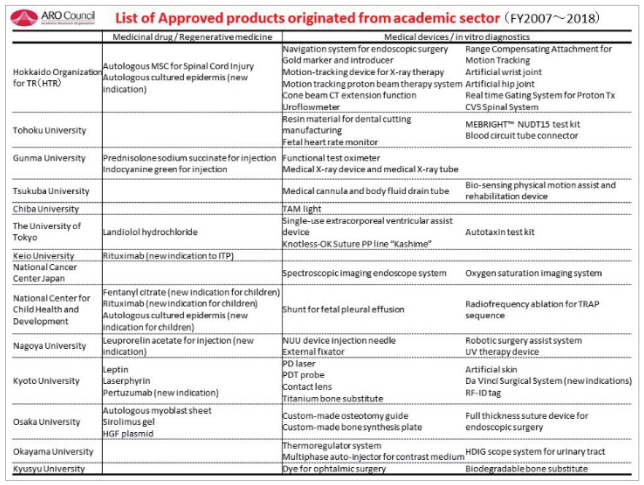

	Medicinal drug / Regenerative medicine	Medical devices / in vitro diagnostics	
Hokkaido Organization for TR(HTR)	Autologous MSC for Spinal Cord Injury Autologous cultured epidermis (new indication)	Navigation system for endoscopic surgery Gold marker and introducer Motion-tracking device for X-ray therapy Motion tracking proton beam therapy system Cone beam CT extension function Uroflowmeter	Range Compensating Attachment for Motion Tracking Artificial wrist joint Artificial hip joint Real time Gating System for Proton Tx CVS Spinal System
Tohoku University		Resin material for dental cutting manufacturing Fetal heart rate monitor	MEBRIGHT™ NUDT15 test kit Blood circuit tube connector
Gunma University	Prednisolone sodium succinate for injection Indocyanine green for injection	Functional test oximeter Medical X-ray device and medical X-ray tube	
Tsukuba University		Medical cannula and body fluid drain tube	Bio-sensing physical motion assist and rehabilitation device
Chiba University		TAM light	
The University of Tokyo	Landiolol hydrochloride	Single-use extracorporeal ventricular assist device Knotless-OK Suture PP line "Kashime"	Autotaxin test kit
Keio University	Rituximab (new indication to ITP)		
National Cancer Center Japan		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	Leuprorelin acetate for injection (new indication)	NUU device injection needle External fixator	Robotic surgery assist system UV therapy device
Kyoto University	Leptin Laserphyrin Pertuzumab (new indication)	PD laser PDT probe Contact lens Titanium bone substitute	Artificial skin Da Vinci Surgical System (new indications) RF-ID tag
Osaka University	Autologous myoblast sheet Sirolimus gel HGF plasmid	Custom-made osteotomy guide Custom-made bone synthesis plate	Full thickness suture device for endoscopic surgery
Okayama University		Thermoregulator system Multiphase auto-injector for contrast medium	HDIG scope system for urinary tract
Kyusyu University		Dye for ophtalmic surgery	Biodegradable bone substitute

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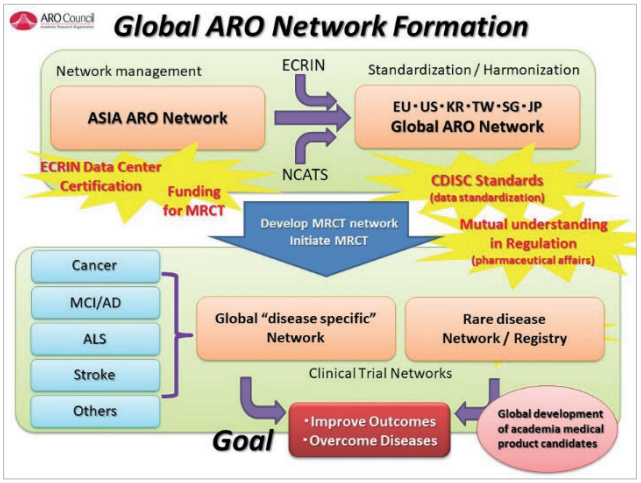

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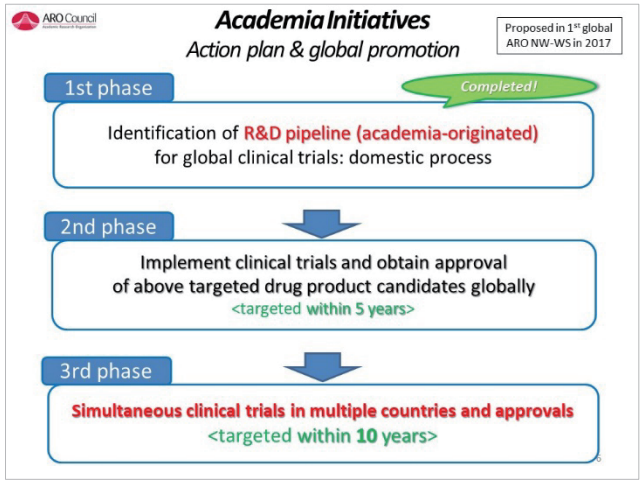

