National Center for Global Health and Medicine
Center for Clinical Sciences
Department of International Trials

Comprehensive and collaborative training on medical innovations adapted to challenges of clinical trials in Asian and African countries [2nd edition]

January 18-31, 2020

A 14 day training on conducting multi-regional clinical research was held in order to provide some guidance to health professionals from five countries, with the ambitious goal of providing new medical treatment to patients with emerging and re-emerging infectious diseases, rare diseases, and intractable diseases around the world.

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[2nd edition]

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日本とアジア・アフリカ諸国での国際共同臨床試験（Multi-regional Clinical Trial（MRCT））の実施にむけて、信頼のおける安定したネットワークを構築することは NCGM 臨床研究センターインターナショナルトライアル部とアジア・アフリカ各国の連携施設の協力において非常に重要な位置づけとなっています。

MRCT を国際的な基準や手順に従って実施するための、専門家の能力向上に寄与するこのプログラムは、MRCT による新しい薬剤や医療機器の開発を通じて国際的な医療環境の改善に貢献する、という当部署の目的を成し得るための大きな柱の一つといえます。

2018 年度と同様に、コンゴ民主共和国、インドネシア、フィリピン、タイ、ベトナムの 5 カ国より研修生を迎えると共に、今年度は日本の機関からも研修生をお迎えすることができました。昨年度は 10 施設より研修生にお越しいただいた一方で、今年度は 14 の連携施設から当プログラムにご参加いただいたことに感謝いたします。

14 日間のプログラムにおいて研修生は、規制当局（独立行政法人 医薬品医療機器総合機構（PMDA））、民間企業（シオノギ製薬株式会社）、国際協力機構（JICA）、教育機関（大阪大学）、日本 ACRP（Association of Clinical Research Professionals Japan Chapter）、ナショナルセンターバイオバンクネットワーク（NCBN）、臨床施設（国立がん研究センター（NCC）、国立国際医療研究センター（NCGM））で講義や施設の視察を中心としたプログラムに参加しました。講師の皆様、5 カ国から 2-3 人 / 国の研修生と日本人研修生を合わせた 14 人の研修生、DIT のスタッフ含め、活発に意見交換をすることができたことも、本プログラムで成し得たことの一つです。

今回のプログラムを成功に導いてくださった皆様に感謝するとともに、この活動が今後も継続し、発展しながら各連携国との協業につながるものと期待いたします。

2020 年 3 月 10 日
国立国際医療研究センター
国立国際医療研究センター病院長
杉山　温人

謝辞

薬剤の開発プロセスが複雑化する中において、研究参加者の安全性と権利を確保した上で質の良いデータを得ることは必須要件であり、効果的かつ専門的な研修を受け、十分な能力を有する臨床研究の専門家は質の高い臨床研究の実施において非常に重要な役割を果たします。

国際的な医療状況を改善するべく、連携各国と協力しながら国際共同臨床試験を推進するにあたり、継続性は重要な意味を持っています。NCGM 臨床研究センターインターナショナルトライアル部は、第 2 回目の “A program focused on comprehensive and collaborative training on medical innovations adapted to challenges of clinical trials in Asian and African countries” を 2019 年度のプログラムとして実施いたしました。

本プログラムではコンゴ民主共和国、インドネシア、フィリピン、タイ、ベトナムの連携 5 カ国に加え日本からも研修生を迎え、14 日間に渡り講義・施設への視察を実施しました。プログラムの最終的な目的は、新興・再興感染症、希少疾患、非感染性疾患、難治性疾患等で苦しむ世界中の患者さんに新しい薬剤や診断機器を届けることです。

本事業の実現は、日本及び各連携国の関係者の皆様の多大なるご協力・ご尽力の賜物です。プログラム参加研修生に講義見学の機会を与えてくださいました PMDA の皆様にも感謝を申し上げます。

また、お忙しい中、ご講義や施設見学の機会をご提供くださいました以下の機関・ご担当者の方々に御礼を申し上げます。

【ご協力いただいた機関・法人】

国立がん研究センター中央病院 / シオノギ製薬株式会社 / 大阪大学医学部附属病院 /
独立行政法人 国際協力機構 / 独立行政法人 医薬品医療機器総合機構 / 日本 ACRP /
ナショナルセンターバイオバンクネットワーク

「団結は力なり」という言葉の通り、このプログラムを共に作り上げてくださった NCGM の皆様、とりわけ国際医療協力局、国際感染症センター、熱帯医学・マラリア研究部、データサイエンス部、バイオバンクの皆様、誠にありがとうございました。

最後に、連携各国より研修生をご推薦くださった機関の皆さまに感謝申し上げます。非常に熱心な研修生をお迎えし、このプログラムを成功裏に終了することができましたのも、皆様のご助力なしには実現しえなかったことと確信しております。

【各国における連携施設】（国名のアルファベット順）

- The Democratic Republic of the Congo: University of Kinshasa, Institut National de Recherche Biomédicale
- Indonesia: University of Indonesia, Sulianti Saroso Infectious Diseases Hospital, Mochtar Riady Research Institute
- The Philippines: University of the Philippines, St. Luke's Medical Center, San Lazaro Hospital
- Thailand: Faculty of Tropical Medicine and Siriraj Hospital in Mahidol University, Prince of Songkla University
- Vietnam: Cho Ray Hospital, Bach Mai Hospital

2020 年 3 月 10 日
国立国際医療研究センター
臨床研究センター
インターナショナルトライアル部長
飯山　達雄

略語一覧

ACR	Academic Clinical Research Center of Osaka University Hospital 大阪大学医学部附属病院 未来医療開発部　臨床研究センター
ACRP	Association of Clinical Research Professionals エイ・シー・アール・ピー（ACRP）
ASEAN	Association of Southeast Asian Nations 東南アジア諸国連合
ATC	Asia Training Center アジア医薬品・医療機器 トレーニングセンター
BIHC	Bureau of International Health Cooperation 国際医療協力局
CCS	Center for Clinical Sciences 臨床研究センター
COVID-19	Coronavirus Disease 2019 新型コロナウイルス感染症 （COVID-19）
CPF	Cell Processing Facility 細胞調整施設
CRC	Clinical Research Coordinator 治験コーディネーター
DCC	Disease Control and Prevention Center 国際感染症センター
DIT	Department of International Trials インターナショナル トライアル部
DRC	Democratic Republic of the Congo コンゴ民主共和国
FY	Fiscal Year 会計年度

GCP	Good Clinical Practice 医薬品の臨床試験の実施の基準
ICH	The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use 医薬品規制調和国際会議
INRB	Institut National de Recherche Biomédicale コンゴ民主共和国にある 国立生物医学研究所
IPS	Induced Pluripotent Stem Cells（iPS Cells） 人工多能性幹細胞（iPS 細胞）
IRB	Institutional Review Board 治験審査委員会
IVR	Interventional Radiology インターベンショナル・ラジオロジー （画像下治療）
JICA	Japan International Cooperation Agency 独立行政法人 国際協力機構
JTF	Joint Task Force 共同タスクフォース
MRCT	Multi-Regional Clinical Trials 国際共同臨床試験
MTR	Medical Center for Translational Research, Osaka University Hospital 大阪大学医学部附属病院 未来医療開発部　未来医療センター
NCBN	National Center Biobank Network ナショナルセンター・バイオバンク ネットワーク
NCC	National Cancer Center Japan 国立研究開発法人 国立がん研究センター
NCGM	National Center for Global Health and Medicine 国立研究開発法人 国立国際医療研究センター
PMDA	Pharmaceuticals and Medical Devices Agency 独立行政法人 医薬品医療機器総合機構
PV	Pharmacovigilance 医薬品安全性監視

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1. はじめに

1.1 研修概要

“A program focused on comprehensive and collaborative training on medical innovations adapted to challenges of clinical trials in Asian and African countries, 2nd edition" は国際共同臨床試験（Multi-regional Clinical Trials（MRCT））の実施にむけて信頼のおける強固なネットワークを構築するため NCGM 臨床研究センターインターナショナルトライアル部が実施した、連携 5 カ国と日本の臨床試験専門家を育成する 14 日間の研修プログラムです。

本年は、コンゴ民主共和国（2 名）、インドネシア（3 名）、フィリピン（3 名）、タイ（3 名）、ベトナム（2 名）の 5 カ国に加えて日本国内の施設からも研修生（1 名）をお迎えすることができました。本プログラムでは、独立行政法人医薬品医療機器総合機構アジアトレーニングセンターが実施する国際共同治験セミナー 2020 を見学する機会を頂き、国際共同治験によって得られたデータに対する調和のとれた審査について規制当局の基本的な考え方を知ることができました。革新的な研究や医療技術の現状を知るため、臨床施設（国立がん研究センター（NCC)、国立国際医療研究センター（NCGM))、教育機関（大阪大学)、民間企業（シオノギ製薬株式会社）で講義や施設の見学視察を中心としたプログラムに参加しました。

国際協力機構（JICA）からは日本の医療協力とプロジェクトの予算配分などについて、臨床試験専門家のための団体である日本 ACRP からは組織の役割とその重要性について講義をして頂きました。本プログラムでは、ASEAN 諸国やアフリカにおける医薬品・医療機器の開発の際の課題や提言をテーマとした公開プレゼンテーションセッションも計画していました。NCGM 内部からの参加者に加え、外部からも 40 名を超える参加登録がありましたが、COVID-19 の流行状況を鑑みて中止となりました。

プレゼンテーション資料は参加登録くださった皆様にお送りするとともに、DIT のホームページにて公開いたします。

1.2 研修の目的

本研修の目的は以下の通りです。

- 日本とパートナー国との間で世界標準の MRCT を実施するためのグローバルな臨床試験ネットワークを確立する
- 臨床試験を設計および実施できる専門家を育成する

1.3 研修生の背景

ASEAN4 カ国、アフリカ 1 カ国、日本、の計 14 施設より医師・薬剤師であり臨床研究の経験のある方々が参加されました。研修生のプロフィールを**表 1** に示しています。

表１　研修生プロフィール

The Democratic Republic of the Congo	
	**Nsengi Yumva Pierre-Michel Ntamabyaliro** [Current position] Study site coordinator, Co-Principal Investigator INRB Lecturer at University of Kinshasa, Pharmacovigilance Unit [Degree(s)] MD, MSc Specialty: Pharmacovigilance and Pharmacoepidemiology
	**Mata Junior Mboloko** [Current position] Lecturer at University of Kinshasa, Consultant at Department of Obstetrics and Gynecology University of Kinshasa [Degree(s)] MD, MSc Specialty: Obstetrics and Gynecology
Vietnam	
	**Thi Hong Linh Le** [Current position] Consultant at Center for Tropical Diseases, Bach Mai Hospital [Degree(s)] MD,MSc Specialty: Infectious and Tropical Diseases
	**Ngo Van Cong** [Current position] Consultant at Department of Otorhinolaryngology- Head and Neck Surgery, Cho Ray Hospital [Degree(s)] MD, PhD Specialty: Otorhinolaryngology
Indonesia	
	**Maria Lawrensia Tampubolon** [Current position] Consultant at RSPI Prof. Sulianti Saroso Hospital External Research Coordinator in Research Unit RSPI Prof. Sulianti Saroso Hospital [Degree(s)] MD, Specialty: Neurology

Indonesia

Melva Louisa Simbolon

[Current position]
Research coordinator, Department of Pharmacology and Therapeutics,
Secretary for Doctoral Program in Biomedical Sciences, Faculty of Medicine
University of Indonesia

[Degree(s)]
Pharmacist, MSc, PhD
Specialty: Pharmacology

Dina Nilasari

[Current position]
Staff and lecturer, Department of Internal Medicine Hasanuddin University Teaching Hospital
Mochtar Riady Institute
Consultant at Outpatient Clinic Nephrology-Hypertension Unit, Wahidin Sudirohusodo and Hasanuddin University Hospital

[Degree(s)]
MD, PhD
Specialty: Internal Medicine, Nephrology

Philippines

Maria Elizabeth Panlaqui Mercado

[Current position]
Lead faculty for Biostatistics and Instructor of Clinical Epidemiology, University of Santo Tomas Faculty of Medicine
University of the Philippines

[Degree(s)]
MD, Masters in Advance Study (MAS)
Specialty: Clinical Research

Gelza Mae Almario Zabat

[Current position]
Consultant at St. Luke's Medical Center
St. Luke's Medical Center
[Degree(s)]
MD
Specialty: Internal Medicine - Infectious Diseases

Jay Ron Olegario Padua

[Current position]
Consultant at San Lazaro Hospital

[Degree(s)]
MD
Specialty: Pediatric Infectious Diseases

Thailand

Weerawat Kiddee

[Current position]
Associate Professor of Ophthalmology, Glaucoma Unit
Deputy Head of Department for Research, Department of Ophthalmology
Faculty of Medicine, Prince of Songkla University

[Degree(s)]
MD
Specialty: Ophthalmology

Noppadon Tangpukdee

[Current position]
Associate Professor Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University

[Degree(s)]
B.N.S. (Nursing and Midwifery)
MSc (Medical Toxicology)
Diploma (Medical Microbiology)
PhD (Tropical Medicine)

Suvimol Niyomnaitham

[Current position]
Consultant Siriraj Clinical Research Center (SiCRC)
Lecturer and researcher at Department of Pharmacology
Principal Investigator in clinical trials and bioequivalence studies
Faculty of Medicine, Siriraj Hospital, Mahidol University

[Degree(s)]
MD
MSc (Clinical Epidemiology and Biostatistics)
PhD (Pharmacoepidemiology)
Diploma on Research and Development of products to meet Public Health Needs

Japan

Chisa Tabata

[Current position]
Associate Professor Center for Global Health, Department of Medical Innovation, Osaka University Hospital

[Degree(s)]
MD, PhD
Specialty: Obstetrics and Gynecology, Medical Genetics

2.　NCGM 内のプログラム

2.1　臨床研究センター　インターナショナルトライアル部（DIT）

2.1.1　DIT の概要

昨年開催の初回プログラムの際と同様に、国際共同臨床試験のプラットフォーム構築・強化するために実施中のプロジェクトを中心に紹介がありました。国際感染症フォーラムの開催等で産官学の情報交換・連携体制を促進し、国際的な医療課題を解決するような共同開発プロジェクトを生み出す取り組みとともに、新興国で国際基準や各国規制を遵守して円滑に国際共同臨床試験を実施する際の DIT の役割の重要性が伝えられました。

アジア・アフリカ各国における臨床試験専門家の能力強化のための継続的なトレーニングプログラム運営は DIT の活動の内の大きな柱の一つであり、重要なものと位置づけられていることについても説明がありました。加えて、実施中の臨床試験についても紹介されました。

図 1a: インターナショナルトライアル部の紹介

図 1b: 日本の暮らし紹介

図 1c: インターナショナルトライアル部のネットワーク

図 1d: 日本でのごみの処理方法

2.1.2　臨床試験のコンピテンシー

臨床試験のコンピテンシー（専門的能力）のための共同タスクフォース（JTF）は、臨床研究に関わる全ての専門家のコンピテンシーを定義し、その基準を一つの枠組みとして取りまとめた「臨床研究専門職のための調和のとれたコアコンピテンシーの枠組み」を 2014 年に発表し、2018 年に改訂しました。改訂版では 47 のコンピテンシーを 8 つの領域に分類して枠組み化し、それぞれのコンピテンシーにおいて基礎、中級、上級それぞれのレベルを定義しています。8

つの領域は、1. 科学的概念と研究デザイン、2. 倫理面および被験者の安全への配慮、3. 治験薬の開発および規制、4. 臨床試験の実施（Good Clinical Practice: GCP）、5. 試験および施設の管理、6. データマネジメントとインフォマティクス（情報科学）、7. リーダーシップと専門性、8. コミュニケーションとチームワーク、から構成されています。DIT の講師が、この枠組みの主な内容を紹介し、なぜ臨床研究の領域においてこのような枠組みが重要となるのか説明しました。中でも、主に領域 1, 2, 4, 5, 6 についてディスカッションを行い、例えば重篤な有害事象 / 有害事象の報告や被験者負担軽減費などについて各国間での現状を共有し比較をするなど、研修生の様々な経験に基づいた意見交換をすることができました。

研修生の多くは、原理原則を遵守しながら、複雑なデザインの試験や被験者個別の状況にどのように対応していくかということに難しさを感じていることがわかりました。このようなディスカッションを続けること自体が、研究の効率的なデザインと適切な実施に向けて重要であると考えられます。

■ JOINT TASK FORCE FOR CLINICAL TRIAL COMPETENCY: https://mrctcenter.org/clinical-trial-competency/

Dr. Noppadon Tangpukdee, Faculty of Tropical Medicine, Mahidol University, Thailand からのコメント：

“臨床試験に携わるにあたり核となる専門的能力を深めるため、考え方やその能力を身に付けるための方法について学びました。互いの経験を共有し、共に理解を深め、そして講師からはとても有益なコメントをもらうことが出来ました。”

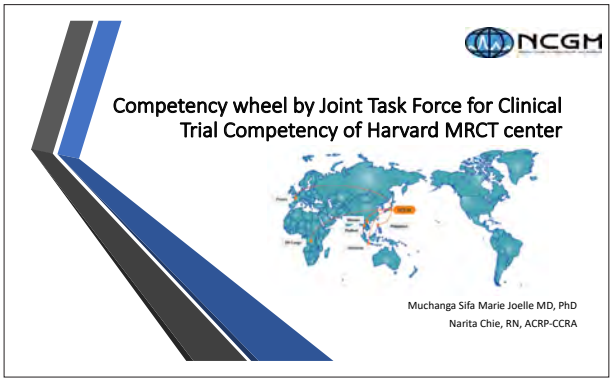

図 2a: 臨床試験のコンピテンシー紹介

図 2b: 臨床試験のコンピテンシーディスカッション

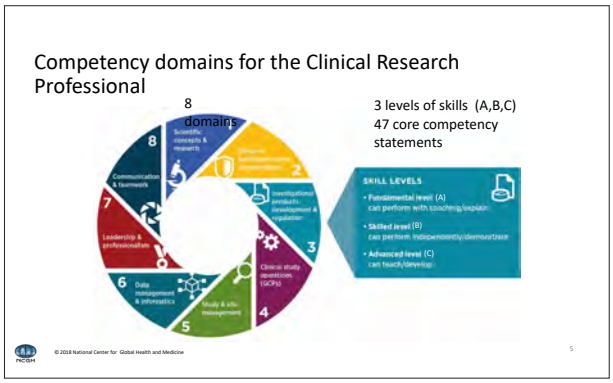

図 2c: 臨床試験のコンピテンシー領域

2.2 国際医療協力局（BIHC）

NCGM は BIHC を通して、40 年を超える国際協力の歴史を築き、技術協力事業から政策提言まで、幅広く活動を行っています。

技術協力事業の主なものとしては人材育成（看護師やその他の医療従事者への教育、医療技術移転）、病院マネジメント、などが挙げられます。このような事業は様々な医療問題の解決や医療ニーズの充足に寄与します。

加えて、BIHC は政策の策定に際して助言を行うため、様々な国に職員を派遣してきました。

図 3a: 国際医療協力局の活動の紹介

また、コンゴ民主共和国におけるエボラウィルス病の流行において検疫所での管理体制をサポートするために日本の医師を派遣するなど、疾病の流行地域に専門家を派遣する国際的な対応としての活動にも参加している事が紹介されました。

図 3b: 国際医療協力局担当者と集合写真

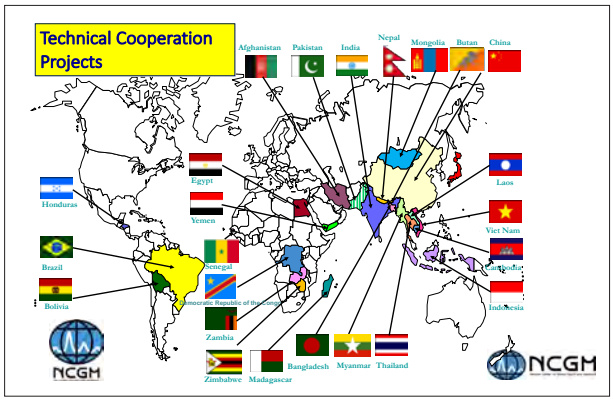

図 3c: NCGM のネットワーク

2.3 研究所 熱帯医学・マラリア研究部

NCGM 研究所熱帯医学・マラリア研究部は、マラリア学を中心とする熱帯医学の研究成果をもって、グローバルヘルスに貢献することを所掌としています。

講義では、さまざまな活動や国際保健協力ネットワークが紹介され、具体例としては、ラオスパスツール研究所やマヒドン大学との協力関係などが挙げられました。

特に、無症候性マラリアの検出のための複数の診断機器に関する研究はマヒドン大学との協力関係を基礎とし、DIT も参加して実施されています。DIT の担当スタッフからも、本研究における DIT の役割と機能についての説明がありました。