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Global Research Experience in a national Clinical Research Network

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

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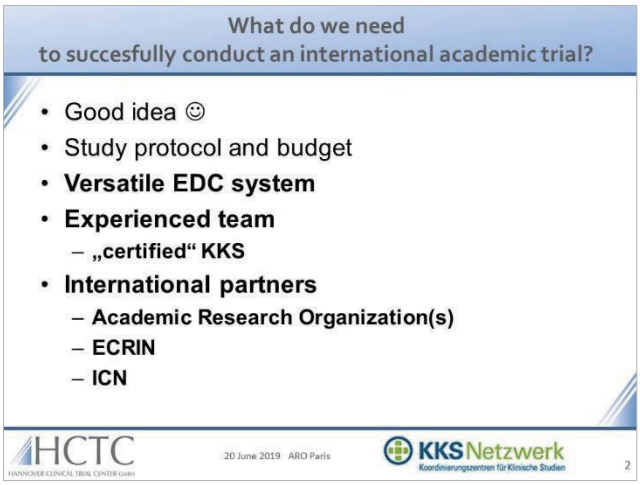

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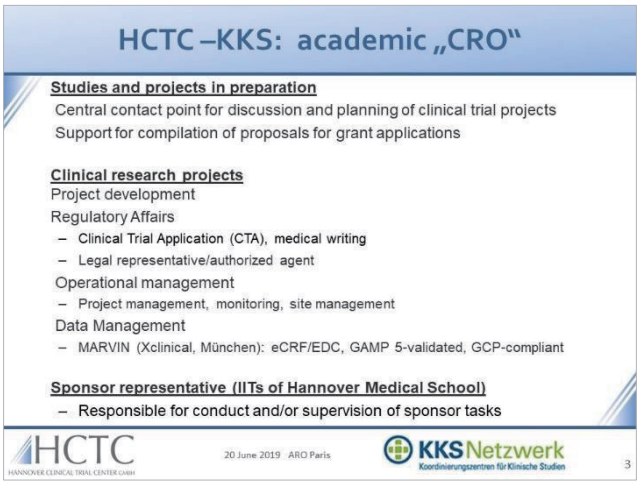

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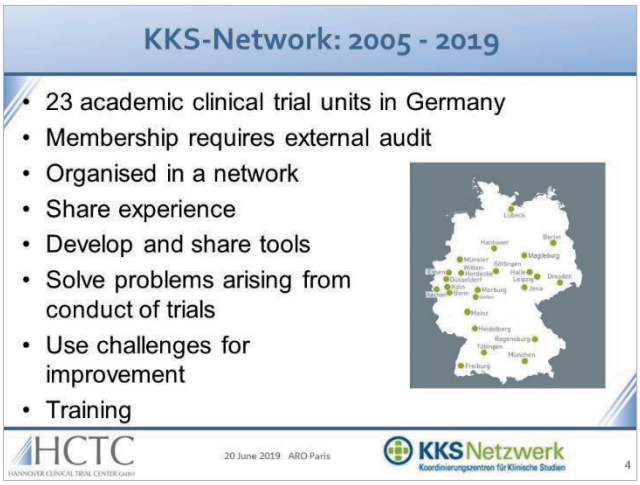

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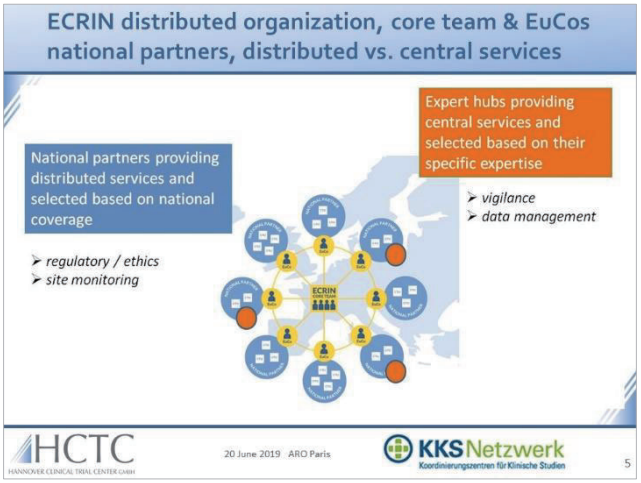

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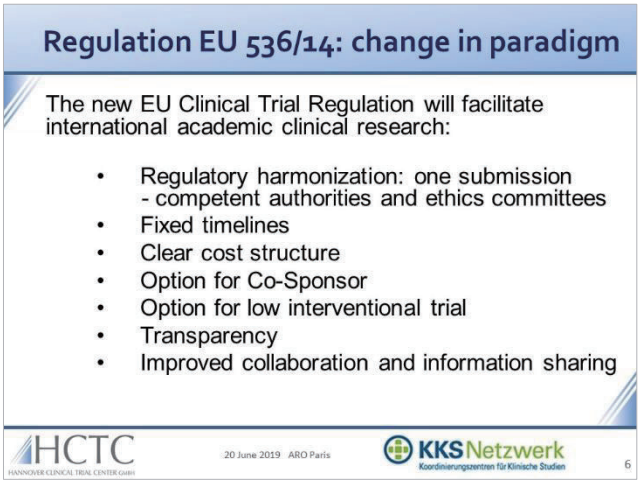

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Rare Cancer ReGISTry NETwork in Asia

Toshirou Nishida

National Cancer Center Hospital

Japan

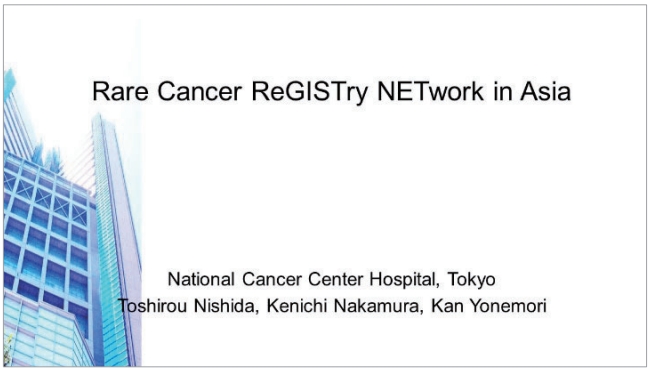
■Profile

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 pharmaceutic 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, pharmaceutic 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



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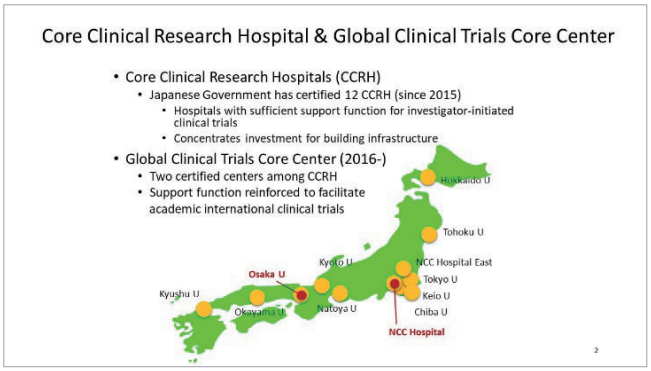

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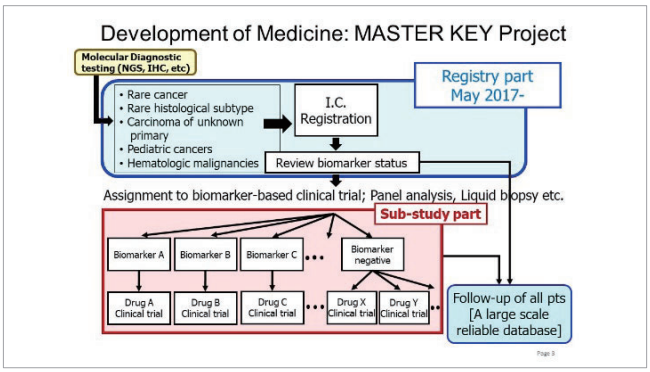

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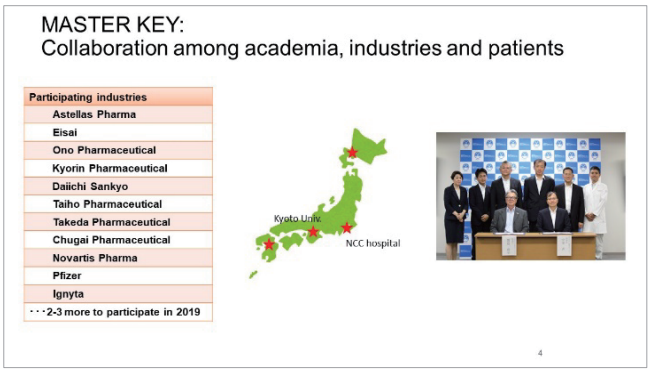

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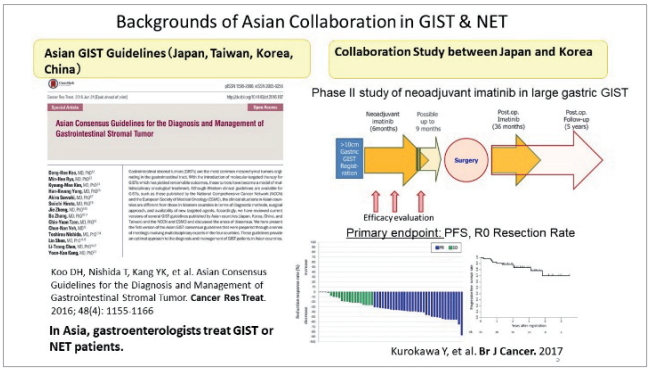