図 4a: 熱帯医学・マラリア研究部の活動紹介

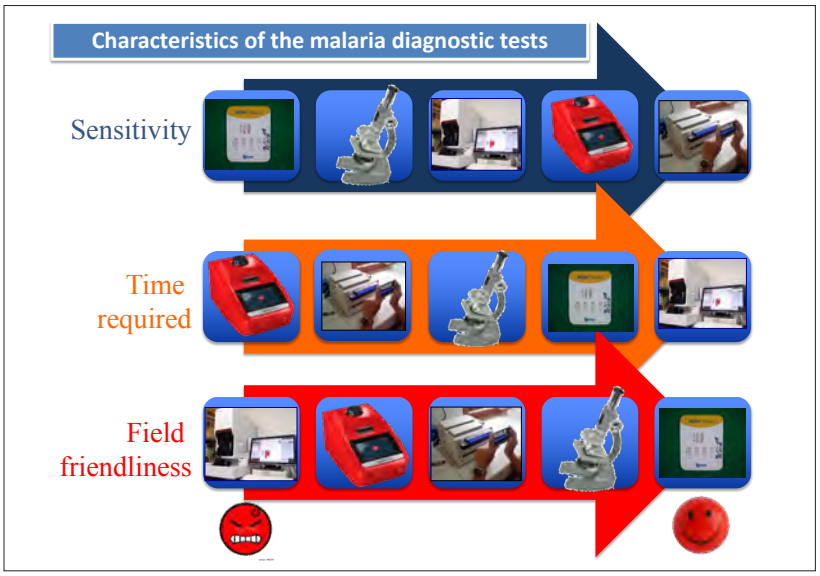

図 4b: マラリア診断法の紹介

2.4 臨床試験実施施設の経験について：マヒドン大学 熱帯医学部

試験の実施においては、最低限の実施要件を満たしながら、安全性と有効性を適切に評価することが重要である一方で、それぞれの施設や試験によって、状況は様々です。臨床試験の専門家は倫理面や規制面から試験固有、依頼者特有のものまで、様々な要件を満たした上で試験を実施する必要があり、その過程においては多くの課題に直面することとなります。

タイから参加した研修生に講師となって頂き、試験実施施設としてのマヒドン大学の紹介の後、課題に直面した経験などを共有して頂きました。試験責任医師としての経験に基づき、プロトコルの作成から試験結果の論文発表まで、責任医師としての役割について述べて頂き、研修生同士のディスカッションを実施しました。

Dr. Maria Lawrensia Tampubolon, Sulianti Saroso Infectious Diseases Hospital, Indonesia からのコメント：

“マラリア撲滅には、その診断、そして治療、という課題が存在します。それぞれの国が持つ資源を活用して共に前進、協調していくことがとても大切です。”

図 5a: マヒドン大学による試験責任医師の役割紹介

図 5b: インターナショナルトライアル部によるタイのプロジェクト紹介

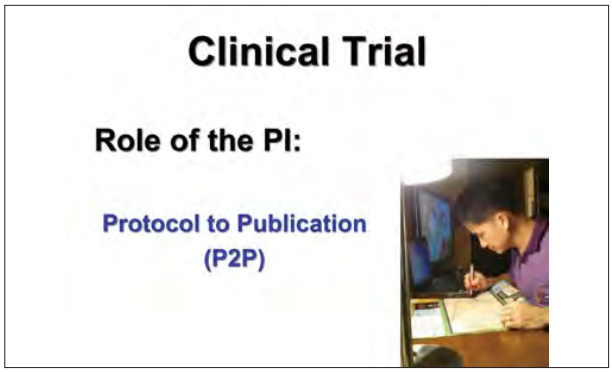

図 5c: 試験責任医師とは

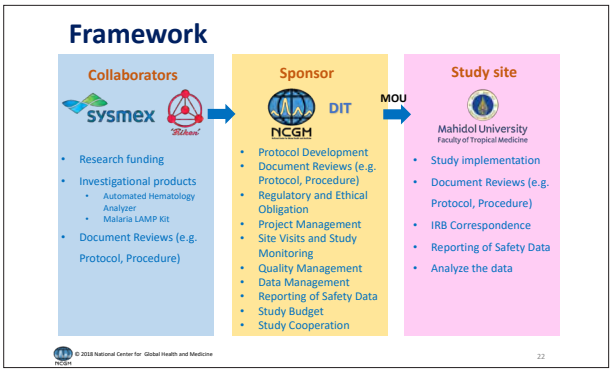

図 5d: NCGM のタイにおけるプロジェクトの枠組み

2.5　国際感染症センター（DCC）

DCC では講義と施設の見学が実施されました。中国での COVID-19 の流行を鑑み、DCC の活動の中でも特に感染症に関する日本の規制や緊急対応の枠組みに焦点を当て、講義が行われました。DCC は、高度な隔離病室や職員への研修、緊急対応チームの構築、初期対応の手順の標準化などについて、経験に基づいた取り組みと改善を行ってきました。研修生は特に DCC の、感染制御への対応に的を絞った職員への初期研修と継続研修に興味を示していました。ディスカッションは、適切な研修を受けた職員が常時対応できるような管理体制を維持するため、職員の交代時はどのように対応しているかなどにも及びました。

施設見学では、高度隔離病室を訪問しました。緊急時には集中治療を実施することができると同時に、隔離中の患者さんの快適性を維持することを考慮した設備となっている旨、説明を受けました。

Dr. Antonio Villanueva, Department of International Trials, NCGM, the Philippines からのコメント：

“講義は幾度か中断されることがありました。COVID-19 がまさに日本に上陸したタイミングだったからであり、研修生は歴史的場面に立ち会うこととなりました。大曲先生は今も日本のコロナ対策の先頭に立って指揮を執っています。研修生は皆、無事に本国へ帰国しました。”

図 6a: 国際感染症センターの活動の一例

図 6b: 国際感染症センターによる様々な取り組みの紹介

2.6 臨床研究センター　データサイエンス部

データの質の確保は臨床現場で使用するエビデンスを構築する際の必須要件です。最新の公開論文を例に、基準化した電子データ収集システムをいくつかご紹介頂きました。使用するシステムの選定方法やデータの構築方法は研究者の考え方によって異なりますが、研究者とデータサイエンティストの緊密なコミュニケーションがより質の高いデータを得るための「要」となることは、研究者である研修生の心に残るメッセージとなりました。

Dr. Weerawat Kiddee, Prince of Songkla University, Thailand からのコメント：
“（研究における）国際協調体制を構築しそして展開していくには、臨床データを管理する標準的ツールが必要である、との認識を新たにしました。”

図 7a: NCGM のデータマネージメント体制紹介

図 7b: データサイエンス部担当者とのディスカッション

2.7 ナショナルセンター・バイオバンクネットワーク（NCBN）

NCBN は国内 6 ナショナルセンターからなるバイオバンクのネットワークであり、収集される検体の種類は各ナショナルセンターの専門性によって異なります。利用のための問い合わせ窓口は NCBN 事務局で一括して実施されており、ナショナルセンター以外の組織に所属する、国内外の企業を含む研究者も検体の利用申請が可能です。NCBN、NCGM バイオバンク双方より講師の方々にお越し頂き、NCBN で利用可能な検体数の一覧が確認できる「カタログベース」の使用方法をデモンストレーションして頂きました。

NCGM バイオバンクでは、感染症や代謝疾患、免疫異常等の患者さんの血液などの検体を保管しています。NCGM バイオバンクへの訪問では、検体の保管状態を厳格かつ詳細に管理している様子を見学することができました。

Dr. Melva Louisa, University of Indonesia, Indonesia からのコメント：
“バイオバンクネットワークを利用した研究は、大きな可能性を秘めていると感じます。”

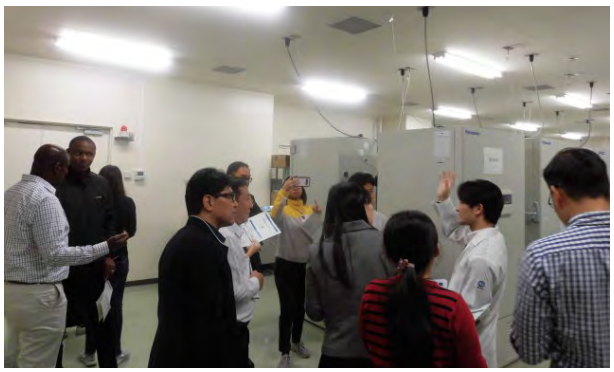

図 8a: NCGM バイオバンク見学

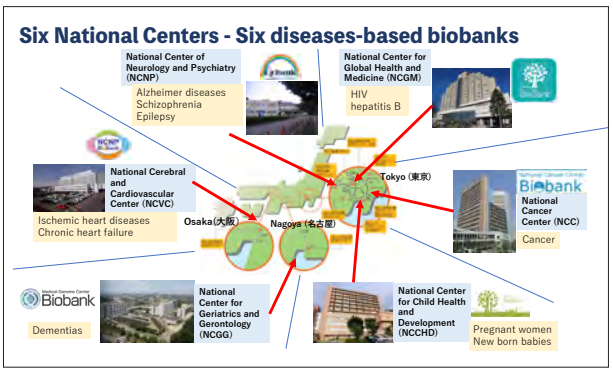

図 8b: ナショナルセンターバイオバンクネットワーク

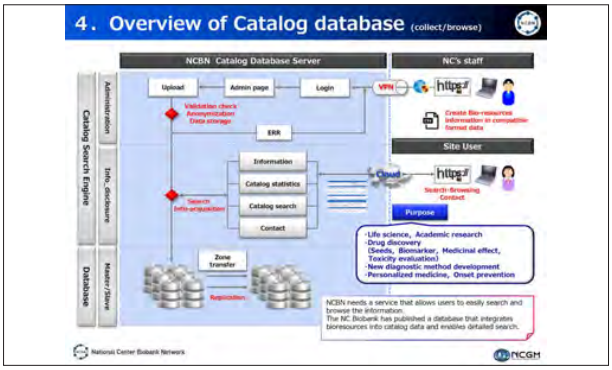

図 8c: NCBN カタログデータベース

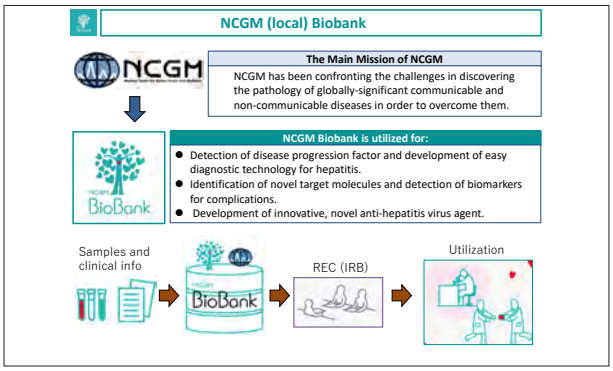

図 8d: NCGM バイオバンク

2.8 医薬品安全性監視 (PV) に関する講義

コンゴ民主共和国 (DRC) からの研修生より、医薬品安全性監視（PV）の要点の説明に続いて当該国で PV を実施した経験について共有して頂きました。

DRC ではシステム上、保健省にある国立 PV 委員会が PV 業務の取りまとめを行っています。安全性に関する報告を全国から集めた上で、規制当局としての判断をする役割を果たしています。そのために、地域レベルの情報を地域 PV センターが集め、その情報を全国 PV センターがまとめ、分析し、国立 PV 委員会へ報告します。全国 PV センターはキンシャサ大学に設置されており医療分野の専門家から成る諮問委員会を有しています。

さらに、北キブ州で発生しているエボラウィルス病の流行中に実施した臨床試験における経験を共有して頂きました。情勢が安定せず、医療者が一般住民の方々の信頼を十分に得られない環境の中で、多くの国のステークホルダーや機関が関わる試験において得られた教訓、課題とその解決策についてお話して頂きました。

図 9a: コンゴ民主共和国 研修生によるプレゼンテーション

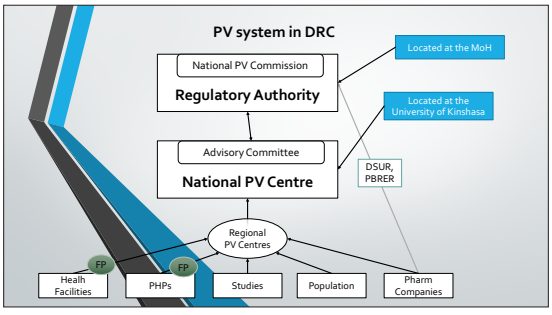

図 9b: コンゴ民主共和国の医薬品安全性監視 (PV) 体制

Dr. Jay Ron O. Padua, San Lazaro Hospital, the Philippines からのコメント：

“Dr. Nsengi の医薬品安全性監視に関する知識の豊かさは素晴らしいものでした。講義の間、一貫して、仕事に対する熱意とひたむきさを伺うことができました。”

3.　NCGM 外のプログラム

3.1　医薬品医療機器総合機構（PMDA）

PMDA と NCGM の包括的連携協定に基づき、PMDA アジア医薬品･医療機器トレーニングセンター（PMDA-ATC）主催の「PMDA-ATC 国際共同治験（MRCT）セミナー 2020」にオブザーバーとしての見学の機会を得ました。本セミナーは規制水準の向上やその調和を促進することを目的として、アジアを中心とした各国規制当局担当者を対象に、国際共同治験をテーマとして取り上げたセミナーです。MRCT の計画・デザイン、実施及び結果の評価における留意点、GCP 調査結果を踏まえた承認審査における留意点、MRCT に基づき承認された医薬品の市販後安全性評価に至るまで、包括的かつ各専門家のご経験や事例に基づいた詳細な講義を聴講しました。特に、PMDA のみならず製薬業界やアカデミアの先生方からのご講義を聴講することで、より実務に即した形で MRCT についての学びを深めることができました。これは研修生にとって、MRCT の成績がどのように規制当局の評価を受けるのかを理解するよい機会となりました。

表 2　セミナープログラム

（上記ウェブページより見学したプログラムのみを抜粋）

History of drug evaluation using overseas data in Japan
Scientific insights about ethnic factors
<**International cooperation and alignment**> Global Platform for Medical Innovation as an Academic Research Organization Challenges for global cooperation of regulatory agencies
<**Points to consider when evaluating results**> Statistical consideration for MRCT based on the ICH E17 G/L PMDA's experiences to review MRCT results
<**Consideration for MRCT operation**> Practical issues and solutions on MRCT operations (investigator's view point) Practical issues and solutions on MRCT operations (industry's viewpoint)
<**Regulatory review based on results of GCP inspection**> How to perform GCP inspection -Role of GCP inspection in review process How to consider GCP inspection results from reviewer's perspective Applicant's experiences to undergo GCP inspection
<**Post market safety evaluation of approved drugs based on MRCT** > Global standard for Pharmacovigilance Risk management plan based on MRCT -industry perspective Risk management based on MRCT -Regulatory Agency Perspective

図 10: PMDA にて

3.2　シオノギ製薬株式会社

くすりの研究開発や製造工程についてより広い視点を得ることを目的に、本プログラムでは大阪にあるシオノギ製薬株式会社のシオノギ医薬研究センターを訪問させて頂きました。シオノギ製薬株式会社は「常に人々の健康を守るために必要な最もよい薬を提供する」という理念を基本方針に掲げる、日本を拠点とする製薬会社です。

シオノギグローバルヘルスアクセスポリシーとして、1. アンメットメディカルニーズを満たす革新的な治療法を開発する、2. 医薬品の適正使用を促進する、3. 医薬品が必要な患者さまにとって入手しやすい環境を整備する、4. ヘルスケアシステムを強化する、が掲げられています。

訪問では、自動フロー合成システムを使用して化合物を合成するデモンストレーションを見学させて頂きました。研究所やオフィスエリアなど、設備の整った施設ツアーの後には、各専門分野で活躍されている研究員の方々より、承認済みの感染症治療薬を例に、薬剤開発のそれぞれのフェーズ（早期開発段階から後期臨床試験まで）における経験や課題についてお話を頂きました。

Dr. Gelza Mae Almario Zabat, St. Luke's Medical Center, the Philippines からのコメント：
“シオノギが手掛けている薬の研究開発は目を見張るものばかりでした。”

図 11: シオノギ医薬研究センター前にて

3.3　国立がん研究センター（NCC）

国立がん研究センター（NCC）は日本で一番多くのがんの臨床試験を実施している施設です。NCC においても施設の視察ツアーと臨床試験に関わる専門家の医師からの講義をして頂きました。NCC の概要説明の後には、センターにおける臨床試験の現状と薬剤開発におけるこれまでの実績についてもご紹介頂きました。NCC は今まで、国内臨床試験、国際共同臨床試験の両方を実施してこられましたが、特に国際共同臨床試験においては、文化や言語の違い、規制要件の違いや資金の確保・管理、被験薬の管理など、様々な課題に直面してこられました。特に昨今では、NCC で実施されている臨床試験数に比べた臨床試験コーディネーター（CRC）の不足を補う工夫として、CRC が担当する試験を研究分野に応じて割り振っているというお話もありました。さらに、着任時の研修と継続研修についても、臨床試験をサポートする際の重要なポイントとしてご紹介頂きました。

施設の視察ツアーでは、フェーズ１臨床試験用の入院施設や外来化学療法センター、内視鏡センター、放射線治療部門、バイオバンク、IVR センター (Interventional Radiology Center) を見学させて頂きました。

Dr. Suvimol Niyomnaitham, Siriraj Hospital, Thailand からのコメント：
“この機関では、臨床試験が当たり前の事のように行われており、この姿は私が所属する機関において是非手本としたいと思うものでした。”

図 12a: NCC 医師によるプレゼンテーション -1

図 12b: NCC 医師によるプレゼンテーション -2

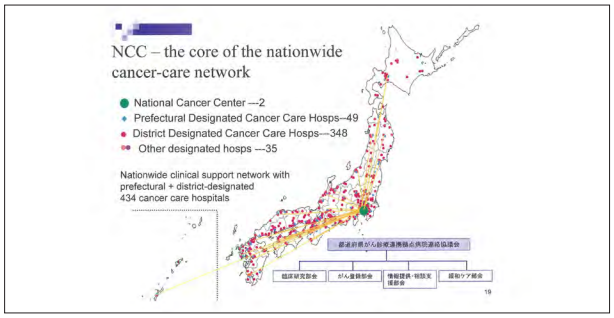

図 12c: NCC のネットワーク

図 12d: NCC の先生方とディスカッション

図 12e: NCC の先生方と集合写真

3.4 大阪大学医学部附属病院

大阪大学は、日本の高等教育をけん引する国立大学の一つです。大阪大学医学部附属病院の見学では、細胞培養調整施設（CPF）と第Ⅰ相臨床試験施設を訪問させて頂きました。

講義では、以下についてご紹介頂きました。

- 国際共同臨床研究実施に向けた取り組み
- 大阪大学医学部附属病院臨床研究センター（ACR）
- 大阪大学医学部附属病院未来医療センター（MTR）

各国の医療事情や IRB/ 倫理委員会の組織について、また将来の協力･協業の可能性と、どのように進めて行くかなど、多岐にわたる話題についてディスカッションが実施されました。

更に、大阪大学医学部附属病院で医師主導治験として iPS 心筋細胞シートが第１症例目の方に移植され、前日にニュース発表されたことを共有して頂きました。

Dr. Maria Elizabeth Mercado, University of the Philippines, Manila, the Philippines からのコメント：
“大阪大学の取り組みは、アカデミアにおいて研究を推し進めるために必要な、サポート体制の先駆けとなる例だと感じます。”