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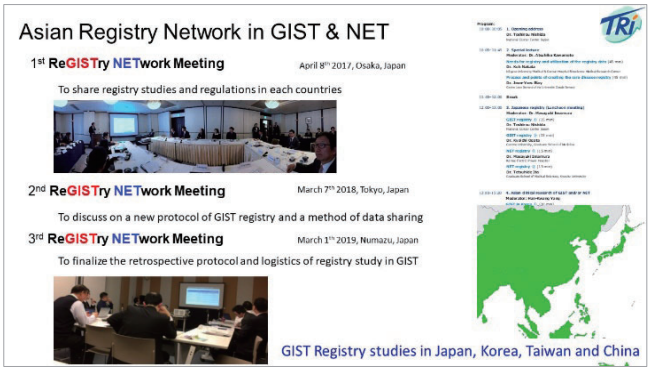

6

Wearables and Sensors in Clinical Trials

Samuel Volchenboum

The University of Chicago

United States of America

■Profile

Dr. Volchenboum 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

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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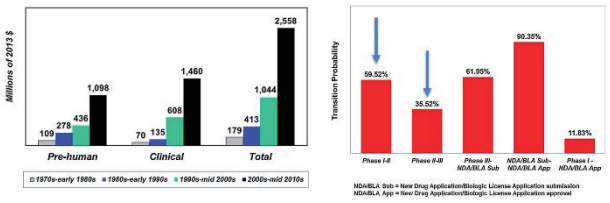
Bad data lead to waste in clinical trials



$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

2

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 Morton, David Blackman May 27, 2016, Applied Clinical Trials

3

Wearables and sensors for COAs

	Clinical outcomes assessments (COAs)			non-COA
mHealth data type	Patient/caregiver-reported outcome (PRO)	Clinician-reported outcome (ClinRO) (requires HCP)	Performance outcome (PerfO) (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? PSQI + sleep		Data mining to document fitness?	HR, steps, sleep

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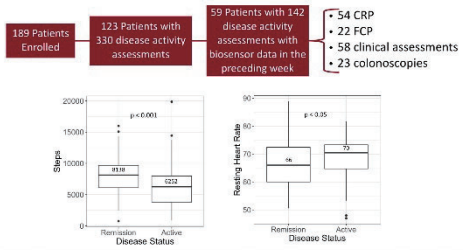
Cox S, Lane A, and Volchenboum SL. "Use of Wearable, Mobile, and Sensor Technology in Cancer Clinical Trials." JCO Clinical Cancer Informatics. June 2018.

4

University of Chicago IBD study



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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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6

Memo

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.

ECRIN EUROPEAN CLINICAL RESEARCH INFRASTRUCTURE NETWORK

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

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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 CDMAs - Design, Development and Validation (8)
DM03 CDMAs - 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)

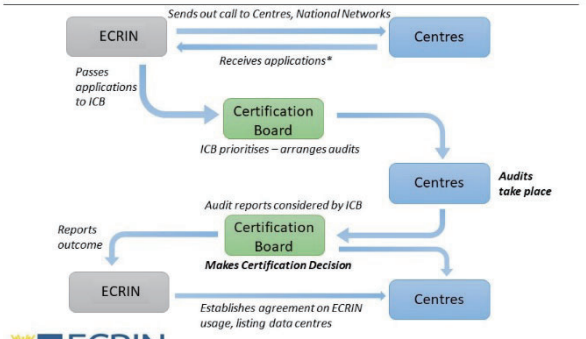
ECRIN EUROPEAN CLINICAL RESEARCH INFRASTRUCTURE NETWORK

*https://zenodo.org/record/1240941#.XOlhmJV7ncs

1

2

ECRIN data centre certification programme.
Procedure



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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

ECRIN EUROPEAN CLINICAL RESEARCH INFRASTRUCTURE NETWORK

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

ECRIN EUROPEAN CLINICAL RESEARCH INFRASTRUCTURE NETWORK

4

5

ECRIN data centre certification programme
Proposed approach for globalisation

ECRIN Europe	Initial supervision by ECRIN	Global CRIGH supervision
ECRIN standards	ECRIN standards Translation validation	ECRIN Standards
Auditors	Regional auditors trained by ECRIN, 1 joint audit	Autonomous regional auditors
ICB	1 Joint ICB assessment ECRIN and region	Autonomous regional boards supervised by global board
ICB Secretariat	Development of aligned ICB secretariat	Autonomous regional ICB secretariat
System development and maintenance	Development of aligned procedures and systems	Autonomous regional system development/maintenance

ECRIN EUROPEAN CLINICAL RESEARCH INFRASTRUCTURE NETWORK

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

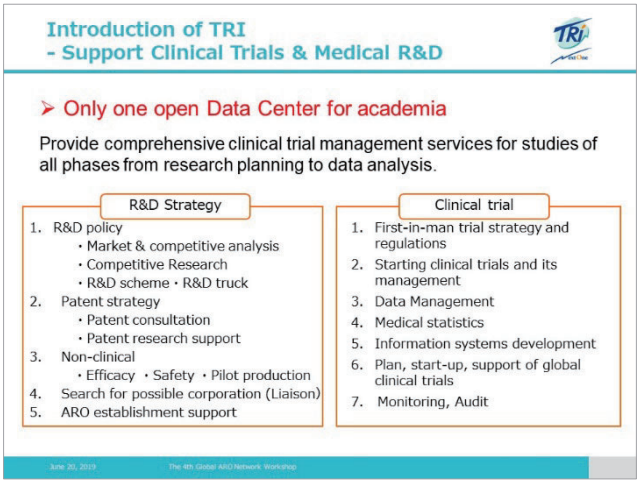
■Profile

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

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



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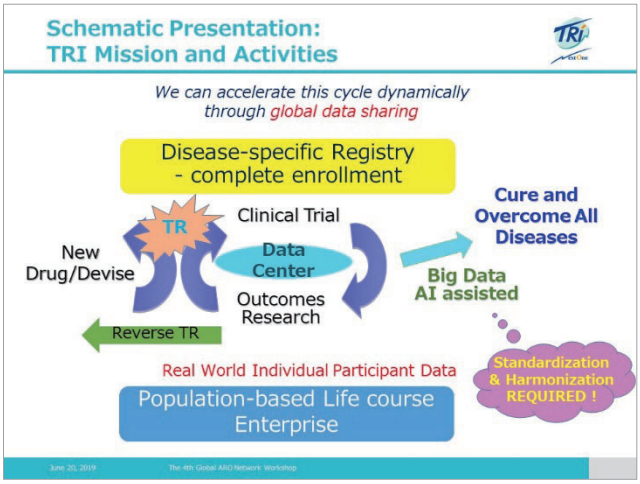

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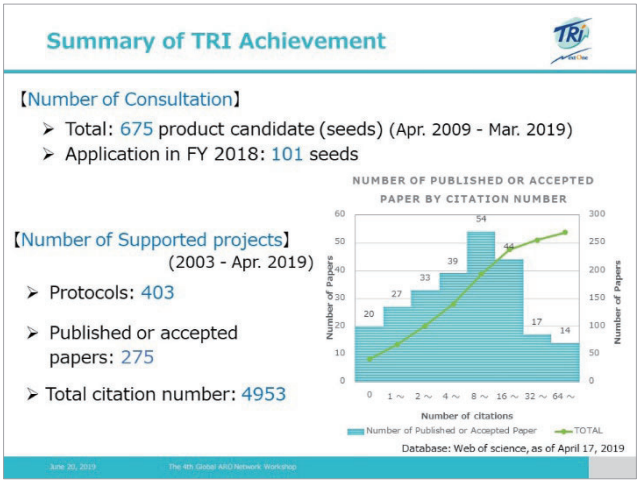

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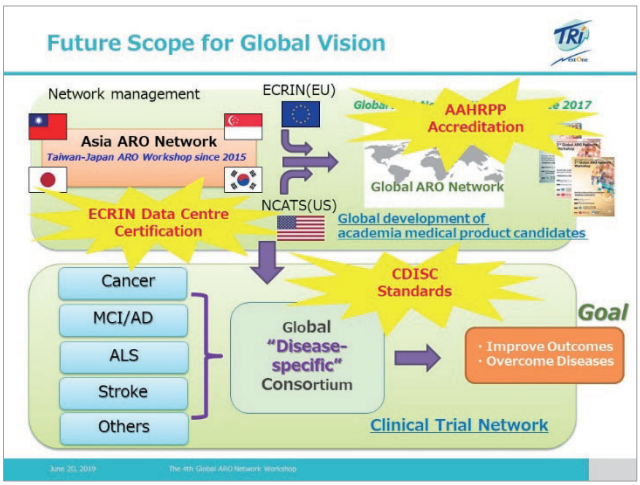


6

CDISC Standards Implementation in Japanese Academia

Masato Shiren

Osaka University

Japan

■Profile

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.

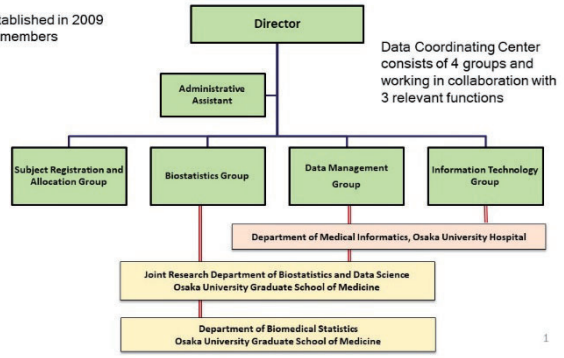
■Abstract

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

Introduction to Data Coordinating Center Osaka University Hospital

Established in 2009
15 members



Data Coordinating Center consists of 4 groups and working in collaboration with 3 relevant functions

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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

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

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

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

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

SNUH's Efforts to Improve the Quality of Data Management

SeungHwan Lee

Seoul National University Hospital

Korea

■Profile

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

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 mangers 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