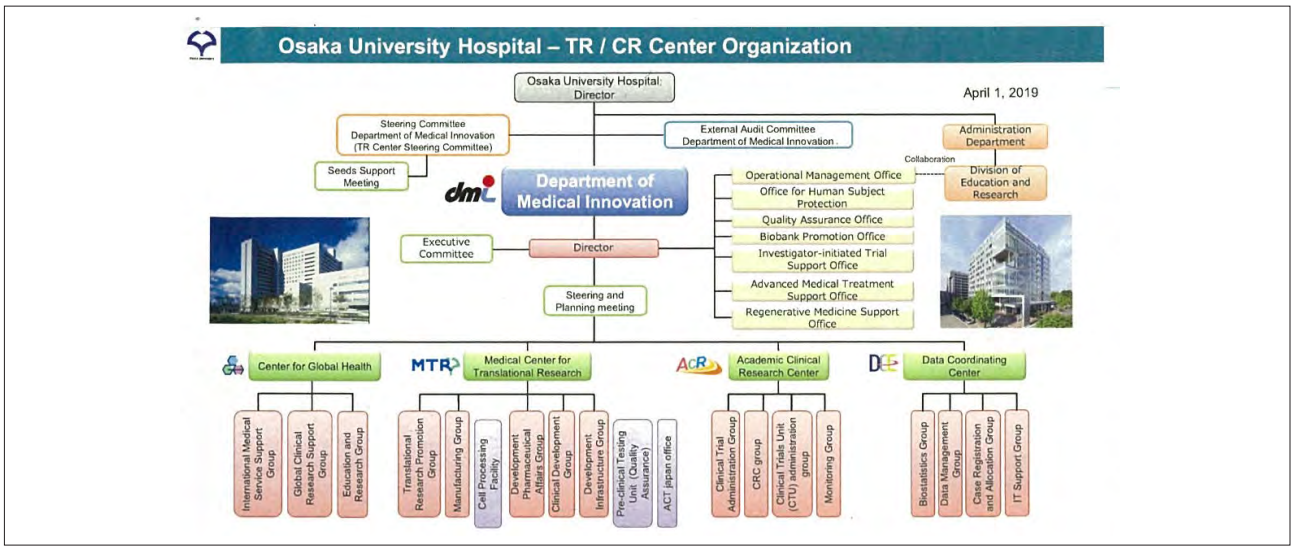

図 13a: 大阪大学医学部附属病院 国際臨床研究体制の紹介

図 13b: 未来医療開発部の紹介

図 13c: 大阪大学医学部附属病院 医師によるプレゼンテーション -1


図 13d: 大阪大学医学部附属病院 医師によるプレゼンテーション -2


図 13e: 大阪大学医学部附属病院 医師によるプレゼンテーション -3

図 13f: 未来医療センター前にて

3.5 国際協力機構

国際協力機構 (JICA) は、資金面において世界最大規模の二国間援助を実施する組織の 1 つで、150 をこえる開発途上国・地域で活動する組織です。

JICA の概要説明の後、JICA が途上国政府と協力して実施されている保健関連の活動についてご紹介頂きました。医薬品や食品の安全を確保するための市販後の管理システムや研究能力の強化、保健関連のマネジメント強化のための技術協力などが活動例の一部として挙げられました。ディスカッションでは、JICA からの協力を受けるためにはどうすればよいのかなどの話題にも研修生の注目が集まり、JICA は政府間で外交的に提出された正式な要請を基に協力を行っていることが説明されました。また、特に、民間セクターとの協力に関して、研修生からの質問がありました。

Dr. Ngo Van Cong, Cho Ray Hospital, Viet Nam からのコメント：
“JICA は数多くの発展途上国を援助しています。的確な、大きな効果をもたらす援助です。”

図 14a: JICA の協力活動の例

図 14b: JICA ご担当者によるプレゼンテーション

3.6 日本 ACRP

Association of Clinical Research Professionals (ACRP) は米国の首都ワシントンに本部を置き、70 カ国以上に 13000 人以上の会員を有する、臨床試験専門家の育成や認定、教育のための非営利組織です。その活動や認定プログラムについて、特に試験責任医師 (PI) に焦点を当てて紹介頂きました。各国にある支部の一つとして、日本支部における教育プログラムや施設の視察、認定試験対策などの活動についてもお話がありました。

Dr. Nsengi Ntamabyaliro, The Institut National de Recherche Biomédicale, DRC からのコメント：
“この組織の存在を知る事が出来、そして研修教材、オンライン教材、オンライン講座、更には様々な資格認定の活動についても知ることが出来たのは大変有意義でした。”

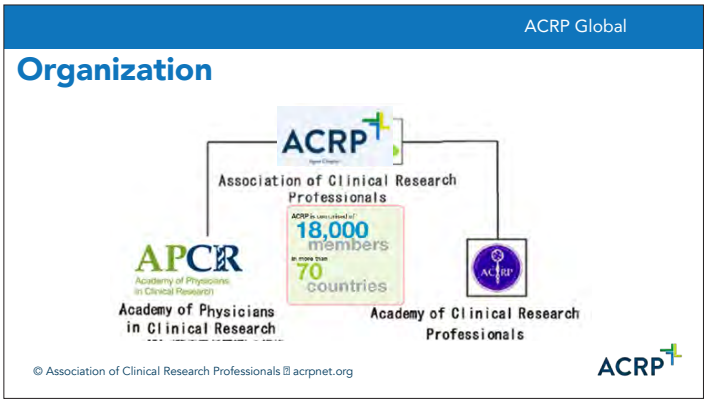

図 15a: ACRP の紹介

図 15b: ACRP- Japan のご担当者の皆様

3.7　科学館 / 博物館

科学の世界、その中でも特に薬剤開発の分野における革新への理解を深めることを目的に、日本科学未来館 “Miraikan” と Daiichi Sankyo くすりミュージアムの 2 つの博物館を見学しました。

Dr. Mboloko Mata Junior, University of Kinshasa, DRC からのコメント：
”未来館“ ではロボットの展示が印象的でした。暮らしをより良くするために科学をいかに活用できるか、という点について学ぶことができ非常に興味深かったです。”

3.7.1　日本科学未来館 “Miraikan”

日本科学未来館 “Miraikan” は、科学、技術への理解を深め、その役割や可能性について考えていくことを目的として作られました。

展示内容は、技術革新、グローバルな環境問題、宇宙、生命科学を含む幅広いテーマにまたがります。研修生たちは iPS 細胞の研究、人工知能の活用、腹腔鏡手術の進歩など、医療における様々な技術革新について理解を深め、体験し、多くを学ぶことができました。

■　日本科学未来館 “Miraikan” ホームページ : https://www.miraikan.jst.go.jp/

図 16a: 見学の様子 -1

図 16b: 見学の様子 -2

3.7.2　Daiichi Sankyo くすりミュージアム

くすりミュージアムは、広く一般の人々に向けて薬やその開発を身近に感じてもらえるような工夫が凝らされた博物館です。見て聞いて触れて、という双方向型の体験を通じて薬について学ぶことができました。

■　Daiichi Sankyo くすりミュージアム　ホームページ : https://kusuri-museum.com

図 17a: 見学の様子

図 17b: 博物館玄関にて集合写真

4. 公開プレゼンテーションセッション

各国の臨床研究 / 臨床試験の現状と課題、医療ニーズ、将来の協力にむけた提案について NCGM 内外の方々に向けて発表する公開セッションを企画していましたが、残念ながら COVID-19 のの流行状況を鑑みて中止となりました。発表予定のスライド資料については本研修プログラムで講師を務めていただいた皆様、研修生、公開セッションへの参加登録者に共有するとともに、DIT のホームページにて公開する予定です。

図 18: 公開プレゼンテーションセッションの案内

5.　結語

昨年に引き続き 2 回目となる本研修においては、5 カ国から 13 名と日本から 1 名の研修生が一堂に会し、14 日間に渡り、MRCT データに対する規制当局の審査の視点や日本での臨床研究・臨床試験の現場の状況、国際医療協力における日本政府の貢献、将来の研究での使用を目的とした検体の適切な保管などについて学びを深めました。加えて、臨床試験の専門家にとって必要な専門的能力は何かを学んだうえで、医薬品の研究開発について現場の状況について知る機会を得ました。

公開プレゼンテーションセッションは中止となりましたが、研修生がプログラムでの学びを生かして作成したスライド資料は講師の皆さま、セッションに参加登録してくださった皆様、研修生で共有し、将来の協力・協業に向けた一歩としての役割を果たすことと期待しています。

■大阪大学医学部附属病院の先生方からのコメント：

田畑先生：

“本研修に参加して最も印象的だったのは、研修生、講師、NCGM のコミュニケーションの素晴らしさです。今後の国際共同臨床試験への良好な協調体制を確信しました。”

名井先生：

“皆さんが NCGM のこのプログラムを満喫されたことを望みます。”

中谷先生：

“この研修が皆さんの経験や知識をより豊かにするものとなりますように願っています。”

今後に向けて

2020 年 1 月に開催しました 14 日間に渡る "A program focused on comprehensive and collaborative training on medical innovations adapted to challenges of clinical trials in Asian and African countries, 2nd edition" では 5 カ国より 13 名に加え、日本からも 1 名の研修生を迎えました。

研修生からは、聴講した PMDA による規制調和の講義や、臨床施設（国立がん研究センター（NCC)、国立国際医療研究センター (NCGM))、教育機関（大阪大学)、国際協力機構（JICA)、日本 ACRP（Association of Clinical Research Professionals Japan Chapter)、民間企業（シオノギ製薬株式会社）の講義、また様々な議論を通じて他国の状況をも知りえる機会が提供できたことなどに高い評価を得た一方、専門家との具体的な事例を取り上げた議論など、双方向型の研修内容への要望がありました。

今後も、より良いプログラムの実施に向け、関係者の皆様のご指導、ご協力を賜りますよう、引き続きよろしくお願い申し上げます。

2020 年 3 月 10 日
国立国際医療研究センター
臨床研究センター
インターナショナルトライアル部長
飯山　達雄

Comprehensive and collaborative training on medical innovations adapted to challenges of clinical trials in Asian and African countries

[2nd edition]

ENGLISH / 英語

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Preface

The establishment of a reliable and stable network for implementation of Multi-Regional Clinical Trials (MRCT) among Japan, Asian and African countries is the crucial element of the collaboration between the Center for Clinical Sciences/Department of International Trials (CCS/DIT) of the National Center for Global Health and Medicine (NCGM) and its partner institutions located in Asia and Africa.

The program for capacity building of health professionals capable of implementing multi-regional clinical researches in accordance with internationally standardized procedures is one of the main pillars for the achievement of the CCS/DIT project. This project aims to contribute to the improvement of medical care around the world by affirming new medicines and diagnostic tools through MRCTs.

Same as for the FY 2018 program, delegates from five countries, namely: The Democratic Republic of the Congo, Indonesia, The Philippines, Thailand, and Vietnam participated, while a delegate from Japan was added. In total, 14 institutions sent representatives to the program compared to 10 previously.

This 14-day training program consisted of lectures and guided visits at Japan's regulatory authority (Pharmaceuticals and Medical Devices Agency (PMDA)), private industry (SHIONOGI & CO., LTD.), governmental agency (the Japan International Cooperation Agency (JICA)), academia (Osaka University), the Association of Clinical Research Professionals-Japan chapter (ACRP-JP), the National Center Biobank Network (NCBN), and clinical settings (National Cancer Center (NCC) and NCGM), was a great opportunity for exchange and rich discussions among the 14 participants (two to three per country), lecturers and DIT staff. The current program introduced two novel approaches: the participation of a delegate from a Japanese institution and the inclusion of lectures from some delegates who shared about their experience on pharmacovigilance and clinical trials in their respective institutions.

We continuously thank each one who contributed to the achievement of this activity and hope that it will continuously grow for cooperation with counterpart countries.

Haruhito Sugiyama
Director, Center for Clinical Sciences,
National Center for Global Health and Medicine
March 10, 2020

Acknowledgments

The complexity of drug development process and the impact it has on human health require the generation of good data while paying careful attention to the research participants' safety and rights. Effective and relevant training of skilled clinical research professionals plays an essential role in the clinical research quality.

Continuity plays a key role in promoting multi-regional clinical research that contributes to the improvement of global health in collaboration with counterpart countries. The Center for Clinical Sciences-Department of International Trials of the National Center for Global Health and Medicine organized the FY2019 training program entitled "The 2020 NCGM/CCS country-specific MRCT capacity building: A program focused on comprehensive and collaborative training on medical innovations adapted to challenges of clinical trials in Asian and African countries, 2nd edition".

This was 14-days full of intensive lectures and site visits, planned for delegates from Japan and five countries, namely The Democratic Republic of the Congo, Indonesia, The Philippines, Thailand, and Vietnam. The ultimate goal of the program is to provide new medical treatment and diagnostic medical devices that will benefit patients with emerging and re-emerging infectious diseases, rare diseases, non-communicable diseases and intractable diseases around the world.

The accomplishment of this work was the result of the cooperative efforts of many stakeholders within Japan and from our partner countries. As such, we sincerely thank the PMDA who kindly provided opportunity to our delegates.

We thank all the organizations and their personnel who, despite their multiple responsibilities, accepted to provide lectures and/or site visits:

- National Cancer Center Hospital, Japan
- SHIONOGI & CO., LTD.
- Osaka University Hospital
- Japan International Cooperation Agency
- Pharmaceuticals and Medical Devices Agency
- Association of Clinical Research Professionals, Japan Chapter
- The National Center Biobank Network

Since "unity is strength", we gratefully thank all NCGM Departments who always come together with us to make the program a success, namely the Bureau of International Health Cooperation, Disease Control and Prevention Center, Department of Tropical Medicine and Malaria, Data Science Department, and Biobank.

Finally, to those institutions from our counterpart countries who accepted to send their professionals; without their collaboration, we would not have such dedicated participants who were definitely the key to make this program successful. We gratefully thank all of you.

Our international partner institutions are as follows (by alphabetical order of country's name):

- The Democratic Republic of the Congo: University of Kinshasa, Institut National de Recherche Biomédicale
- Indonesia: University of Indonesia, Sulianti Saroso Infectious Diseases Hospital, Mochtar Riady Research Institute
- The Philippines: University of the Philippines, St. Luke's Medical Center, San Lazaro Hospital
- Thailand: Faculty of Tropical Medicine and Siriraj Hospital in Mahidol University, Prince of Songkla University
- Vietnam: Cho Ray Hospital, Bach Mai Hospital

Tatsuo Iiyama

Director, Department of International Trials,
Center for Clinical Sciences,
National Center for Global Health and Medicine
March 10, 2020

List of Acronyms

ACR	Academic Clinical Research Center of Osaka University Hospital
ACRP	Association of Clinical Research Professionals
ASEAN	Association of Southeast Asian Nations
ATC	Asia Training Center
BIHC	Bureau of International Health Cooperation
CCS	Center for Clinical Sciences
COVID-19	Coronavirus Disease 2019
CPF	Cell Processing Facility
CRC	Clinical Research Coordinator
DCC	Disease Control and Prevention Center
DIT	Department of International Trials
DRC	Democratic Republic of the Congo
FY	Fiscal Year
GCP	Good Clinical Practice
ICH	The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
INRB	Institut National de Recherche Biomédicale
IPS	Induced Pluripotent Stem Cells（iPS Cells）
IRB	Institutional Review Board
IVR	Interventional Radiology
JICA	Japan International Cooperation Agency
JTF	Joint Task Force
MRCT	Multi-Regional Clinical Trials
MTR	Medical Center for Translational Research, Osaka University Hospital
NCBN	National Center Biobank Network
NCC	National Cancer Center Japan
NCGM	National Center for Global Health and Medicine
PMDA	Pharmaceuticals and Medical Devices Agency
PV	Pharmacovigilance

List of Figures and Tables

1. Introduction

1.1 Description of the Training Program

The 2020 NCGM/CCS country-specific MRCT capacity building: “A program focused on comprehensive and collaborative training on medical innovations adapted to challenges of clinical trials in Asian and African countries, 2nd edition" was a 14-day training program which aimed to solidify the international network and to improve capacity of clinical research professionals from five counterpart countries and Japan in the conduct of multiregional clinical research.

This year’s program invited 14 delegates, from The Democratic Republic of the Congo (2), Indonesia (3), The Philippines (3), Thailand (3), and Vietnam (2) and from Japan (1). The program included lectures, discussions, and visits to the PMDA, a pharmaceutical company, and clinical research facilities.

Participants attended the 2020 Multiregional Clinical Trials (MRCT) Seminar organized by the PMDA Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs (PMDA-ATC) and gained insight into the harmonization of regulatory review of MRCT data.

In order to know the current status of research and medical innovations, lectures and visits were provided from the clinical setting (NCGM, NCC), academia (Osaka University), and from a private company (SHIONOGI & CO., LTD).

The representative of the Japan International Cooperation Agency (JICA) lectured about Japanese international health cooperation and their project financing procedure while the lecturer from the Association of Clinical Research Professionals (ACRP) explained the importance and concept of their organization.

A public seminar where delegates were supposed to discuss challenges and suggestions on drug/device development in ASEAN and African countries was planned. In addition to those from NCGM, 40 participants registered for this session; however, the session was cancelled due to the outbreak of the COVID-19 since it is managed at NCGM’s Center Hospital.

Presentation slides were shared with registrants and uploaded to DIT’s homepage.

1.2 Program Objectives

The program aimed:

- To establish a global clinical research network to conduct global standard MRCTs between Japan and partner countries.
- To build capability of professionals able to design and conduct clinical research.

1.3 Participants

Medical doctors and pharmacists from 14 institutions in four South East Asian, one African country and Japan who have been involved in clinical research participated in the program.

Following in Table 1 are their profiles.

Table 1. Delegates Profiles

The Democratic Republic of the Congo	
	**Nsengi Yumva Pierre-Michel Ntamabyaliro** [Current position] Study site coordinator, Co-Principal Investigator INRB Lecturer at University of Kinshasa, Pharmacovigilance Unit [Degree(s)] MD, MSc Specialty: Pharmacovigilance and Pharmacoepidemiology
	**Mata Junior Mboloko** [Current position] Lecturer at University of Kinshasa, Consultant at Department of Obstetrics and Gynecology University of Kinshasa [Degree(s)] MD, MSc Specialty: Obstetrics and Gynecology
Vietnam	
	**Thi Hong Linh Le** [Current position] Consultant at Center for Tropical Diseases, Bach Mai Hospital [Degree(s)] MD,MSc Specialty: Infectious and Tropical Diseases
	**Ngo Van Cong** [Current position] Consultant at Department of Otorhinolaryngology- Head and Neck Surgery, Cho Ray Hospital [Degree(s)] MD, PhD Specialty: Otorhinolaryngology
Indonesia	
	**Maria Lawrensia Tampubolon** [Current position] Consultant at RSPI Prof. Sulianti Saroso Hospital External Research Coordinator in Research Unit RSPI Prof. Sulianti Saroso Hospital [Degree(s)] MD, Specialty: Neurology

Indonesia

Melva Louisa Simbolon

[Current position]
Research coordinator, Department of Pharmacology and Therapeutics,
Secretary for Doctoral Program in Biomedical Sciences, Faculty of Medicine
University of Indonesia

[Degree(s)]
Pharmacist, MSc, PhD
Specialty: Pharmacology

Dina Nilasari

[Current position]
Staff and lecturer, Department of Internal Medicine Hasanuddin University Teaching Hospital
Mochtar Riady Institute
Consultant at Outpatient Clinic Nephrology-Hypertension Unit, Wahidin Sudirohusodo and Hasanuddin University Hospital

[Degree(s)]
MD, PhD
Specialty: Internal Medicine, Nephrology

Philippines

Maria Elizabeth Panlaqui Mercado

[Current position]
Lead faculty for Biostatistics and Instructor of Clinical Epidemiology, University of Santo Tomas Faculty of Medicine
University of the Philippines

[Degree(s)]
MD, Masters in Advance Study (MAS)
Specialty: Clinical Research

Gelza Mae Almario Zabat

[Current position]
Consultant at St. Luke's Medical Center
St. Luke’s Medical Center
[Degree(s)]
MD
Specialty: Internal Medicine - Infectious Diseases

Jay Ron Olegario Padua

[Current position]
Consultant at San Lazaro Hospital

[Degree(s)]
MD
Specialty: Pediatric Infectious Diseases

Thailand

Weerawat Kiddee

[Current position]
Associate Professor of Ophthalmology, Glaucoma Unit
Deputy Head of Department for Research, Department of Ophthalmology
Faculty of Medicine, Prince of Songkla University

[Degree(s)]
MD
Specialty: Ophthalmology

Noppadon Tangpukdee

[Current position]
Associate Professor Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University

[Degree(s)]
B.N.S. (Nursing and Midwifery)
MSc (Medical Toxicology)
Diploma (Medical Microbiology)
PhD (Tropical Medicine)

Suvimol Niyomnaitham

[Current position]
Consultant Siriraj Clinical Research Center (SiCRC)
Lecturer and researcher at Department of Pharmacology
Principal Investigator in clinical trials and bioequivalence studies
Faculty of Medicine, Siriraj Hospital, Mahidol University

[Degree(s)]
MD
MSc (Clinical Epidemiology and Biostatistics)
PhD (Pharmacoepidemiology)
Diploma on Research and Development of products to meet Public Health Needs

Japan

Chisa Tabata

[Current position]
Associate Professor Center for Global Health, Department of Medical Innovation, Osaka University Hospital

[Degree(s)]
MD, PhD
Specialty: Obstetrics and Gynecology, Medical Genetics

2. Activities at NCGM

2.1 Center for Clinical Sciences Department of International Trials (DIT)

2.1.1 Overview of the DIT

The DIT's project to build a collaborative platform for multi-regional clinical trials was extensively explained to participants by the DIT representatives. It was explained that DIT promotes information exchange and cooperation among government agencies, companies, and academic institutions by, for example, organizing international forums on infectious diseases, while supporting the seamless execution of multi-regional clinical trials in emerging countries in compliance with international standards and country-specific regulations.