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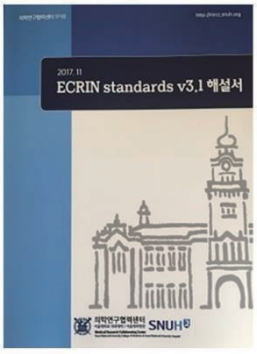
2

ECRIN data center certification

- Translation of ECRIN standards
  - Version 3.1 & Version 4



1. Introduction and Background

3

ECRIN data center certification

- Revision of SOPs
  1) Mapping of SOPs of MRCC and CTC to ECRIN standard
  2) Comparison
  3) Review real working process
  4) Revision of SOPs in accordance with ECRIN standard

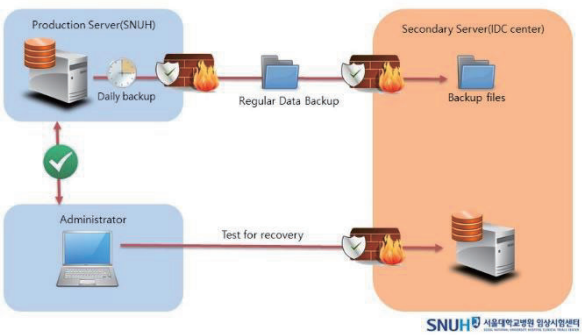
ECRIN standard v4.0	MRCC/CTC SOP
GE01 Centre Staff training and support	SNUH_MRCC/TRM.0010 Staff Training SNUH_MRCC/TRM.0030 New Staff Training : Data Manager
GE01.01: Policies for training:	MRCC TRM0010 Staff Training MRCC TRM0030 New Staff Training : Data Manager MRCC TRM0040 Education of SOPs
GE01.02: 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/CON.0010 Study Coordination

SNUH 서울대학교병원 임상시험센터

4

ECRIN data center certification

- Upgrade infrastructure
  - Build secondary server outside of hospital



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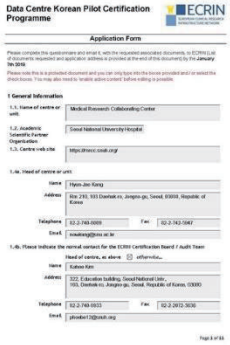
ECRIN data center certification

- Applied for ECRIN data center certification in January 2019


Data Centre Korean Pilot Certification Programme

Application Form


Data Centre Korean Pilot Certification Programme

Application Form

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

Taiwan Clinical Trial Consortium

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

Ueng-Cheng Yang

National Yang-Ming University, Taiwan. cims@ym.edu.tw

The 4th global ARO workshop, June 20, 2019

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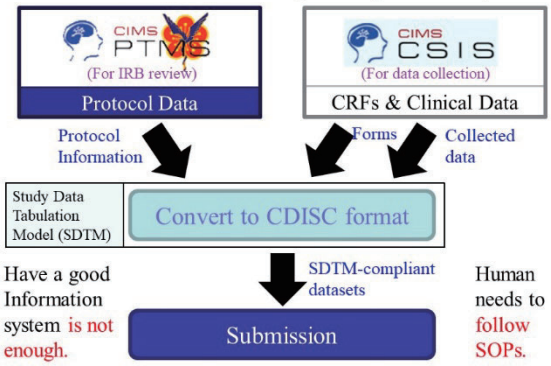
Merging protocol data and trial data for the submission to the regulatory authority



Have a good Information system is not enough.

Human needs to follow SOPs.

2

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

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

4

Preparation for the ECRIN certification

Gap analysis
↓
Operations and process mapping
↓
Document revision
↓
Implement workflow using BPM

→ **Typical design of a document system**

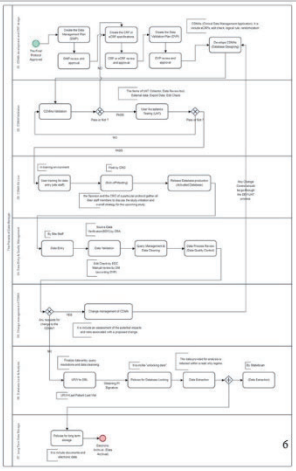
Level 1: policy
Level 2: process
Level 3: procedure
Level 4: forms

5

5

High level processes of a trial

1. CDMA development and CRF design
2. CDMA validation
3. CDMA go live
4. Data entry and quality management
5. Change management of CDMA
6. Database lock and analysis
7. Long term data storage



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6

Standards for Academic Research

Xuanhui Ng

Singapore Clinical Research Institute (SCRI)

Singapore

■Profile

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

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 improve efficiencies and benefit patients and our society.