In order to develop a better and solid environment for multi-regional clinical trial programs, DIT is continuously organizing training programs for capacity building of clinical trial professionals in Asian and African countries.

Fig. 1a: DIT presentation

Fig. 1b: Introduction of life in Japan

Fig. 1c: The DIT network

Fig. 1d: Garbage management in Japan

2.1.2 Clinical Trial Competency

In order to achieve a single, high-level set of standards to serve as a framework for defining professional competency throughout the clinical research enterprise, the Harmonized Core Competency Framework was released in 2014 and reviewed in 2018 by the Joint Task Force for Clinical Trial Competency (JTF). The later version defined competencies at Fundamental, Skilled and Advanced levels for the 47 competencies of the 8

domains in the framework. The 8 domains comprise: 1. Scientific Concepts and Research Design, 2. Ethical and Participant Safety Considerations, 3. Investigational Products Development and Regulation 4. Clinical Study Operations (Good Clinical Practice), 5. Study and Site Management, 6. Data Management and Informatics, 7. Leadership and Professionalism, and 8. Communications and Teamwork. DIT lecturers shared about the content of the competency wheel and why it is a nice tool for the clinical research enterprise.

Discussion was mainly focused towards domains 1, 2, 4, 5, and 6; various experiences were shared. For example, Serious Adverse Events (SAE)/AE reporting and subject compensation were compared between countries.

Most participants highlighted difficulties on how to align with the principles related to the complexity of the trial design and the adaptation to each individual situation.

Therefore, discussion remains on how to create an efficient design and for appropriate implementation of the research.

Fig. 2a: Competency wheel presentation

Fig. 2b: Discussion during the competency wheel presentation

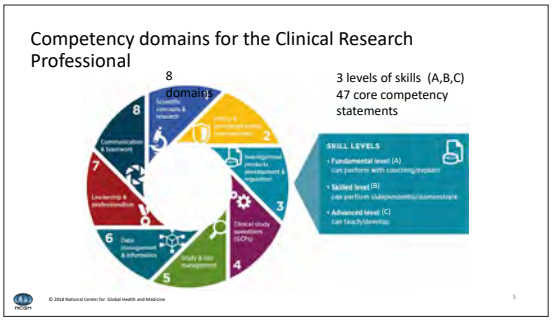


Fig. 2c: Competency domains for clinical research professionals

JOINT TASK FORCE FOR CLINICAL TRIAL COMPETENCY:
https://mrctcenter.org/clinical-trial-competency/

Comment from: Dr. Noppadon Tangpukdee, Fauclty of Tropical Medicine, Mahidol University, Thailand

"We have learned about the guidance and tools to ensure our professional competency in clinical research."

"We have learned, and we have shared our experience together and received very good comments from the team."

2.2 Bureau of International Health Cooperation (BIHC)

With more than a 40-year history of international health cooperation, the NCGM through its BIHC is conducting a wide range of technical cooperation projects and policy proposals.

Technical cooperation projects include human resource development (e.g., education of nurses and other medical professionals, medical technology transfer), hospital management, and these cover many kinds of health problems and needs.

In addition, the BIHC has dispatched their staff in different countries to provide health-related counselling to policymakers.

Fig. 3a: BIHC presentation; BIHC's activities

BIHC participates also in the global response to outbreak by sending skilled professionals to help fight against the threat, as is the case for the Ebola Virus Disease outbreak in the DRC, where Japanese doctors were sent to help manage quarantine.

Fig. 3b: Group photo with the BIHC representative

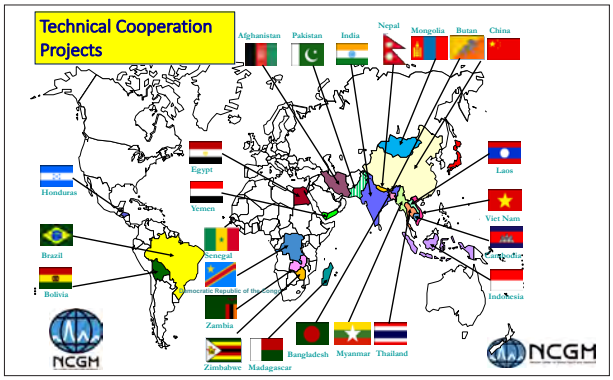


Fig. 3c: NCGM's collaboration network

2.3 Department of Tropical Medicine and Malaria, Research Institute

The NCGM-Research Institute by its Department of Tropical Medicine and Malaria has a mission to contribute to global health by the research on tropical medicine and malariology.

Various activities in the department and the international health cooperation network were introduced. The lecturer touched on different devices used to diagnose asymptomatic malaria and the collaboration with the Institut Pasteur du Laos and Mahidol University.

Fig. 4a: Department of Tropical Medicine and Malaria presentation

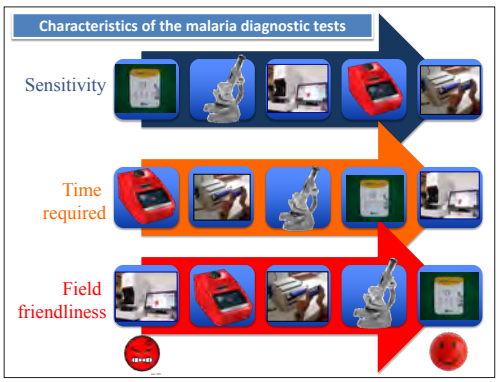


Fig. 4b: Malaria diagnostic tests available at the NCGM

Specifics on research involving DIT's participation and international health cooperation with Mahidol University were shared.

During the same session, DIT's facilitation functions and responsibilities in the previously mentioned research projects were presented by the regional manager involved.

2.4 Experience from a Clinical trial site: Mahidol University, Faculty of Tropical Medicine case

Conducting clinical trials needs to fulfill minimum requirements to reach the standard of safety and efficacy. Each site and/or each study has its peculiarities.

Clinical trial professionals are facing multiple challenges in order to comply with ethical, regulatory, sponsor and study requirements.

The delegate from Mahidol University shared about the challenges and experiences of their institution. After a brief introduction on their study site, he shared about his experience as Principal Investigator (PI) in clinical studies. From the protocol writing to the publication of research results, the role of the PI was actively commented and discussed among delegates.

Comment from: Dr. Maria Lawrensia Tampubolon, Sulianti Saroso Infectious Diseases Hospital, Indonesia

"The problem of diagnosis and therapy can be a challenge in eradicating the disease. So, the innovation and collaboration based on each country's resource become important."

Fig. 5a: Mahidol University delegate presentation; Responsibility of Principal Investigator

Fig. 5b: DIT presentation; Overview of NCGM DIT's projects in Thailand

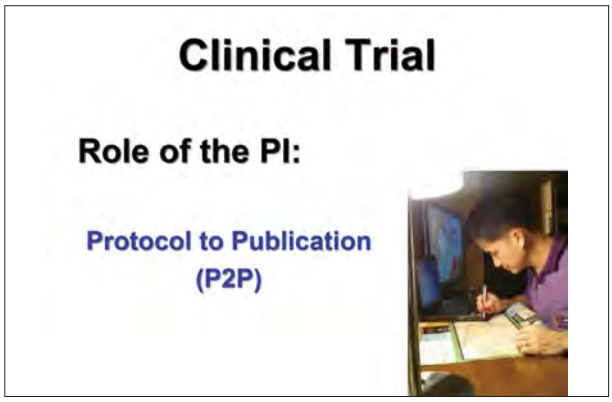


Fig. 5c: Role of the PI slide from Mahidol University

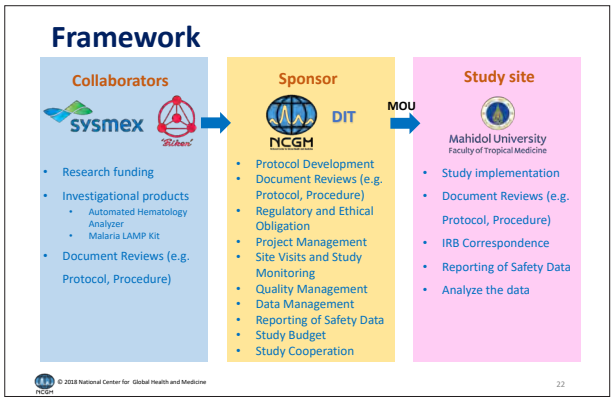


Fig. 5d: NCGM's Thai projects framework

2.5 Disease Control and Prevention Center (DCC)

Activities at the DCC were divided into two parts; the lecture and the facility visit. Since this was during the time of the outbreak of the 2019 new Coronavirus in China, the lecture mainly focused on a brief introduction of the Japanese regulations and framework in response to emerging infectious diseases. DCC has developed and improved their activities based on their experiences such as construction of a high-level isolation unit, training course for the staff, response team structure, and standard flow for the first response. Participants were interested in DCC's training course and its maintenance program which emphasizes readiness in terms of infection control. The discussion extended into the management of turnover of trained staff. During the facility tour, participants visited the high-level isolation unit and observed that it is well-equipped to give the patients intensive care in case of an emergency, as well as comfort during their isolation.

Fig. 6a: DCC's activities

Comment from: Dr. Antonio Villanueva, Department of International Trials, NCGM, the Philippines

"Unlike previous years, his discussion was interrupted several times because COVID-19 had just entered Japan. Just in time for the trainees to take part in history in the making. To this day, Dr. Ohmagari continues to lead anti-COVID efforts in Japan and the trainees were sent home safely."

Fig. 6b: DCC presentation

2.6 Department of Data Science, Center for Clinical Sciences

Quality data is a must for building evidence to be used in clinical practice.

Referring to a newly published paper, the lecturer introduced some types of data collection with emphasis on the standardized electronic data capturing systems. He reminded about one thing to keep in mind; "Researchers have their preferences on each of the systems and data structure, therefore, close communication between researchers and data scientists is key for a better outcome."

Fig. 7a: Data management system in the NCGM

Fig. 7b: Discussion with Data Science Department representative

Comment from: Dr. Weerawat Kiddee, Prince of Songkla University, Thailand

"At the end of the lecture, we have realized that to generate and to promote international collaboration, for sure, we need the standard tool to manage the clinical data."

2.7 National Center Biobank Network (NCBN)

The National Center Biobank Network (NCBN) is a group of six biobanks located at six national centers in Japan. The six national biobanks store samples related to their respective specialties. While each national center biobank collects its related sample, there has been developed a common platform for the management of specimen.

Any researcher who wishes to use biodata can apply to the secretariat and the acquisition of samples is possible for anyone who fulfills the requirements.

Lecturers from the NCBN and from NCGM's biobank explained how the biobank works and demonstrated how to use their catalog database. This is a repository of the list of specimens available in the bank.

The NCGM biobank stores samples (blood, etc.) obtained from patients with infectious diseases, metabolic disorders, and immune-related disorders. A site visit at the NCGM biobank facility could show an overview on how the

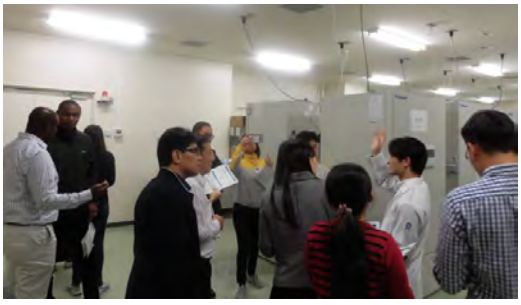


Fig. 8a: NCGM biobank visit

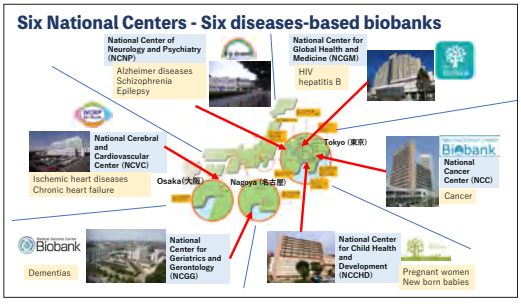


Fig. 8b: National Center Biobank Network

biobank stores the samples with strict and close monitoring.

Comment from: Dr. Melva Louisa, University of Indonesia, Indonesia

"My opinion is the research using the biobank network can be very promising in the future."

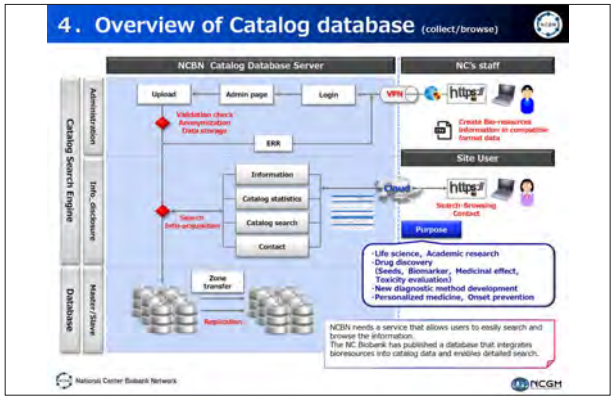


Fig. 8c: NCBN catalog database portal

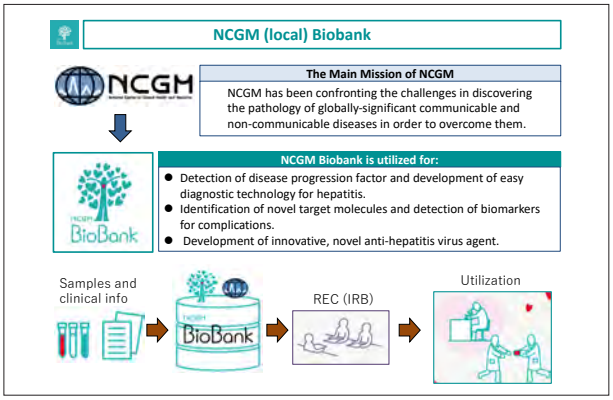


Fig. 8d: NCGM biobank description

2.8 Lecture on Pharmacovigilance

After introduction on the essentials of pharmacovigilance (PV), the delegate from the Democratic Republic of the Congo (DRC) shared his experience on conducting pharmacovigilance in their country.

The PV system in DRC is organized as follows: The National PV Commission is responsible for taking regulatory decisions based on information provided by the National PV Center. It is located at the Ministry of Health (in the Directorate of Pharmacy and Medicines). The National PV Center is responsible for collecting and analyzing safety reports from all over the country. It is located at the University of Kinshasa (Department of Clinical Pharmacology). It is assisted by an Advisory Committee composed of experts from different medical fields. Regional PV Centers collect data at province level and report to the National PV Center. The lecturer also shared his experience on conducting the clinical trial during the Ebola Virus Disease outbreak in North Kivu. Lessons learned, challenges, and solutions applied into a clinical trial involving various countries' stakeholders, organizations in an unstable conflict zone, and where populations have lack of trust in health workers.

Comment from: Dr. Jay Ron O. Padua, San Lazaro Hospital, the Philippines

"His knowledge on pharmacovigilance was exceptional. His passion and enthusiasm in his field of work is apparent throughout his lecture."

Fig. 9a: DRC delegate presenting the Pharmacovigilance system in DRC

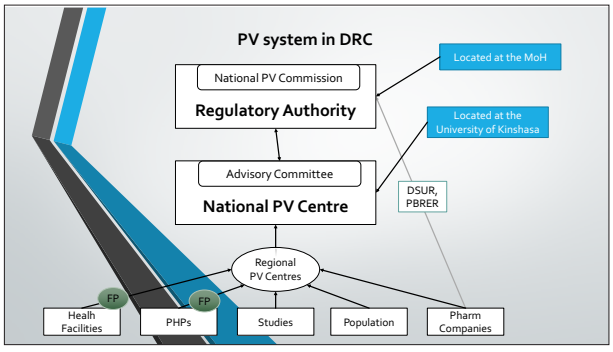


Fig. 9b: Pharmacovigilance system in DRC

3. Activities outside of NCGM

3.1 Pharmaceuticals and Medical Devices Agency (PMDA)

Comprehensive partnership program between PMDA and NCGM allowed delegates to observe "PMDA-ATC Multi-Regional Clinical Trials (MRCT) seminar 2020" organized by the PMDA Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs (PMDA-ATC). This seminar, focusing on multi-regional clinical trials, was designed for representatives of Regulatory Authorities, with the objective to contribute to enhancement and mutual understanding of regulations and strengthening of cooperation in Asia and other parts of the world.

They provided lectures on the topics such as points to consider at protocol designing and planning of MRCT, clinical operation, clinical data evaluation, regulatory review based on results of GCP inspections, and post-market safety evaluation of approved drugs based on MRCT. Lectures were provided by experts not only from PMDA but also diverse specialists from academia and industry with detailed information acquired by their comprehensive and extensive experiences.

This was a good opportunity for delegates to understand how the Regulatory Authority evaluates the clinical data on New Drugs with MRCT.

■ **Web page on the PMDA-ATC MRCT Seminar:** https://www.pmda.go.jp/english/symposia/0160.html

Table 2 "PMDA-ATC Multi-Regional Clinical Trial (MRCT) Seminar 2020

Organizer: The Asia Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs

Date: January 20-23, 2020

Seminar program

(The following information comes from the above PMDA web page and lists only the program activities attended by the participants.)

History of drug evaluation using overseas data in Japan
Scientific insights about ethnic factors
<**International cooperation and alignment**> Global Platform for Medical Innovation as an Academic Research Organization Challenges for global cooperation of regulatory agencies
<**Points to consider when evaluating results**> Statistical consideration for MRCT based on the ICH E17 G/L PMDA's experiences to review MRCT results
<**Consideration for MRCT operation**> Practical issues and solutions on MRCT operations (investigator's view point) Practical issues and solutions on MRCT operations (industry's viewpoint)

<Regulatory review based on results of GCP inspection>
How to perform GCP inspection -Role of GCP inspection in review process
How to consider GCP inspection results from reviewer's perspective
Applicant's experiences to undergo GCP inspection

<Post market safety evaluation of approved drugs based on MRCT >
Global standard for Pharmacovigilance
Risk management plan based on MRCT -industry perspective
Risk management based on MRCT -Regulatory Agency Perspective

Fig. 10: Group photo after PMDA lecture

3.2 SHIONOGI & CO., LTD.

In order to have a broad view of the manufacturing process for research and drug development, the training team traveled to Osaka to visit SHIONOGI & CO., LTD. This is a Japan-based pharmaceutical company whose mission is to constantly strive to provide the best possible medicines to protect the health and well-being of people worldwide.

Shionogi's Global Health Access Policy Statement says its efforts to improve access are focused in the four following areas: 1. Developing innovative therapies to address unmet needs, 2. Promoting proper use of medicines, 3. Improving affordability for patients in need, and 4. Strengthening healthcare systems.

During the visit, delegates experienced a demonstration on how to synthesize new compounds using the automated flow chemistry system.

After the visit of the well-equipped facility (offices, laboratories), experts from the company shared their experience on challenges during each phase of drug

Fig. 11: Shionogi Co.Ltd. visit

development (from early stage of development to the later phases of clinical trials) using examples of some of their approved anti-infectious drugs.

Comment from: Dr. Gelza Mae Almario Zabat, St. Luke's Medical Center, the Philippines

"The advances made by Shionogi is definitely impressive."

3.3 National Cancer Center Japan (NCC)

The National Cancer Center is the top facility in terms of number of cancer clinical trials in Japan. Activities at the NCC comprised of a facility tour and lectures from clinical trials professionals. After a brief explanation about the hospital structure and services, the current situation of clinical trials in the NCC and the achievements which have been made in terms of drug development were introduced. NCC has been involved in local and international clinical trials (MRCTs). Concerning the MRCTs, clinical trials professionals have been facing many challenges such as the cultural and language differences, varying regulatory requirements, and management of funds and trial drugs received from pharmaceutical companies.

One of the current challenges is the shortage of Clinical Research Coordinators (CRC) compared to the huge number of studies conducted at the NCC.

In order to overcome the situation, the NCC appoints CRCs by research area. Also, onboarding with continuous training further supports clinical research.

During the facility tour, participants visited the inpatient ward for phase 1 clinical trials, outpatient treatment center, Endoscopy center, Invasive Radiotherapy Center, Biobank, and Interventional Radiology Center.

Comment from: Dr. Suvimol Niyomnaitham, Siriraj Hospital, Thailand

"They make clinical trial look so routine that is the model that I have to propose to my faculty here in Thailand."

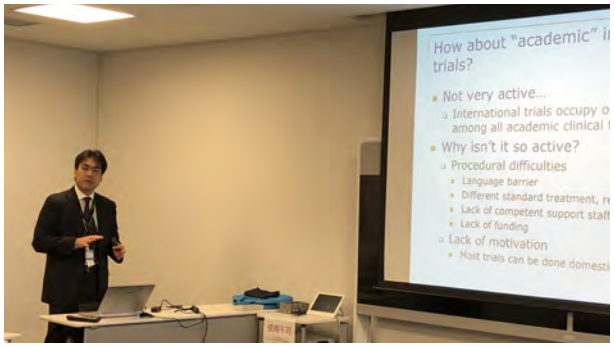


Fig. 12a: NCC presentation -1

Fig. 12b: NCC presentation -2

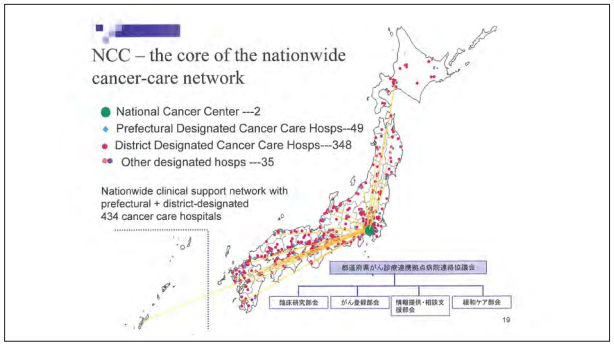


Fig. 12c: The national cancer - care network

Fig. 12d: Discussion with NCC doctors

Fig. 12e: Group photo with NCC represantives

3.4 Osaka University Hospital

Osaka University, a Japanese national university, is ranked as one of Japan's most prestigious institutions of higher learning. A facility tour at Osaka University Hospital included visit to the Cell Processing Facility and the Phase 1 unit for clinical trials.

Lectures introduced activities related to three main topics:

- Efforts on conducting Multi-Regional Clinical Research
- Academic Clinical Research Center, Osaka University Hospital
- Medical Center for Translational Research, Osaka University Hospital

Discussions were oriented on each country's health situation, the organization of the Institutional Review Board/ Ethical Committee, and on how to develop a possible future collaboration.

In addition, Osaka University Hospital staff were happy to share in a big achievement done by one of their supported investigator-initiated clinical trials: one day before our visit, the first transplantation of Induced Pluripotent

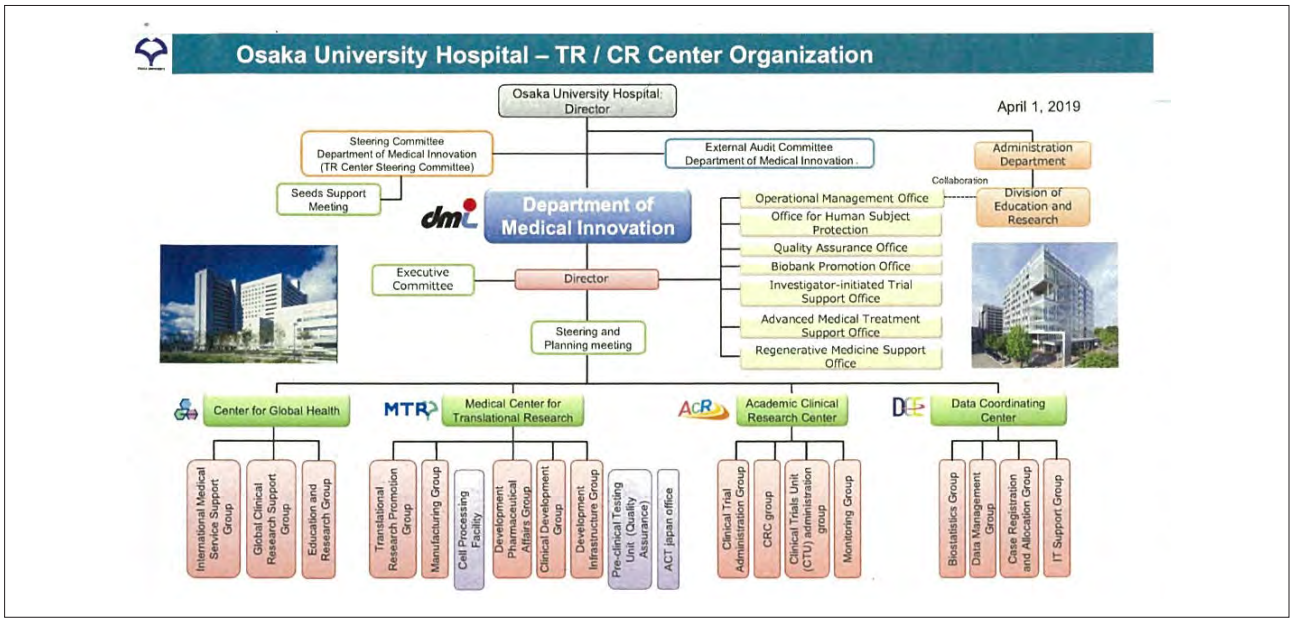


Fig. 13a: Overseas Engagement of Clinical Research to Develop Academic Seeds

Stem cells- based (iPS) - heart sheet had been successfully done.

Comment from: Dr. Maria Elizabeth Mercado, University of the Philippines, Manila, the Philippines

"Osaka University tour has set the example of what kind of support can facilitate a thriving research environment in the academia."

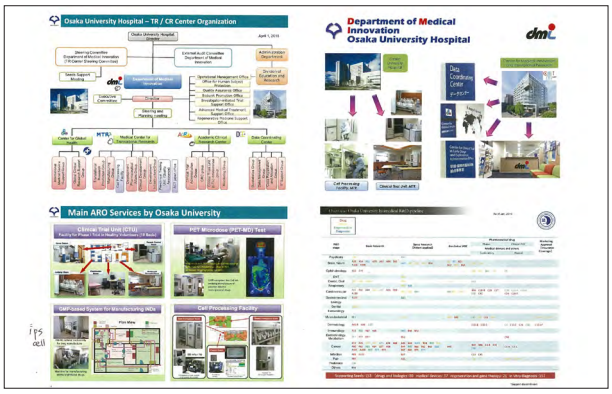


Fig. 13b: Osaka University Hospital Department of Medical Innovation

Fig. 13c: Osaka University Hospital presentation -1

Fig. 13d: Osaka University Hospital presentation -2

Fig. 13e: Osaka University Hospital presentation -3

Fig. 13f: Group photo in front of the Center of Medical Innovation and Translational Research

3.5 Japan International Cooperation Agency

Japan International Cooperation Agency (JICA) is one of the world's largest bilateral aid agencies supporting socioeconomic development in over 150 developing countries and regions.

After presenting an overview of JICA, the lecturer presented some examples of health-related projects supported by JICA. These include technical cooperation on post-market control systems for drug and food safety, research capacity enhancement, and strengthening health management.

Discussions focused on how to request JICA's various types of assistance programs. It explained that JICA's projects are based on the official requests from the recipient government

Fig. 14a: Example of yen loan by JICA

submitted through the diplomatic channel. The question on partnership with the private sector was also brought up by participants.

Comment from: Dr. Ngo Van Cong, Cho Ray Hospital, Viet Nam

"JICA organization helps a lot of developing countries. They produce right efficiency."

Fig. 14b: JICA representative presentation; Introducing JICA activities

3.6 Association of Clinical Research Professionals, Japan Chapter

The Association of Clinical Research Professionals (ACRP) is a Washington, D.C.-based non-profit organization with more than 13,000 members in more than 70 countries which supports clinical research professionals through membership, training, development, and certification. Activities and certification programs of ACRP, especially for the Certified Principal Investigator (CPI), were introduced. Also, as one of the global chapters, information of ACRP Japan's activities including educational programs and site visits abroad were shared at the session, as well as support for certification exam.

Comment from: Dr. Nsengi Ntamabyaliro, The Institut National de Recherche Biomédicale, DRC

"For me, it was good not only to discover that this association exists, but also that there is training materials, online trainings, webinars, and also certifications for different positions."

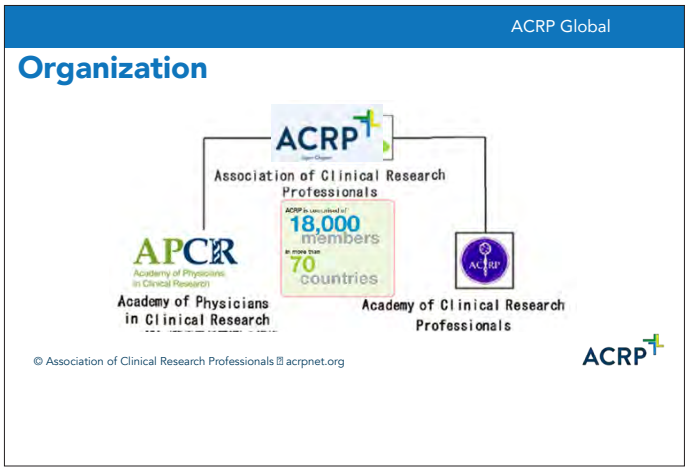


Fig. 15a: ACRP organization

Fig. 15b: ACRP - Japan members

3.7 Science Museum

With the intention of feeling the evolution of new technologies in relation to science in general and particularly in medicine and drug development, participants visited two museums, named National Museum of Emerging Science and Innovation: "MIRAIKAN" and Daiichi Sankyo Medicine Museum: "KUSURI MUSEUM".

Comment from: Dr. Mboloko Mata Junior, University of Kinshasa, DRC

"In "Miraikan", I was impressed by robots; it was so interesting to see how you can make science for better life."

3.7.1 National Museum of Emerging Science and Innovation: “MIRAIKAN”

Miraikan was created with the objective of deepening understanding of science and technology and fulfilling the Japan's aim of becoming a scientifically and technologically creative nation. Exhibitions include various discoveries highlighting technological progress, global environment, space exploration and life science.

Participants experienced medical discovery history such as the iPS cells, the importance of Artificial Intelligence in medical practice, laparoscopic surgery, etc.

Miraikan website: https://www.miraikan.jst.go.jp/en/aboutus/

Fig. 16a: Miraikan visit -1

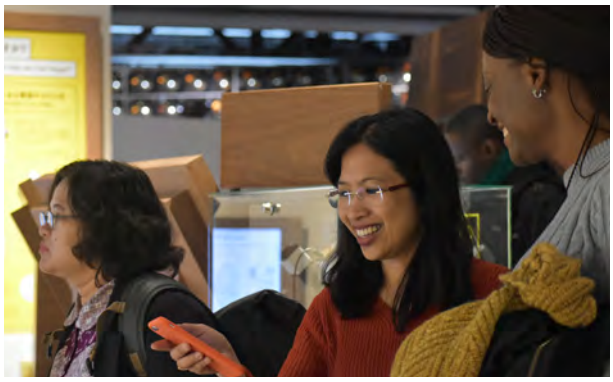


Fig. 16b: Miraikan visit -2

3.7.2 Daiichi Sankyo Medicine Museum: “KUSURI MUSEUM”

Kusuri Museum offers free facility visits in order to develop the proximity of medicine and drug development process to the general public. Inside the museum, participants could experience while playing the history of drug development.

Kusuri Museum website: https://kusuri-museum.com/intro

Fig. 17a: Kusuri Museum visit -1

Fig. 17b: Kusuri Museum visit -2

4. Open presentation session

The open presentation session had been planned to share the Challenges and Suggestions on Drug/Device Development situation in their respective countries with the registrants from inside and outside of NCGM. Unfortunately, it was canceled due to the outbreak of COVID-19. Presentations were instead shared with lecturers, participants, and registrants for the event, as well as uploaded to DIT's homepage.

Fig. 18: Open seminar flyer

5. Conclusion

The 2019 NCGM/CCS country-specific MRCT capacity building: “A program focused on comprehensive and collaborative training on medical innovations adapted to challenges of clinical trials in Asian and African countries, 2nd edition", a 14-day training program which brought 13 participants from 5 countries and 1 from Japan to enrich knowledge on regulatory management of MRCT’s data, the organization of Japanese clinical research/trials settings, Japanese government efforts for global health contribution, and storage of specimen for future research. In addition, they experienced the real world of research and drug development after learning which competencies are needed for clinical research professionals.

Although the open session was canceled, presentation slides were shared among lecturers, registrants and participants.

Comment from: Osaka University team,

Dr. Chisa Tabata:

“The most impressive part for me was the very good communication among trainees, lecturers, and NCGM members; I believe we can have a very good collaboration for MRCT in the future.”

Dr. Myoui:

“I hope you all enjoyed the program of NCGM.”

Dr. Nakatani:

“I hope this program will help you to deepen your experience and knowledge.”

Future Prospects

Thirteen researchers from five countries and one researcher from Japan were invited to participate in the 14-day training program held in January 2020, "A program focused on comprehensive and collaborative training on medical innovations adapted to challenges of clinical trials in Asian and African countries, 2nd edition".

The participants greatly appreciated the lecture on regulatory harmonization given by experts from the PMDA, as well as other lectures from the clinical setting (NCGM, NCC), academia (Osaka University), JICA, ACRP Japan, private company (SHIONOGI & CO., LTD), together with other opportunities to learn about situations in various countries. At the same time, however, they suggested that we should include more active training activities such as discussions with experts based on case studies.

We appreciate the continued guidance and encouragement provided by the relevant organizations and professionals.

Tatsuo Iiyama

Director, Department of International Trials,
Center for Clinical Sciences,
National Center for Global Health and Medicine

別添 / Appendix

別添 1 / Appendix 1　インターナショナルトライアル部　バナー / Department of International Trials banner

別添 2 / Appendix 2　スケジュール / Training Program Schedule

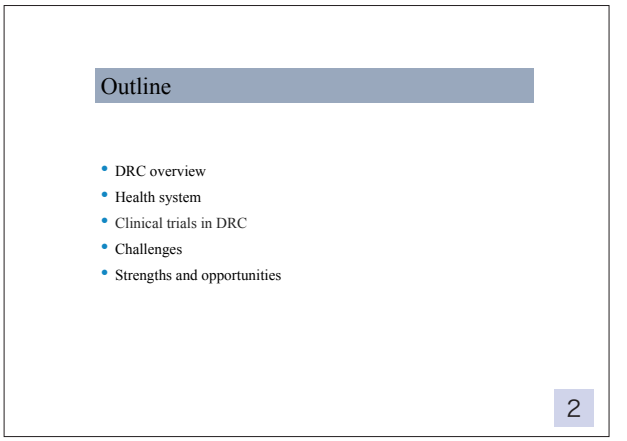
The 2020 NCGM/CCS Counry-Specific MRCT Capacity Building

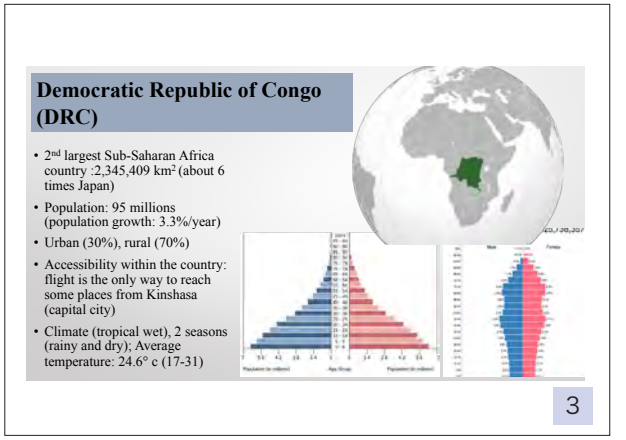
Duration: Jan. 18- Jan.31, 2020

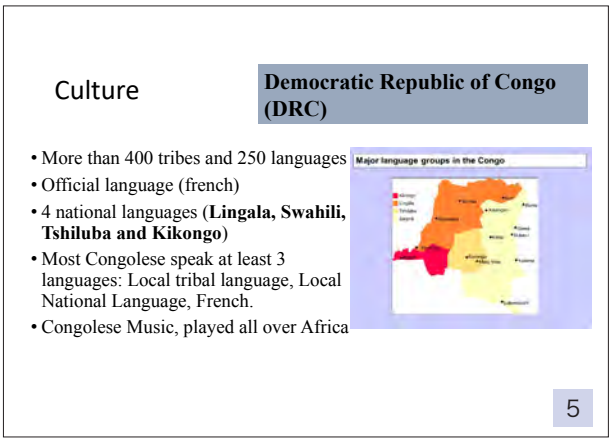
Date	Program
【Day1】 Jan. 18, 2020	Arrival
【Day 2】 Jan. 19, 2020	Orientation: Life in Japan, self-introduction, paperwork Lunch from 7-11 (convenience store) or LIFE (nearby supermarket) Introducing NCGM(Video) and DIT (lecture) Ice breaking activities
【Day 3】 Jan. 20, 2020	Lecture: PMDA Lunch Lecture: NCGM: DIT: Competency Wheel Lecture: PMDA
【Day 4】 Jan. 21, 2020	Lecture (plus facility visit): NCC Lunch Lecture: PMDA
【Day 5】 Jan. 22, 2020	Lecture: PMDA Lecture (plus facility visit): NCGM: DCC Lecture: NCGM: BIHC Lunch Preparation for presentation
【Day 6】 Jan. 23, 2020	Lecture: PMDA Lunch Lecture: PMDA
【Day 7】 Jan. 24, 2020	Greeting: NCGM President and NCGM Hospital Director Lecture: JICA Lecture: DRC delegate: Safety reporting and pharmacovigilance activities in practice Lunch Lecture (plus facility visit): National Center Biobank Lecture: ACRP, Japan Chapter
【Day 8】 Jan. 25, 2020	Kusuri Museum Lunch Miraikan museum
【Day 9】 Jan. 26, 2020	Presentation preparation day
【Date 10】 Jan. 27, 2020	Lecture: NCGM: Department of Data Science Lunch Lecture: NCGM: Research Institute: Tropical Medicine and Malaria Department Lecture: NCGM: DIT: Project collaboration with Thailand Lecture: Thai delegate: Case study of clinical trials from experience in Thailand
【Date 11】 Jan. 28, 2020	Travel to Osaka Lecture (plus facility visit): Shionogi & CO., LTD.
【Date 12】 Jan. 29, 2020	Lecture (plus facility visit): Osaka University Return to Tokyo
【Date 13】 Jan. 30, 2020	Presentation Session Certificate Ceremony
【Date 14】 Jan. 31, 2020	Departure

1. Challenge and Suggestions on Drug or Device Development in the Democratic Republic of the Congo (DRC)

Mboloko Mata Junior / Nsengi Ntamabyaliro







Health system

General secretariat
Centrel Directorates
Health Programs

Provincial Division

Health Zone

Health area

University Hospital

Provincial Hospital

General Referreal Hospital (Health Zone

Health Centre

Health system

University Clinics of Kinshasa

- Patients pay all healthcare services out of their pocket
- No public insurance
- Big firms provide healthcare to personnel
- Assistance provided by NGOs & donors to fight high-burden diseases
- Private sector still growing (in each level), agreements with PHD to be involved in the national policy

7

Health problems

✓**10 most causes of deaths, all ages**

- **Malaria**
- **Lower respiratory infection**
- **Tuberculosis**
- **Diarrheal diseases**
- **Cerebrovascular diseases**
- **Ischemic heart diseases**
- **Protein-energy malnutrition**
- **HIV/AIDS**
- **Preterm birth complications**
- **Birth asphyxia and trauma**

✓**Ten most causes of deaths < 5**

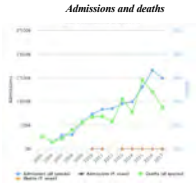
- **Malaria**
- **Lower respiratory infection**
- **Tuberculosis**
- **Diarrheal diseases**
- **Protein-energy malnutrition**
- **Neonatal preterm birth**
- **Neonatal encephalopathy**
- **HIV/AIDS**
- **Neonatal sepsis**
- **Congenital defects**

8

Health problems

Communicable diseases

Admissions and deaths



Malaria

Policies and strategies

12% of all malaria cases worldwide just after Nigeria (25%),
Reduction in malaria deaths but still slower.

https://www.severemalaria.org/countries/democratic-republic-of-congo

9

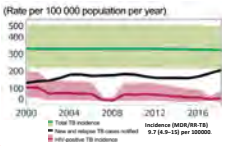
Health problems

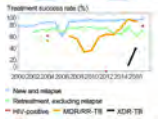
Communicable diseases

Tuberculosis

Situation (Deaths)

(Rate per 100 000 population per year)





1. Top 10
2. All 3 of WHO's high burden
3. Treatment coverage 57%, low treatment success rate, Low detection rate 48%

Mortality Rate per 100 000 population per year

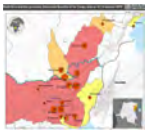
10

Health problems

Two major outbreaks ongoing

Ebola outbreak: Eastern regions

- As of 09 January 2020:
- **3416** cases,
- **2240** deaths,
- **1142** survivors



Measles outbreak: allover the country

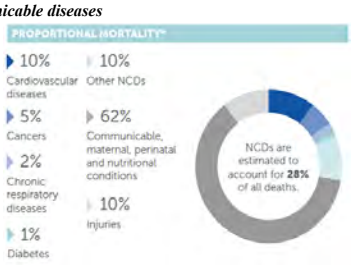
(The worst outbreak, WHO says)
As of 07 Jan 2020

- Over **6000** deaths
- **310 000** suspected measles cases
- **18 million** children under 5 vaccinated

11

Health problems

Non communicable diseases



12

Health problems

Neglected diseases

Human African Trypanosomiasis (HAT) towards elimination:

- from 27,000 case in 1996 to
- **650** in 2018.