■Key Slides

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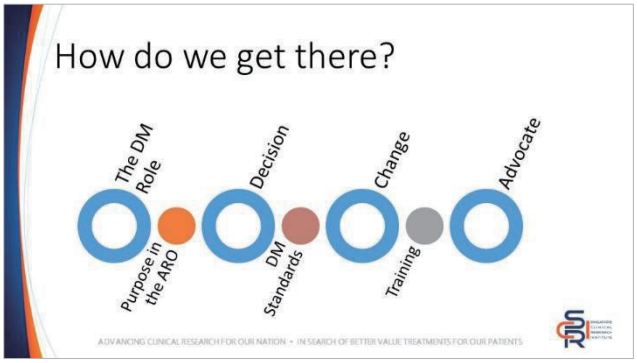

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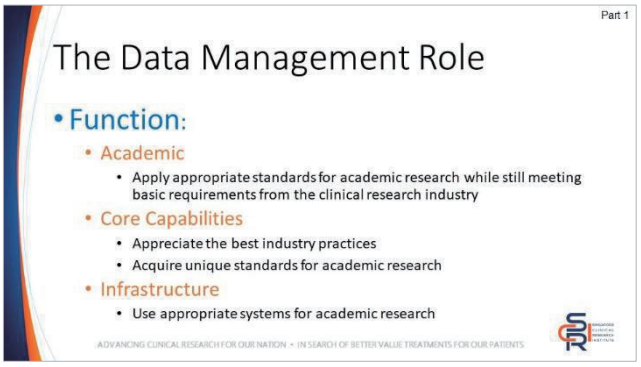

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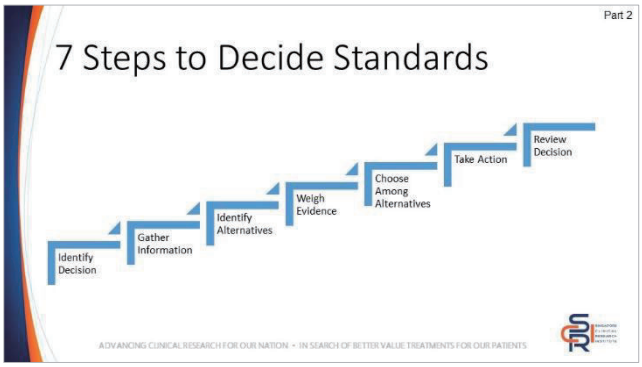

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Standards and Data Strategies for Global Regulated Research, from Protocol through Analysis

Michael Kurilla

National Center for Advancing Translational Sciences, National Institutes of Health

United States of America

■Profile

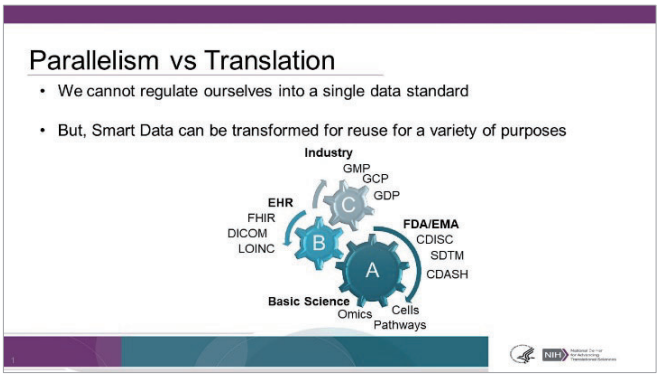
Michael Kurilla is the director of the Division of Clinical Innovation at NCATS. In this capacity, he oversees the Clinical and Translational Science Awards (CTSA) Program, which supports innovative solutions to advance the efficiency, quality and impact of translational science, with the ultimate goal 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

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



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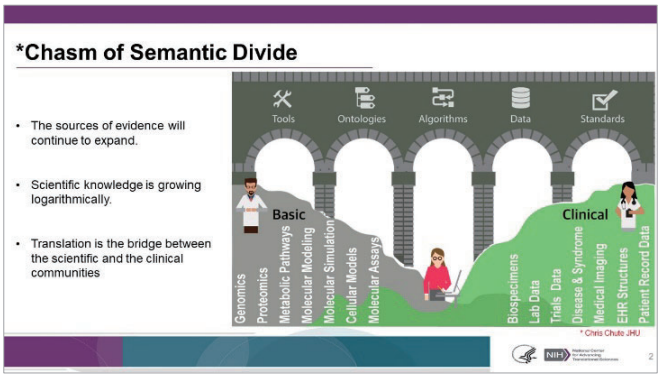

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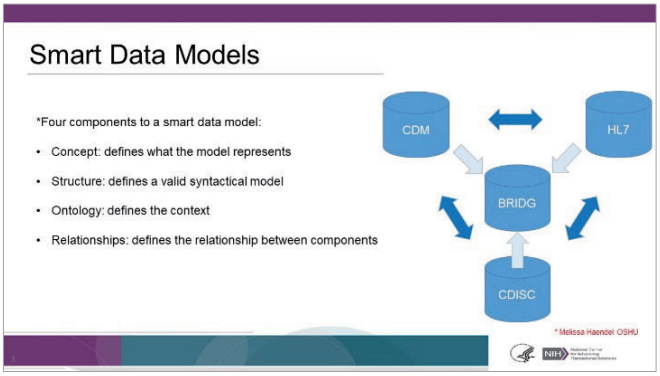