Elimination: 2020

38.4 million people received treatment in D.R. Congo in 2016

11.5 million people in need did not receive treatment in D.R. Congo in 2016

13

Clinical trials: status and infrastructures

73 studies registered in Clinicaltrials.gov. with 13 phase 2 studies and 2 phase 1studies.

113 CT registered in the International Clinical Trials Registry Platform (WHO)

Laboratories and research institutions
- Institut national de recherche biologique(INRB)
- Pronanut: (National program for nutrition)

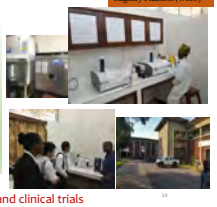
Institut de recherche sur les sciences de la santé (IRSS)

Centre national de transfusion sanguine(CNTS)

Centre de recherche en Maladies Tropicales de l'Ituri

Research institutions (Public and Private Universities)

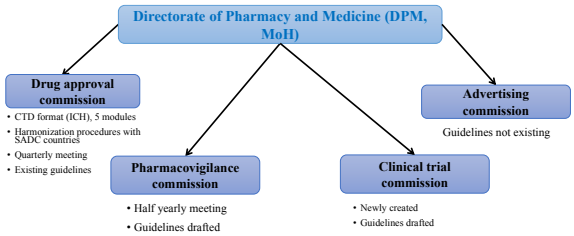
Research institutions(Universities)
University of Kinshasa
University of Lubumbashi
University of Bukavu
University of Goma
Catholic University of Graben
University of Kisangani
Kongo University
Others provincials and privates Universities



There is a lack of facilities and equipment for drug development and clinical trials

14

Clinical trials: regulatory matters



15

15

Research centres and consortia exemples

Institut National de Recherche Biomédicale
- Expertise in Ebola, Monkeypox, Typhoid Fever ...
- Now with a Clinical Trial Centre (Jica funds)

School of Public Heqalth. Clinical trials in collaboration with Oxford University; UNC

Alliance for Clinical Research and Clinical Epidemiology in the DRC (ARCEAU),
- Swiss Tropical and Public Health Institute (TPH), Kinshasa School of Public Health, and the UPC-PV

Central Africa Clinical Research Network (CANTAM)
- Collaboration with colleagues from Congo-Brazzaville and Cameroon, Gabon, Zambia
- Phase IV study of Pyramax
- Training for pharmacovigilance

Centre de Recherche en Santé, Kimpese. Collaboraton with Tropical medicine Intitute, Antwerp, Belgium

PALM consortium
- Collaboration with the INRB: PV working group
- RCT of experimental anti-Ebola drugs
- Training for GCP and safety
- Collection and analysis of AEs, SAEs, deaths, pregnancies and unanticipated problems

16

Clinical trial: examples

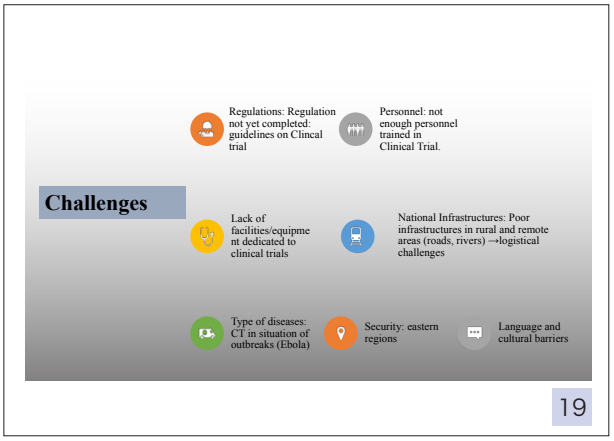
Study title	Condition	Intervention	Location	Sponsor
Investigational Therapeutics for the Treatment of People With Ebola Virus Disease (multioutbreak, multicentre RCT)	Ebola	mAb114, REGN-EB3	Beni, Butembi, Katwa, Mangina	NIH
Cohort Event Monitoring Study of Pyramax®	Malaria	Pyramax	DRC (Kinshasa, Kimpese), Congo, Gabon, Cameroon, Ivory Coast, Switzerland (Closeout visit soon	MMV/Shin Poong
Prospective Study on Efficacy and Safety of SCYX-7158 in Patients Infected by Human African Trypanosomiasis Due to T.b. Gambiense	Human African Trypanosomiasis	Acoziborole	Many locations (12) in DR Congo and 1 site in Guinea	DNDi
DIAgnostics for Multidrug Resistant Tuberculosis in Africa	MDR Tuberculosis	Diagnostic Tesst: Deeplex test, InSilixa chip assay, GeneXpert Fluorescein DiAcetate (FDA)	INRB, ITM Antwerp, some countries	Laboratoire de Référence des Mycobactéries

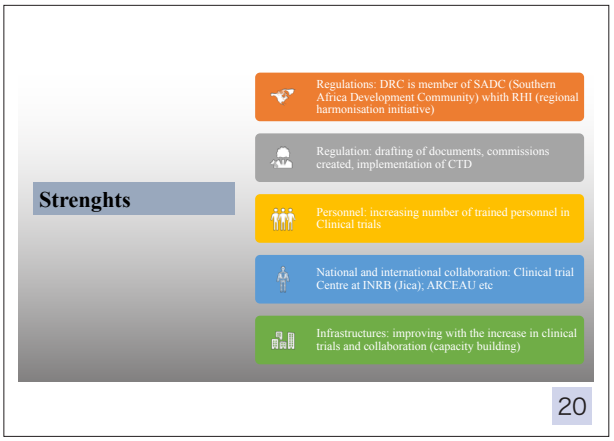
17

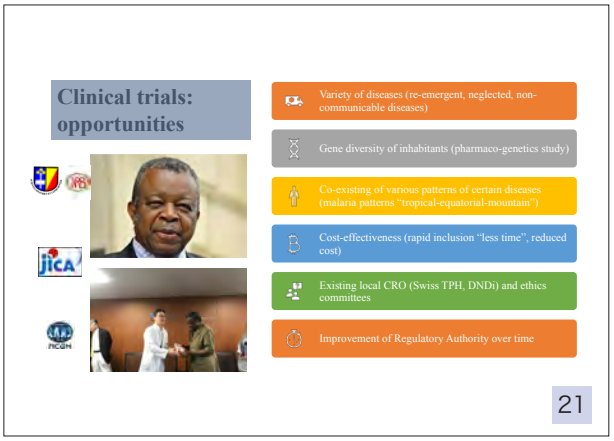
Clinical trial: examples

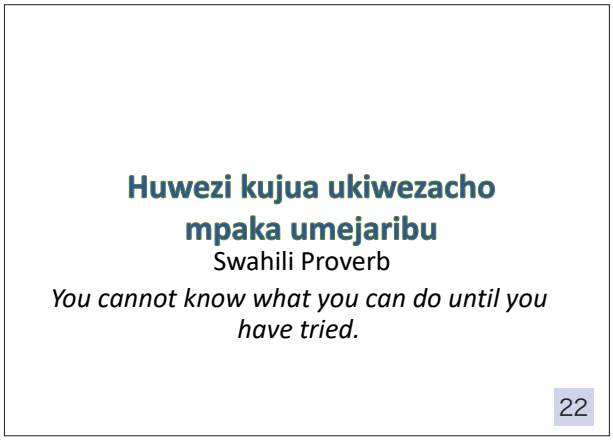
Study title	Condition	Intervention	Location	Sponsor
Diagnostic Tools for Human African Trypanosomiasis Elimination and Clinical Trials: Early Test-of-cure (DiTECT-WP4)	African Trypanosomiasis	Diagnostic Test: RNA and neopterin detection	Many sites in the country	Institute of Tropical Medicine (Belgium)
Arresting Vertical Transmission of Hepatitis B Virus (AVERT-HBV)	Hepatitis B	Tenofovir Disoproxil Fumarate, Monovalent HBV vaccine	Kinshasa	University of North Carolina
Community Access to Rectal Artesunate for Malaria (CARAMAL)	Malaria	Rectal artesunate	DR Congo, Nigeria, Uganda	UNITAID, SWISS TPH, CHAI, UNICEF
Fexinidazole in Human African Trypanosomiasis Due to T.b. Gambiense at Any Stage (FEX009)	Human African Trypanosomiasis	Feninidazole	Many locations in DR Congo	DNDi

18


Challenges
Regulations: Regulation not yet completed: guidelines on Clincal trial
Personnel: not enough personnel trained in Clinical Trial.
Lack of facilities/equipme nt dedicated to clinical trials
National Infrastructures: Poor infrastructures in rural and remote areas (roads, rivers) →logistical challenges
Type of diseases: CT in situation of outbreaks (Ebola)
Security: eastern regions
Language and cultural barriers
19


Strenghts
Regulations: DRC is member of SADC (Southern Africa Development Community) whith RHI (regional harmonisation initiative)
Regulation: drafting of documents, commissions created, implementation of CTD
Personnel: increasing number of trained personnel in Clinical trials
National and international collaboration: Clinical trial Centre at INRB (Jica); ARCEAU etc
Infrastructures: improving with the increase in clinical trials and collaboration (capacity building)
20


Clinical trials: opportunities
JICA
Variety of diseases (re-emergent, neglected, non-communicable diseases)
Gene diversity of inhabitants (pharmaco-genetics study)
Co-existing of various patterns of certain diseases (malaria patterns "tropical-equatorial-mountain")
Cost-effectiveness (rapid inclusion "less time", reduced cost)
Existing local CRO (Swiss TPH, DNDi) and ethics committees
Improvement of Regulatory Authority over time
21


Huwezi kujua ukiwezacho mpaka umejaribu
Swahili Proverb
You cannot know what you can do until you have tried.
22

2. Challenge and Suggestions on Drug or Device Development in Indonesia

Maria Lawrensia Tampubolon / Melva Louisa Simbolon / Dina Nilasari

Challenge and suggestion on drug or device development in Indonesia

Maria Lawrensia Tampubolon (SS-IDH)
Melva Louisa Simbolon (Faculty of Medicine University of Indonesia)
Dina Nilasari (Mochtar Riady Institute)

1

INDONESIA :
About 17.000 islands,
rainy and dry season, 714
ethnic

2

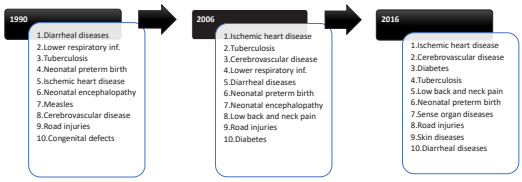
Indonesia

Statistics	
Total population (2016)	261,115,000
Gross national income per capita (PPP international $, 2013)	9,280
Life expectancy at birth m/f (years, 2016)	67/71
Probability of dying under five (per 1 000 live births, 2016)	23
Probability of dying between 15 and 60 years m/f (per 1 000 population, 2016)	205/146
Total expenditure on health per capita (Intl $, 2014)	299
Total expenditure on health as % of GDP (2014)	2.9

https://www.who.int/countries/idn/en/

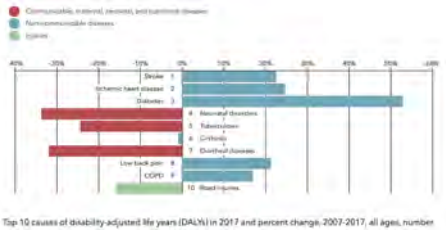
3

Leading cause of Disability Adjusted Life Years (DALYs): 1990 – 2006 - 2016



4

Top 10 Cause of Death and Disability in Indonesia



Top 10 causes of disability-adjusted life years (DALYs) in 2017 and percent change, 2007-2017, all ages, number

https://www.who.int/countries/idn/en/

5

Risk factors for deaths and disability combined

https://www.who.int/countries/idn/en/

6

Unmet Needs in Drug Development in Indonesia

- The rise of NCD → Management of risk factors and treatment for CVD
- Tuberculosis, neonatal preterm birth complications, diarrheal, and lower respiratory tract infections are still substantial contributors to DALYs
- Neglected tropical diseases: filariasis, leprosy
- Rare diseases
- Drug resistant organisms (MDR TB, Drug resistant malaria)

Mboi N. On the road to universal health care in Indonesia. Lancet 2018; 392: 581–91
Maharani A, Tampubolon G. Unmet Needs for Cardiovascular Care in Indonesia. PLOS ONE; 2014: 9(8): e105831.
Riskesdas 2018.

7

10 Most Infectious Disease cases at Outpatient unit in SS-IDH in 2016 - 2018

2016	2017	2018
• HIV • Tuberculosis • Acute respiratory Infection • Ear diseases & Prosesus Mastoid • Pneumonia • Diarrhea • Gastritis • Urinary Tract Infection • Pharyngitis • Dengue Hemorrhagic Fever (DHF)	• HIV • Tuberculosis • Acute Respiratory Infection • Ear diseases & Prosesus Mastoid • Diarrhea • Bronkitis, Emfisema & Others Obstructive Pulmonary Diseases • Pneumonia • Urinary Tract Infection • Pharyngitis • Dermatitis	• HIV • Tuberculosis • Other Primary arthrosis • Acute Respiratory Infection • Chronic Obstructive Pulmonary Disease • Diarrhea • Pneumonia • Otitis Media • Urinary Tract Infection • Pulpitis

8

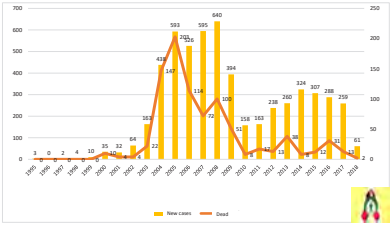
10 Most Infectious Disease cases at Inpatient unit in SS-IDH in 2016 – 2018

2016	2017	2018
• HIV • Dengue Hemorrhagic Fever (DHF) • Tuberculosis • Diarrhea • Gastritis • Pneumonia • Sepsis • Typhoid Fever • Acute Respiratory Infection • Urinary Tract Infection	• HIV • Dispepsia • Tuberculosis • Diarrhea • Pneumonia • Acute Respiratory Infection • Urinary Tract Infection • Typhoid Fever • Dengue Hemorrhagic Fever (DHF) • Sepsis	• HIV • Diarrhea • Chronic Obstructive Pulmonary Disease • Tuberculosis • Acute respiratory Infection • Typhoid Fever • Dyphteria • Dengue Hemorrhagic Fever (DHF) • Pneumonia • Urinary Tract Infection

9

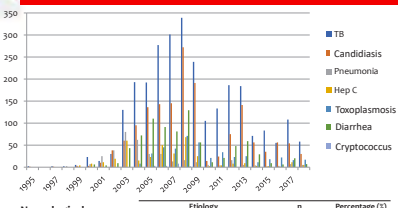
Number of New Cases and Deaths Due to HIV-AIDS in RSPI-SS in 1995-2018

until Feb 2018



10

Opportunistic infection in HIV-AIDS pts

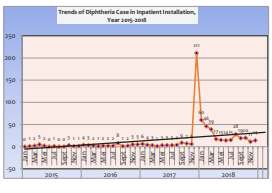


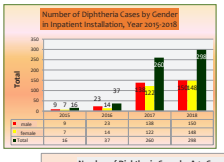
Neurological complication in HIV 2016-2019

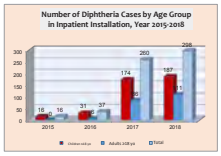
Etiology	n	Percentage (%)
• Toxoplasma	51	83,6
• Tuberculosis Meningitis	4	6,6
• N/A	6	9,8

11

DIPHTHERIA SURVEILLANCE







12

Clinical Trials in Indonesia

Source: http://clinicaltrials.gov
Assessed: 24th January 2020

13

Advantages and challenges for CT in Indonesia

Advantages

- Large patient population
- Wide variety of diseases
- Lower trial cost per patient
- Availability of research subjects
- Many tropical diseases that can not be explored in non-tropical countries
- Regulatory bodies: in compliance with ICH-GCP

Challenges

- Lack of insurance companies that covers clinical trial patients
- Material Transfer Agreement (MTA)
- Variable research capability of investigators to conduct CT

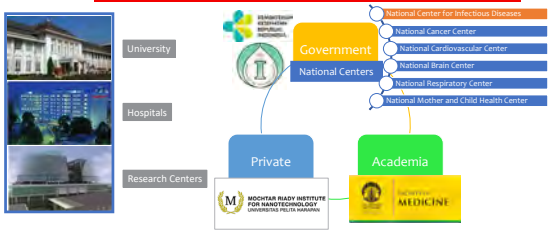
14

Regulatory and EC timelines (Sequential)

Ali S et al. Challenges of conducting clinical trials in Asia. Int J Clin Trials. 2018 Nov;5(4):194-199

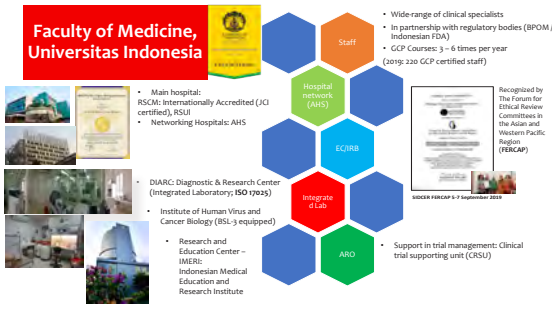
15

Pool of Clinical Investigators and Patients



16

Faculty of Medicine, Universitas Indonesia



17

RSCM

ACADEMIC HEALTH SYSTEM UNIVERSITY OF INDONESIA (AHS-UI)

Member of AAHCI (Association of Academic Health Center International)

18

IMERI MILESTONES

2016 — 2021 — 2026

ESTABLISHMENT ORGANIZATION

Indonesian Medical Science Techno-Park

Research focus

- Drug development: NCD and IDs
- Vaccine development
- Contraceptive method development
- Medical technology (medical instrumentation, tele-medicine, IT)

Indonesian human genetic research center
Indonesian human reproduction and family planning research center
Indonesian stem cell research center
Indonesian medical education research and development center
Indonesian clinical research supporting unit

19

Other Clinical Studies

Clinical research
On going studies
Diagnostic Research

22

FMUI's current international collaboration

(based on number of publications indexed in Scopus)

20

Sulianti Saroso Infectious Disease Hospital (SS-IDH)

Location Map

JL. BARU SUNTER PERMAI RAYA
NORTH JAKARTA
14340
Indonesia

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Clinical Trials

Early phase | Phase 2 | Phase 3 | Post Marketing Surveillance

Otsuka Japan

Otsuka Japan

21

Hospital profile

- Technical Unit of the Ministry of Health, Republic of Indonesia.
- Specific Hospital for Infectious Diseases, Type A hospital with National Accreditation (SNARS ED.1)
- Teaching Hospital (AHS – UI)
- 156 beds
- Primary health care network

24

Ward

ROOM TYPE	NUMBER
HCU	7
VVIP	2
VIP	3
CLASS I	26
CLASS II	19
CLASS III	72
PERINA	5
MDR TB ISOLATION	2
HIGH-RISK ISOLATION	10
ICU HIGH RISK ISOLATION	1
GENERAL ISOLATION	4
TOTAL	156

25

HIV clinic

26

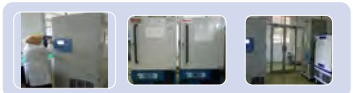
TB-MDR CLINIC

27

Clinic monitoring for clinical research/clinical trial

28

Biobank facilities in Sulianti Saroso hospital disease



Freezer -80°C, 2 unit	Fridge -20°C, 1 unit	Refrigerator 4°C, 1 unit

29

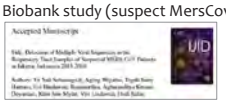
SS-IDH Institutional collaboration

- NCGM
- National Institute Health and Research Development - Ministry of Health Republic of Indonesia
- INA RESPOND : multicenter clinical research network in Indonesia
- Academic health system – University of Indonesia (AHS –UI)
- Eijkman institute
- Bandung technology Institute
- Primary health care network in North Jakarta

30

SS-IDH On going Research Activities

- Proactive study (HIV)
- TB study
- AMR study
- Diptheria study
- NeuroAIDS study
- Biobank study (suspect MersCov study has been published)



31

MRIN

32

Hospitals profiles

Name	Class	Region	Year Opened	Bed Capacity	Operational Beds	GPs & Specialists	Nurses
SH Lippo Village	B	1. Greater Jakarta	1996	308	274	279	373
SH Kelton Jeruk	B	1. Greater Jakarta	2002	265	214	212	333
MRCCC Siloam Semanggi	B	1. Greater Jakarta	2011	334	178	187	248

33

Collaboration opportunities

Infectious Diseases (IDs)	Non Communicable Diseases (NCDs)
• TB • HIV incl. opportunistic infection • Emerging and re-emerging infectious diseases (ERID) • Vaccine (avian flu; "halal product" issue) • Evaluate failed therapy for infectious disease (HIV TB, diphtheria, etc.) • Research that utilizes Biobank (note: research on biobank negative suspects of Mers have been published) • Drug Resistance in Malaria	• Tobacco related diseases • Treatment and Risk Factor Management of NCDs (Metabolic syndrome) • Stunting • Pregnant women morbidity

34

Suggestions

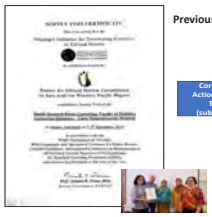
- Clinical research/clinical trial proposal should be made together
- Affordable and low technology medical/health devices
- Capacity building for how to build a good system for clinical research/ clinical trial

35

Thank You

36

Ethics Committee: Recognized by FERCAP



Previous Recognition:
2012
2016

Corrective Action Plans & Time (submitted)

Re-Recognition FERCAP Certificate 2019

SIDCER FERCAP 5-7 September 2019

37

DIARC: Diagnostic & Research Center (Integrated Laboratory)

Implemented ISO 17025

Molecular Biology Unit	Protein and Immunology Unit	Cell Culture Unit	Imaging & Electrophysiology Unit
PCR RT-PCR Sequencer (Mi-Seq) Microarray	Immulite VIDAS Multiscan ELISA Reader Flowcytometry Luminex	*Culture room* Biosafety Cabinet MACS	Patch-Clamp Instrument Confocal microscope Dissecting Microscope

38

Institute of Human Virus and Cancer Biology

Equipped with BSL-3 facility

Topics of Research:
- HIV, CMV, Dengue --> mainly on the study of pathogenesis & vaccine development
- Cervical Cancer

Public Service
- Plasma Cluster Air Conditioner testing (Sharp)
- NanoEx Ion activity testing (Panasonic)
- GLP, ISO, Biosafety Consult

39

Research and Education Center – IMERI: Indonesian Medical Education and Research Institute

40

RSCM – Cipto Mangunkusumo General Hospital

- National Referral Hospital,
- Under Ministry of Health
- Internationally Accredited
- FMUI's main teaching hospital

KENCANA- Private Ward

KIRANA- Ophtalmologic Ward

KIARA- Mother & Child Ward

Cardiology Ward

Radiotherapy

Kidney Transplant

Liver Transplant

HIV Unit

Stem Cell Unit

Cochlea Implant

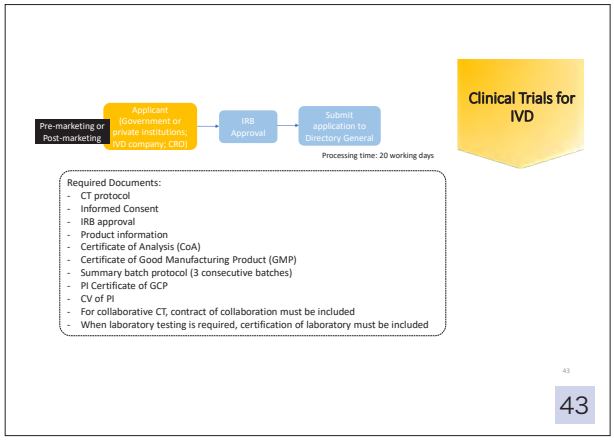
41

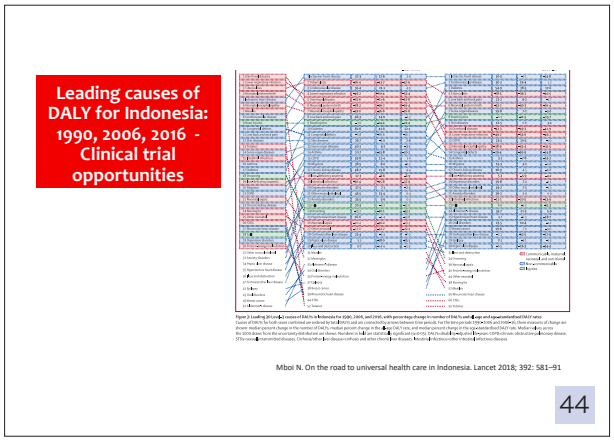
RSUI: Universitas Indonesia Hospital

- Teaching hospital
- Official opening: 13 Feb 2019
- Neuro-cardiovascular diseases, geriatrics, mother-child health, dental health

- 1st clinical trial that will be conducted:
  - Dose-ranging study of drug XXX
  - Phase 2
  - A randomized, double-blind, placebo-controlled for obesity
  - Planned FPFV: end Jan 2020
  - Sponsor: Malaysian Pharmaceutical Company

42


Pre-marketing or Post-marketing
Applicant (Government or private institutions; IVD company; CRO)
IRB Approval
Submit application to Directory General
Processing time: 20 working days
Clinical Trials for IVD
Required Documents:
- CT protocol
- Informed Consent
- IRB approval
- Product information
- Certificate of Analysis (CoA)
- Certificate of Good Manufacturing Product (GMP)
- Summary batch protocol (3 consecutive batches)
- PI Certificate of GCP
- CV of PI
- For collaborative CT, contract of collaboration must be included
- When laboratory testing is required, certification of laboratory must be included
43
43


Leading causes of DALY for Indonesia: 1990, 2006, 2016 - Clinical trial opportunities
Mboi N. On the road to universal health care in Indonesia. Lancet 2018; 392: 581–91
44

3. Challenge and Suggestions on Drug or Device Development in the Philippines

Maria Elizabeth Mercado / Jay Ron O. Padua / Gelza Mae Almario Zabat

Philippine Delegates

University of the Philippines, National Institutes of Health (UP-NIH)

MARIA ELIZABETH P. MERCADO, MD, MAS- Clinical Research

- Project Staff for Executive Director of UP Manila National Institutes of Health; Teaching Assistant to John S. Witte PhD in Molecular and Genetic Epidemiology
- Masters in Clinical Research University of California, San Francisco Department of Epidemiology and Biostatistics.
- Certifications: Advanced GCP (UP Manila DCE), Human Subjects Protection Training Stage 1 (CITI Program)
- Member, Asian Association for the Study of Diabetes (AASD)

San Lazaro Hospital (SLH)

JAY RON O. PADUA, MD, FPPS, FPIDSP- Pediatric Infectious Disease Specialist

- Medical Specialist III, San Lazaro Hospital
- Fellow, Philippine Pediatric Society and the Pediatric Infectious Disease Society of the Philippines
- Life member, Asian Society for Pediatric infectious Diseases
- Visitor Observership and Clinical Preceptorship, Baylor College of Medicine, Texas Children's Hospital
- Participant, The 18th Nagasaki International Course on Research Ethics, Nagasaki University

St. Luke's Medical Center (SLMC)

GELZA MAE A. ZABAT, MD, FPCP, FPSMID- Internal Medicine- Infectious Disease Specialist

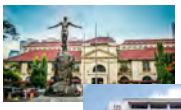
- Member, SLMC Institutional Ethics Review Committee; Head, HIV/AIDS Treatment Hub, SLMC-QC
- Member, Infectious Disease Society of America
- Recent trainings: The Role of Diagnostics in the Antimicrobial Resistance Response, London School of Hygiene & Tropical Medicine; The 18th Nagasaki International Course on Research Ethics, Nagasaki University; Comprehensive Tuberculosis Course, Curry International Tuberculosis Center, UCSF

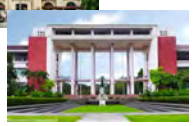
1

National Institutes of Health

University of the Philippines Manila

- an institutional home of a network of various research and extension units specializing in health and socio-biomedical concerns.





- **Strengths of the Institutes**
  - Recognition as Center of Excellence/Influence/Policy
  - Multidisciplinary nature and approach
  - Community-based/oriented programs
  - Research management available
  - Committee on research implementation and development/Ethics boards
  - Recognition for outstanding researches

Registered Clinical Trials			
Industry Funded	Academia	Local Collaborations	International Collaborations
91	5	21	12

http://nih.upm.edu.ph/about-nih/organization

2

St. Luke's Medical Center

Quezon City · Global City

Joint Commission International

Ongoing clinical trials	103
Phase I	3
Phase I/II	1
Phase II	6
Phase II/III	2
Phase IIB	1
Phase III	70
Phase IIIB	1
Phase IV	2
PMS	1
Others	16

- Internationally recognized private academic medical center
  - Accredited by Joint Commission International (JCI) as an academic medical center hospital
  - Trust, Effective Medicine, and Optimized Services (TEMOS)- accredited for excellence in medical tourism and quality in international patient care
- Research and Biotechnology Group (R&B)
  - offers a Master of Science Program in Molecular Medicine
  - Center for Clinical Trials (CCT)
  - Level 3 Institutional Ethics Review Committee (IERC), recognized by SIDCER and FERCAP
  - Biobank for Cancer
  - Center for Human Research Protection and Office of Research Integrity

www.stlukes.com.ph

3

SAN LAZARO HOSPITAL

- Founded 1577
- 500-bed capacity
- National referral facility for Infectious and Tropical Diseases
- One of the retained special tertiary hospital of the Department of Health (DOH), subsidized by the national government
- National Reference Laboratory for Tests on HIV/AIDS, Hepatitis and STIs
- Treatment Hub for HIV/AIDS, TB-DOTS, MDR-TB
- Animal Bite and Treatment Center, including snake bite management
- With an in-hospital mini-laboratory run by Nagasaki University
- Has a Research Ethics and Review Unit, Level III accredited by PHREB
- Has residency training program on Family Medicine and Fellowship training program in Adult Infectious Diseases
- Clinical rotation for medical clerks from 9 medical schools as well as students from Nagasaki, Oita, Kansai, Kobe, Tohoku, and Tottori universities

4

NCGM

Challenges and Suggestions on Drug/Device Development in the PHILIPPINES

5

PHILIPPINES

- Land area: 300,000 km²
  - 7,107 islands
  - Three major islands: Luzon, Visayas, Mindanao
- 13th most populous country in the world and 7th in Asia
  - Population: 104.0 million (as of 2017)
  - Population density: 342 persons/km²
- Life expectancy of 69.1 years (from 62.2 years in 1980)
  - improvements in living conditions, better access to health services, and improved management and treatment of infectious diseases

(Padilla & Cutiongco-de la Paz, 2016; Dayrit et. al, 2018)

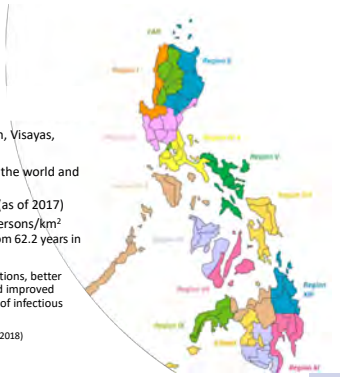


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Figure 2.2 Organizational structure showing the health offices devolved to the LGUs

(Dayrit et. al, 2018)

7

Current Health Situation

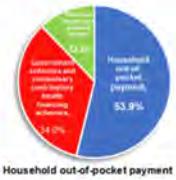
Physical Infrastructure

- 1,224 hospitals
- 2,587 city/rural health units
- 20,216 barangay health stations

Health Professional	Total	HCW density/ 10000 pop
Nurses	90 308	8.6
Midwives	43 044	4.1
Doctors	40 775	3.9
Medical Technologists	13 413	1.3

(Dayrit et. al, 2018)

FIGURE 3 Current Health Expenditures by Financing Scheme, Philippines: 2018



- Household out-of-pocket payment
- Government schemes and compulsary contributory health financing schemes
- Voluntary health care payment schemes

8

Leading Causes of Death in Philippines, 2017

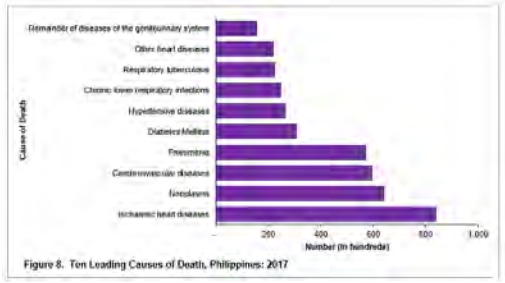


Figure 8. Ten Leading Causes of Death, Philippines: 2017

Philippine Statistics Authority, June 10, 2019

9

2019 is a challenging year for the Health Sector

Measles outbreak – February

- 42, 000 cases
- 560 deaths

Dengue outbreak – August

- 350, 000 cases
- More than 1, 300 related deaths

Polio Outbreak – September

- **19 years** after being declared **"Polio-Free"**
- 16 cases cVDPs

10

Triple Burden of Disease

COMMUNICABLE DISEASES

- HIV/AIDS, TB, Malaria
- Diseases for Elimination
- Dengue, Lepto, Ebola, Zika

NON-COMMUNICABLE DISEASES & MALNUTRITION

- Cancer, Diabetes, Heart Disease and their Risk Factors - obesity, smoking, diet, sedentary lifestyle
- Malnutrition

DISEASES OF RAPID URBANIZATION & INDUSTRIALIZATION

- Injuries
- Substance abuse
- Mental Illness
- Pandemics, Travel Medicine
- Health consequences of climate change / disaster

(Cabral, 2016; Department of Health, 2019)

- Current health burden is summarized and addressed by the Philippine Health Agenda made by the Department of Health (DOH)

11

GOALS

The Health System We Aspire For

FINANCIAL PROTECTION

Filipinos, especially the poor, marginalized, and vulnerable are protected from high cost of health care

BETTER HEALTH OUTCOMES

Filipinos attain the best possible health outcomes with no disparity

RESPONSIVENESS

Filipinos feel respected, valued, and empowered in all of their interaction with the health system

12

National Unified Health Research Agenda (NUHRA)

- outlines the areas and topics that needs to be addressed in the Philippines for the next five years.
- Put together by the Philippine National Health Research Systems (PNHRS)
  - Core agencies:
    - Department of Health (DOH)
    - Philippine Council for Health Research and Development (PCHRD)
    - Commission on Higher Education (CHED)
    - University of the Philippines Manila – National Institutes of Health (UPM – NIH)

(Lopez et al., 2019; PNHRS)

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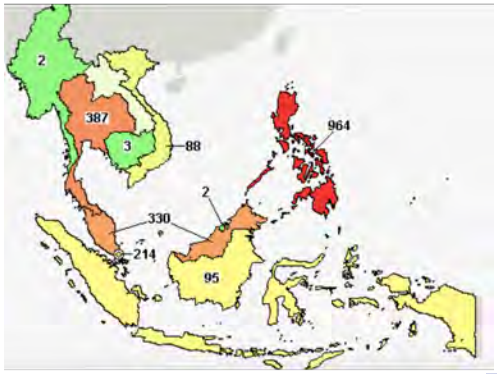

https://clinicaltrials.gov/ct2/results?cntry=PH&Search=Clear&age_v=&gndr=&type=&rslt=

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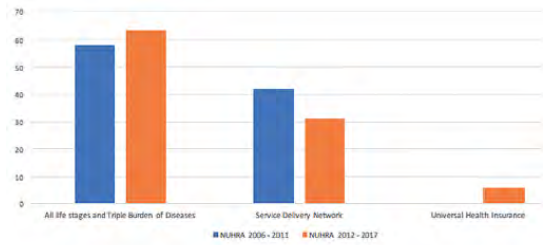

Figure 3. Percentage of NUHRA health research outputs towards addressing the Philippine Health Agenda.

(Lopez et al., 2019; PNHRS)

14

International Trials in the Philippines as of January 2020 from ClinicalTrials.gov

Study Phase	Completed	Ongoing	Total
Early Phase 1	1	0	**1**
Phase 1	15	2	**17**
Phase 2	111	27	**138**
Phase 3	401	96	**497**
Phase 4	84	6	**90**
Others	73	32	**105**
Total	**685**	**163**	**848**

https://clinicaltrials.gov/ct2/results?cntry=PH&Search=Clear&age_v=&gndr=&type=&rslt=

17

(Lopez et al., 2019; PNHRS)

15

http://www.registry.healthresearch.ph/index.php/registry?view=reports&layout=yearly

18

Ongoing Collaborative Researches with Japan-based Institutions (N = 31)

Dokkyo Medical University	1	Santen Pharmaceutical Co., Ltd.	1
Eisai Co., Ltd.	2	Santen Philippines Inc.	1
Hi-Eisai Pharmaceutical, Inc	1	Shionogi	1
Kyushu University, Faculty of Agriculture	1	Shire	2
Kyushu University, Mishima-Kaiun Foundation	1	Shire Human Genetic Therapies, Inc	1
Nagasaki University, Institutes of Tropical Medicine	1	Takeda Development Center Asia, Pte. Ltd.	3
Otsuka Pharmaceutical Co., Ltd.	1	Takeda Global Research and Development Center	1
Otsuka Pharmaceutical Development and Commercialization, Inc.	2	Takeda Pharmaceutical (Philippines), Inc.	1
Philippine Nikkei Jin Kai Polyclinic and Diagnostic Center, Inc.	4	Takeda Vaccines, Inc.	1
		Takeda Vaccines, Pte. Ltd	3
		Tohoku University	1
		Tokyo Metropolitan University	1

http://www.registry.healthresearch.ph/index.php/registry?view=reports&layout=institution

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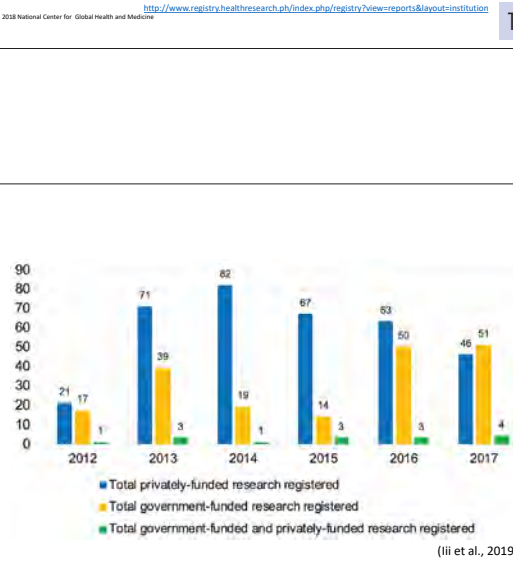

(Iii et al., 2019)

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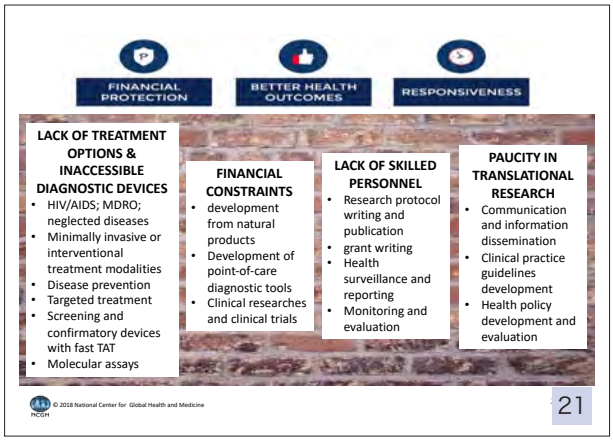

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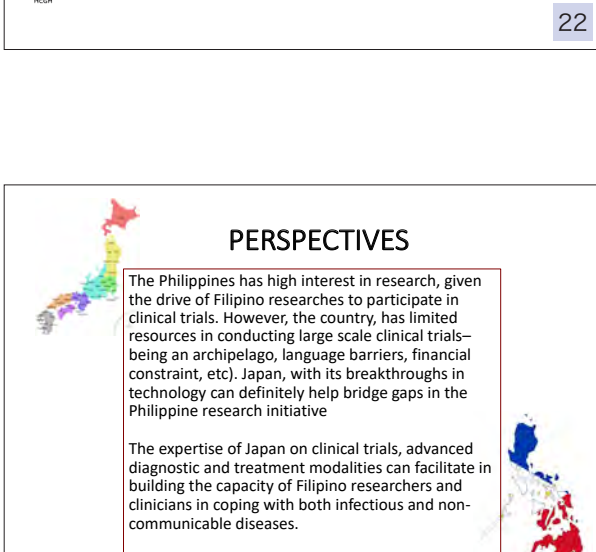

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PERSPECTIVES

The Philippines has high interest in research, given the drive of Filipino researches to participate in clinical trials. However, the country, has limited resources in conducting large scale clinical trials– being an archipelago, language barriers, financial constraint, etc). Japan, with its breakthroughs in technology can definitely help bridge gaps in the Philippine research initiative

The expertise of Japan on clinical trials, advanced diagnostic and treatment modalities can facilitate in building the capacity of Filipino researchers and clinicians in coping with both infectious and non-communicable diseases.