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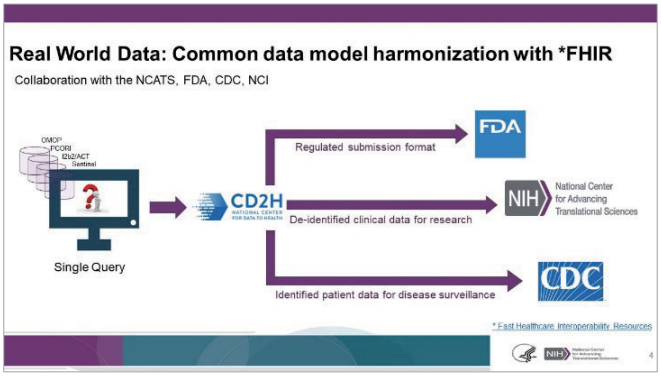

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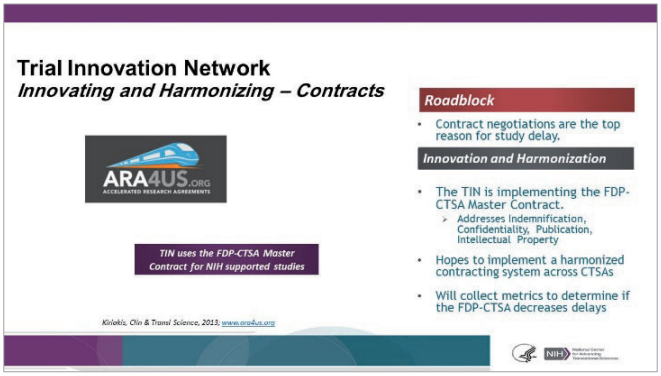

6

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

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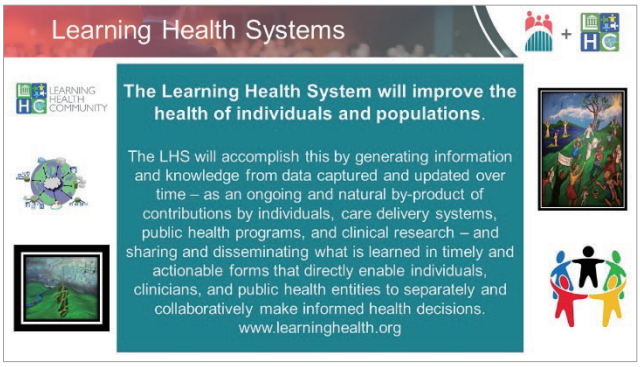

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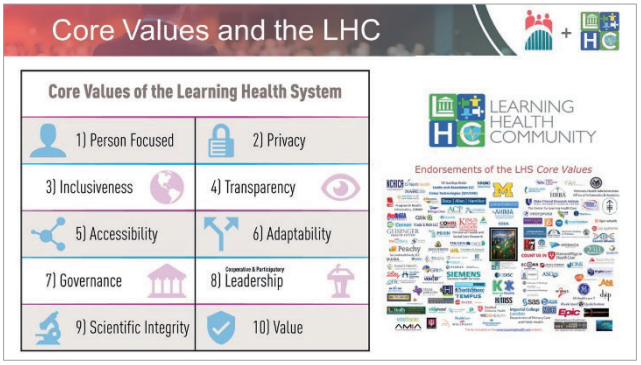

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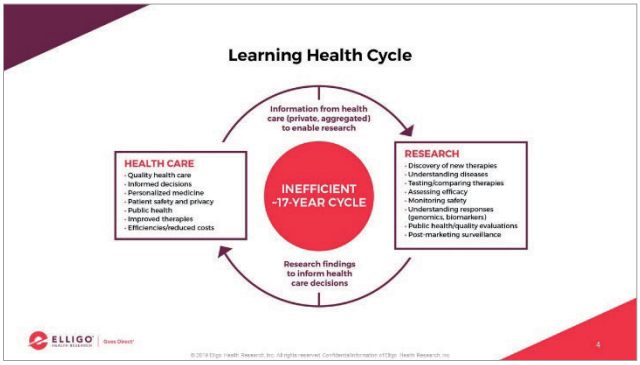

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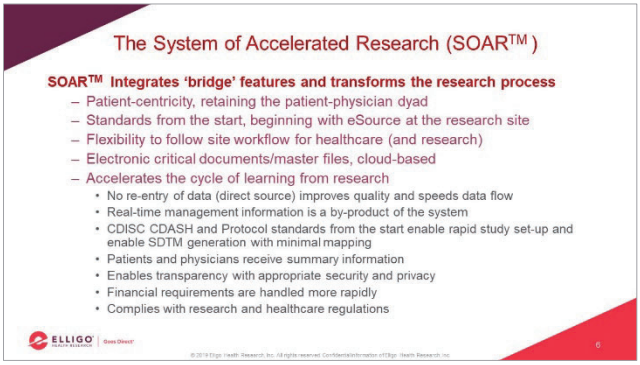

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