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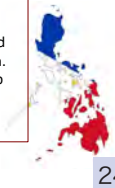
PERSPECTIVES

The collaboration between the Philippines and Japan has always been present. We hope to strengthen these towards the fulfillment of UHC in the Philippines. Financial support, digitalization, technology and knowledge transfer including disaster preparedness and response to disease outbreaks and climate change.

Clinical researches on preventive medicine, infectious diseases and NCDs, newer treatment and diagnostic modalities- gearing more to targeted and personalized medicine are great avenues for research collaboration. Translational and operational researches can also help improve the current health system in the Philippines.



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SALAMAT! THANK YOU! ARIGATO! MERCI! KHOB KUN! CAM ON! TERIMA KASIH! ASANTE!

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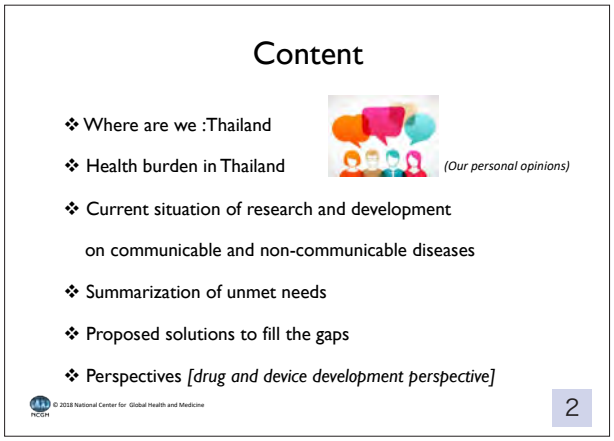
4. Challenge and Suggestions on Drug or Device Development in Thailand

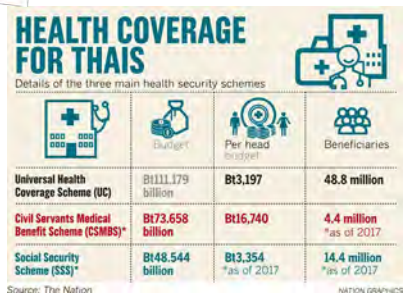
Suvimol Niyomnaitham / Noppadon Tangpukdee / Weerawat Kiddee



Credit:https://theitravelchannel.tv

7

Health care coverage for Thais



https://www.nationthailand.com/national/30346131

10

Phase I clinical trial facilities

https://sicres.org

8

Thailand health burden

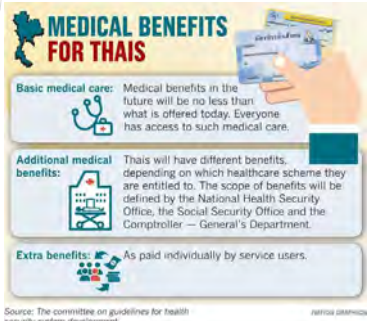
Non-communicable disease > communicable disease

Leading cause of death

1) Cancer
2) Road traffic accident
3) Cardiovascular disease

11

Health care benefits for Thais



https://www.nationthailand.com/national/3034

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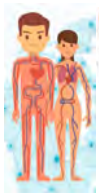
Thailand health burden *(Cont.)*



Non-communicable disease > communicable disease

Number one cause of death among Thais is cancer-related diseases

The Ministry of Health has identified that cancer is the number one killer of Thai citizens since 1998, adding that out of 122,757 new cases diagnosed in 2019, 73,000 patients have died

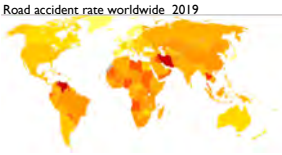
Source: https://thethaiger.com

12

Thailand health burden *(Cont.)*

2.1 Non-communicable disease > communicable disease

Road accident rate worldwide 2019



Emerging problem: respiratory diseases related to PM 2.5 pollution

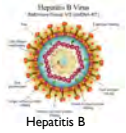
Source: https://www.nationthailand.com

13

Thailand health burden *(Cont.)*

2) Communicable diseases

- ○AMR
- ○TB, RR-/MDR-TB
- ○Hepatitis B
- ○Dengue



Hepatitis B

In 2019, the dengue case is around 114,449 cases with 122 case death (until 11 Nov.) which is highest case during 5 years.

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Current situation of research and development on communicable and non-communicable diseases

3.1 Communicable diseases

- ❖ HIV research
  - ❖New regimen/to cure HIV
- ❖ Hepatitis B
- ❖ Dengue
- ❖ Malaria
- ❖ TB

3.2 Non-communicable diseases

- ❖ Cancer
- ❖ Cardiovascular diseases: HT, CAD: anticoagulants
- ❖ Metabolic diseases e.g. DM
- ❖ Road traffic accident prevention study : ?

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Current situation of research and development **on communicable diseases**

THAILAND'S ACHIEVEMENTS IN HIV TREATMENT, PREVENTION, AND CURE RESEARCH

Author(s):
Praphan Phanuphak[1]

[1]Thai Red Cross AIDS Research Center, Bangkok, Thailand

Leveraging early HIV diagnosis and treatment in Thailand to conduct HIV cure research

Camilla Muccini, Trevor A. Crowell, Eugène Kroon, Carlo Sacdalan, Reshmie Ramautarsing, Pich Seekaew, Praphan Phanuphak, Jintanat Ananworanich, Donn J. Colby & Nittaya Phanuphak

AIDS Research and Therapy 16, Article number: 25 (2019) | Cite this article

2112 Accesses | 3 Altmetric | Metrics

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Current situation of research and development **on communicable diseases**

- Thailand show the potential for conducting the clinical research in dengue due to there are various type of patient e.g. naïve patients and secondary dengue infected patients
- Dengue vaccination related research : well established
- There are many AMR strain founded in Thailand and some have been collected in biobank. So Thailand is ready for the innovation for AMR testing

(Our personal opinions)

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Unmet needs of R&D

1. Accessibility of the new cancer treatment/early diagnosis
2. Patient accessibility to participate in the clinical trial
3. Awareness of antimicrobial resistance (AMR)
4. Under screening for the preventable diseases
   e.g. breast cancer, cervical cancer
5. Under detection of the early stage of some diseases
   Glaucoma, DM, CAD, AF
6. Need (short/long term) policies to reduce the rate of road traffic injury/ pollution prevention

(Our personal opinions)

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Proposed solutions to fill the gaps

Research

- ❖ Health care system research to strengthening health services
- ❖ Increase the number of clinical trials *(both IIT, and sponsor trials)*
  - ○ To increase the accessibility of the new treatment
  - ○ To collect the specific data of Thai population
  - ○ To meet the need of some specific diseases or problems in Thai population

Collaboration

- ❖ with the local private/governmental institution
- ❖ with international health institutions : knowledge sharing

(Our personal opinions)

Proposed solutions to fill the gaps *(Cont.)*

Awareness/preventive plan

- ❖ National plan for prevention program esp. preventable disease
  - ○ Road- traffic accident long term plan
  - ○ Screening program for the breast cancer and the cervical cancer
- ❖ Antimicrobial resistance awareness and prevention
  - ○ Antimicrobial resistance control and prevention
- ❖ Health education/awareness for national-wide

Proposed solutions to fill the gaps *(Cont.)*

- ❖Health education for national-wide population
- ❖Healthcare supporting systems
  - ○ Increase healthcare personnel
  - ○ financial support
  - ○ strengthening competency of health care personnel
- ❖Budget allocation to healthcare/research system
- ❖Involve the scientist and healthcare professional in the policy making process

Perspectives to fill the unmet needs

[From drug and device development perspective]

1. Clinical research and drug/device development can

✓Clinical research (MRCT) might help establishing the genomic landscape of Thai population
(such as mutations in Thai cancers, data on the drug response that studied in our population)

✓IIT related to drug/device development will help lowering the cost of some treatments/device

Perspectives to fill the unmet needs

[From drug and device development perspective] *(Cont.)*

2. Barriers in Thailand that might related to drug and device development

- ➢ ***Regulatory perspective***
  - ○ Delay processes within the local regulatory
  - ○ Contact personnel
- ➢ ***Economy perspective***
  - ○ Budget allocation into the research
- ➢ ***Regarding developing drug/device***
  - ○ Less number of IIT
  - ○ Need local collaborator

Perspectives to fill the unmet needs *(Cont.)*

[From drug and device development perspective]

3. Collaboration which seems possible between Thailand/ institution in Thailand and Japan/NCGM
   - ➢ Technology transfer
   - ➢ MRCT/ multicenter-RCT

4. Help/support which could be the efficient collaboration
   - ➢ Innovation
   - ➢ Compact or portable device is very advantageous for remote area and surveillance program
   - ➢ Japan experiences *(regarding trial initiation/management in drug and device development)*

Perspectives to fill the unmet needs *(Cont.)*

[From drug and device development perspective]

5. Area/points to learn from Japanese colleagues working in the clinical research and development field.

- How to prepare the efficient system of clinical trial that relevant to drug/device for **aging society**?
- Role of *drug/device development* relating the community care system for the **aging society**

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In case the Japanese product needs Thailand's approval

- Oversea clinical study data is acceptable
- Clinical development (trial) Must aligned with **ICH and/or WHO** guidance
- Bridging data & local regulatory trials are not always required *(exception: drugs that have demonstrated the ethnic differences might be requested more data)*

26

Thai FDA approval related to the generic drugs?

Regarding **the *systemic*** generic drug /new generic drug which manufacture and/or import in Thailand

Thai FDA requires the bioequivalence study and *in vitro* dissolution/release study compared to original new drugs to ensure the quality and efficacy of product

"Which need to be studied by Thai institution or Thai laboratory except some which cannot be tested in Thailand"

27

Thai FDA approval related to the generic drugs?

Regarding **the topical/local applied** generic drug /new generic drug which manufacture and/or import in Thailand

Thai FDA required *the comparative studies* in **pharmacodynamics** and/or in clinical together with ***in vitro* studies**.
The applicant need to give the reasons why the submitted method is selected.

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Situation of clinical trials in Thailand for additional indication

- Oversea clinical study data is **acceptable**
- Must aligned with **ICH and/or WHO** guidance
- Bridging data & local regulatory trials are not always required *(exception: drugs that have demonstrated the ethnic differences might be requested more data)*

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Benefits to conduct the clinical trials in Thailand

- ✓ Well trained research physician, familiar with trials
- ✓ No language barrier for personnel
- ✓ Large naïve patient population across many disease profiles
- ✓ High cost-effectiveness in hosting trials
- ✓ High incidence of tropical diseases
- ✓ Access to state of the art, readily available medical equipment and facilities infrastructure

NOTED: **Among ASEAN country, the same dossier can be used for submission**

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NCGM

We thank NCGM for arranging this productive fruitful meeting – and to meet distinguish participants here in Tokyo 2020.

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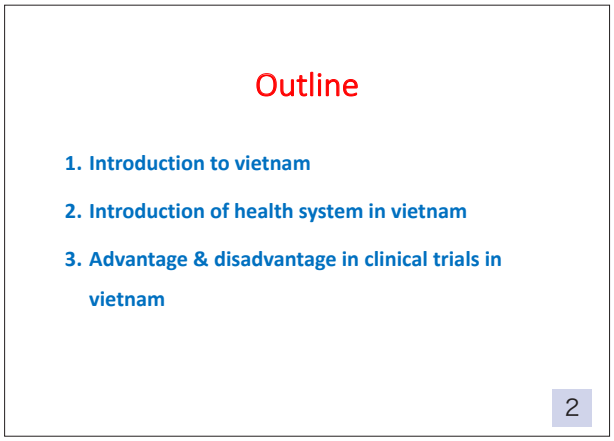
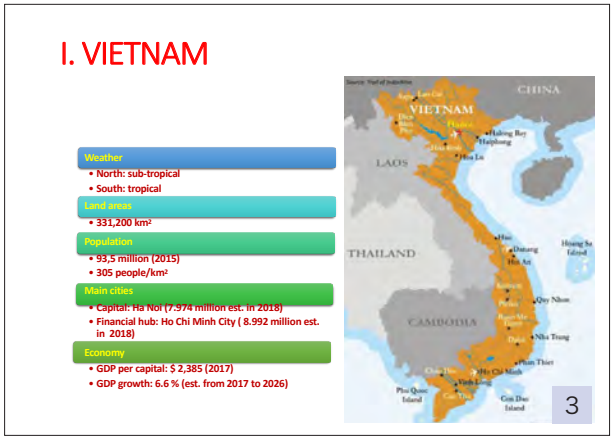
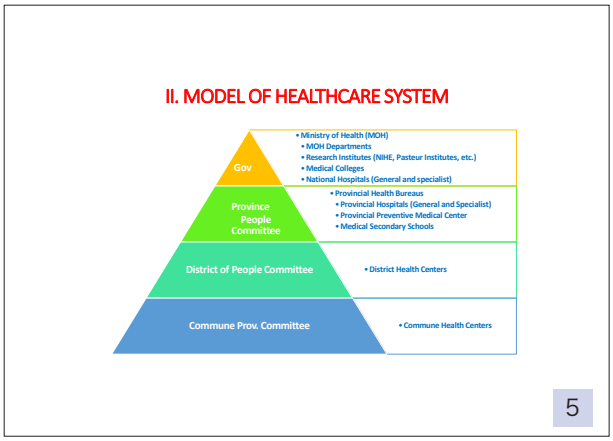
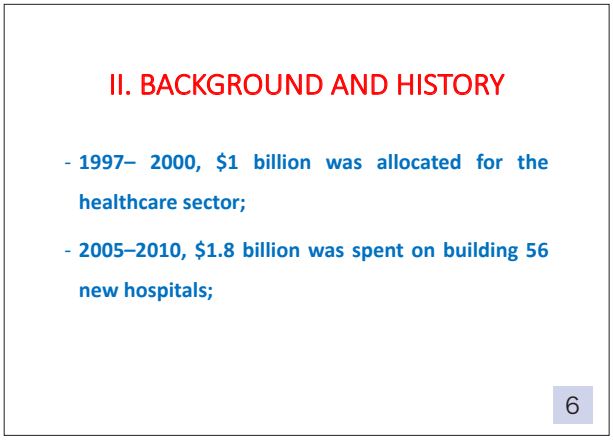
5. Challenge and Suggestions on Drug or Device Development in Vietnam

Ngo Van Cong / Thi Hong Linh Le









BACKGROUND AND HISTORY

- Hospitals in Vietnam (1,161 public hospitals and 185 private hospitals in 2016);
- The number of healthcare clinics and medical centres is increasing (> 20,000 private healthcare clinics and > 11,000 traditional medicine centres);

7

KEY HOSPITALS IN VIETNAM

- 115 People Hospital;
- Da Nang Hospital;
- Cho Ray Hospital;
- Dong Nai Hospital;
- Kien Giang Hospital;
- Ho Chi Minh Heart Institute;
- Ho Chi Minh Oncology Hospital;
- UBHN Cancer Centre;
- Hue Central Hospital;
- K Hospital;
- National Institute of Hygiene and Epidemiology Hospital;
- Bach Mai Hospital;
- Viet Duc Hospital....

- Hanoi and Ho Chi Minh City are two major markets for medical products.
- Cho Ray Hospital, Bach Mai Hospital

8

CHO RAY HOSPITAL

9

10

11

STAFF	
Doctors	872
Nurses	1668
Technicians	400
Pharmacists	96
Others	904

12

Daily activities

350 emergency patients

1,197,134 1,239,541 1,341,947 1,401,038 1,526,894

6.000 out-patients

123,122 117,803 123,075 125,963 135,195

3.000 in-patients

Length of Hospital stay: 7,1 days

300 surgeries

40,544 39,212 38,722 42,890 45,465

2013 2014 2015 2016 2017

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BACH MAI HOSPITAL

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CRH & NCGM COOPERATION ON QUALITY MANAGEMENT & PATIENT SAFETY

Training course on patient safety & quality management in 2012

Training course on QM & PS at CRH

Training course by WHO and NCGM in 2016

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OVERVIEW OF BACH MAI HOSPITAL

Bach Mai Hospital is the first special level general hospital

- *3200 inpatient beds*
- *Total staffs: 3,500*
- *Current structure: 3 Institutes, 11 Centers, 22 Clinical Departments and 5 Paraclinical Departments, 12 Functional Divisions, 1 Medical College, 2 other units, 1 Journal of Clinical Medicine.*
- *Creadited Laboratory (ISO 15189:2007)*

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TECHNICAL ASSISTANT PROJECT

1. On job training in Hospital Quality Management and Patient Safety
2. Lectures
3. Research

Summary meeting at CRH on 14th Dec 2016

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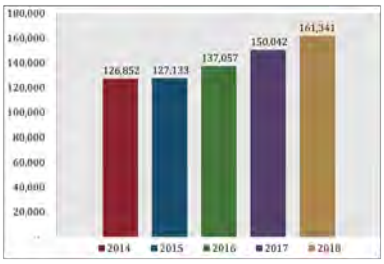
Number of outpatient in 5 years

18

Number of inpatient in 5 years



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III. REGULATORY APPROVAL PROCESS IN VIET NAM

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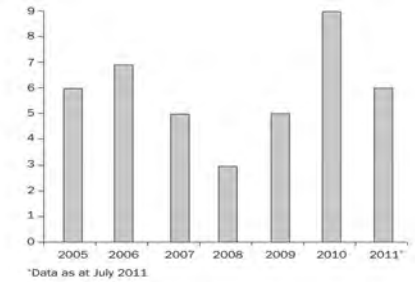
III. NUMBER OF CLINICAL TRIALS



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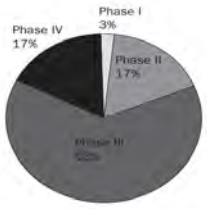
III. CLINICAL TRIALS IN VIETNAM

- Vietnam is participating in approximately 7–8 new industry sponsored trials every year.
- There were 142 trials



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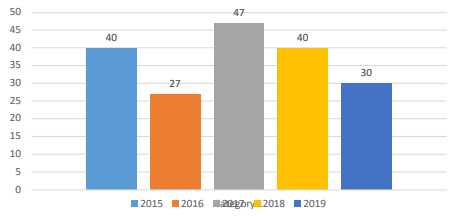
NUMBER OF CLINICAL TRIALS (2015 -2019)



Interventitional clinical trial in HCM, HNC

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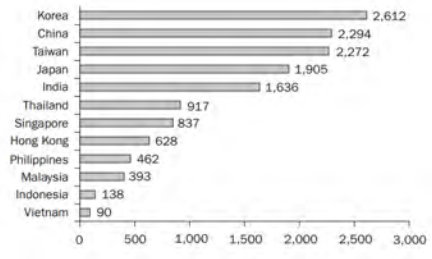
NUMBER OF CLINICAL TRIALS IN THE ASIA REGION



Source: *www.clinicaltrials.gov* (accessed 20 July 2011)

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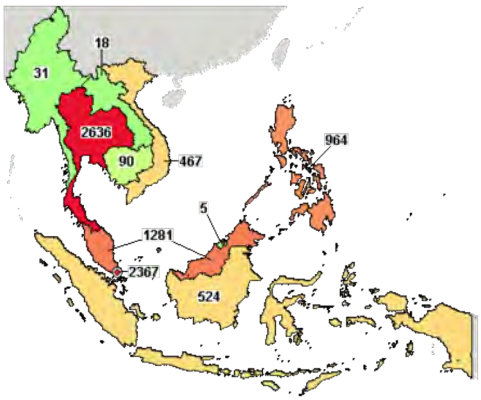

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ADVANTAGE

- Wide range of diseases and potential patient pool;
- Adequate facilities (central);
- Qualified staff (medical license; GCP Certificate for Central Hospitals and Institutes);
- Experience (National Hospitals and Institutes);
- Cost saving and low competitors

- Improvement:
+ Timeline start-up
+ Clinical trial experience of provincial or district health care centers
+ Facilities of district hospitals in remote areas

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DISADVANTAGE

- CSA needs to be translated into the local language as legal documents;
- Some basic researching fees (10% administrative fees for MOH and 30% overhead fee included in CSA);
- Too much steps in researching:
+ Requirement of renewing IL yearly and renewing EL for biosamples every 6 months;
+ Restriction of relabeling IMP/non-IMP at sites for shelf-life extension;
+ CSR submission requirement for closing study in the country;
→ To creates complicated and overlapping procedures for sponsors during the approval process.

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Clinical Trials is increasing about quantity and quality

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DISADVANTAGE

- Network system is weakness;
- Need of having local vendor/broker for shortening IL review process for study specific auxiliaries;
- The MOH is in the process of developing guidelines for best practices in clinical trials;

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Comprehensive and collaborative training on medical innovations adapted to challenges of clinical trials in Asian and African countries [2nd edition]

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