海外出張報告書(1)

渡航者	佐瀬　一洋
所属機関名	順天堂大学大学院臨床薬理学

渡航目的及び見込まれる成果

米国FDAにおいて HBD (Harmonization by Doing, 医療機器審査開発の実践と調和) 会議に参加

日　程 (予定)	出発地	到着地 (宿泊地)	訪問機関名 訪問者名等	訪問目的及び見込まれる成果 (個別欄)
平成18年 7月12日	東京(成田) UA 9682	ワシントンDC	CDRH/FDA	別添　Agenda 参照
平成18年 7月14日	ワシントンDC UA 7346 ニューヨーク 乗継 UA 801	東京(成田)		

平成18年7月11日から13日まで開催された、Harmonization by Doing (HBD) 会議に学術専門家として出席した。

FDAの医療機器審査部門であるCDRHの責任者であるダニエル・シュルツ博士が開会の挨拶と趣旨説明を行い、その後、厚生労働省、医薬品医療機器総合機構、Advamed、医機連、そして日米の学術専門家により、平成19年1月に公開でHBD会議を開催するための準備を行った。

HBDの組織図、ロードマップについて議論がなされ、概略が決定した。

主要な議題は以下のとおり。

1. 薬剤溶出型ステントおよび心血管領域における医療機器の開発と審査
2. 補助人工心臓の市販後レジストリ(INTERMACs)
3. 日本における臨床研究のインフラストラクチャー
4. 日米規制当局によるハーモナイゼーション

July 11-13, 2006 Japan MHLW-PMDA Visit to FDA/CDRH

Conference Room (110G)
Division of Small Manufacturers, International, and Consumer Assistance (DSMICA)
Office of Communication, Education and Radiation Programs (OCER)
1350 Piccard Drive, Rockville, MD 20850, U.S.A
Phone: (240) 276-3141

Draft AGENDA

PC and Projector will be available for use. Pre-loading of presentations, please send to Joyce.Raines@fda.hhs.gov Deadline - July 6 (Thursday).

The conference room is located on the first floor. Enter the building facing Piccard Dr. (Look for the flag). You will see the Guard's desk. An entry door to DSMICA is across the guard's desk (a slight jog to the right). Badge is required to enter. Go straight ahead (overhead signs). You will enter a large room with some boxes along the walls. The conference room is at the end (right side).

Visitors need to sign in with the guard and will be escorted by FDA staff.

July 11, 2006 (Tuesday)

9:30 – 11:30	**Welcome (J. Stigi, Director, DSMICA) & Introductions** MHLW PMDA and FDA HBD Roundtable Discussion with Dr. Daniel Schultz CDRH Director (Regulators Meeting)
11:30 – 13:30	Break for Lunch
13:30 – 16:30	HBD General Meeting FDA, MHLW-PMDA, DCRI, JAG, ADVAMED, JFMDA a) 5-10-minute presentations "Defining roles of participants in the HBD program" b) Follow-up discussion on HBD Structure (from June 20 Teleconference) Break -- c) Mini-workshop - Planning the program for HBD West (tentative schedule October 19-20)
18:00 -	Dinner (Optional Attendance) – Where? TBD

July 12, 2006 (Wednesday)

9:30 – 11:30	Roundtable Discussion MHLW-PMDA and FDA Regulators (HBD Cooperation/Formalizing Relationships, Terms of Reference, other practical issues)
11:30 – 13:00	Lunch break
13:00 – 14:00	LVAD Registry (INTERMACs) Working Group
14:00 – 15:00	Global DES Working Group
15:00 – 15:30	Break
15:30 – 17:00	Regulators Meeting with FDA ICDB Reviewers (Drug Eluting Stents)

July 13 (Thursday)

9:30 – 10:15	Clinical Research Infrastructure/Statistical Pooling Working Group
10:15 – 10:30	Break
10:30 – 11:30	Regulatory Convergence Working Group (STED subpart)
11:30 – 12:30	Regulatory Convergence Working Group (Medical Device GCP subpart)
12:30 – 14:00	Lunch break
14:00 – 15:00	Regulators Meeting with FDA Reviewers (Orthopedic Specialty area - TBA)
15:00 – 16:00	Other topics beyond HBD (TBA)
16:00 – 16:30	**Summary of HBD meetings / Wrap-Up (Dr. Schultz)**
16:30 – 17:15	Regulators Meeting with PDLB Reviewers and OSB statistician (Pacemaker)

ADJOURN

海外出張報告書(2)

渡航者	所　属	備考
松田 暉	兵庫医科大学	審査ガイドラインWG
中谷 武嗣	国立循環器病センター 臓器移植部	
高江 慎一	厚生労働省 医療機器審査管理室	
佐瀬 一洋	順天堂大学大学院 臨床薬理学	
高谷 節雄	東京医科歯科大学	開発ガイドラインWG
阿部 裕輔	東京大学医学部	
小沢 由紀	テルモ(株)	
山根 隆志	産業技術総合研究所	

渡航目的及び見込まれる成果

米国FDAの CDRH (Center for Devices and Radiological Health) において 医療機器国際整合化の実践会議(Harmonization by Doing)し、人工心臓に代表される

次世代医療機器の開発に関する最新の動向を調査し、INTERMACsについて協議する

日　程 (予定)	宿泊地	訪問先	訪問機関名 訪問者名等	訪問目的及び見込まれる成果 (個別欄)
平成18年 10月19日	ワシントンDC 郊外(ロックビル、MD)	FDA (Food and Drug Administration)	CDRH	別添 Agenda 参照

平成18年10月19日にFDAの医療機器審査部門であるCDRH (Center for Devices and Radiological Health) で開催されたHarmonization by Doing (HBD) 会議第二作業部会(WG2)に、審査ガイドライン策定ワーキンググループと開発ガイドラインワーキンググループが合同で出席した。

HBDは、日米の産学官が共同で取り組むプロジェクトで、国際共同治験や共同審査等を実践することにより、GHTF (Global Harmonization Task Force)やISO (International Organization for Standardization)等を補完する役割が期待されている。米国では学会等でFDAを招いたタウンホール・ミーティングが盛んであるが、日本でも2004年3月の日本循環器学会にFDAの医療機器審査部門であるCDRHの審査官が来日したことをきっかけに、産学官による患者指向型のシンポジウムが頻繁に開催されるようになった。

2006年からは運営委員会が電話会議を毎月実施している。第一作業部会は薬剤溶出型ステント等、循環器系医療機器の国際共同治験、第二作業部会は人工心臓の市販後登録調査、第三作業部会は医療機関における臨床研究実施支援体制、第四作業部会は日米規制当局間の整合性向上が主要なテーマで、2007年1月に第1回HBD-West公開シンクタンクに向けた準備が進行中である。

今回参加した第二作業部会は、米国で開始されたINTERMACs(Interagency Registry for Mechanically Assisted Circulatory Support)について、日米の連携の可能性を協議した。INTERMACsはDestination Therapyや在宅管理を視野にいれた省庁横断型のプロジェクトで、研究費はNIHの一部門であるNHLBI(National Heart, Lung, and Blood Institute)が公募した。研究計画はアラバマ大学バーミングハム校のカークリン教授を主任研究者として、生物統計家のDavid Naftel氏を中心とするグループが立案、実施運営を担当している。FDAは研究の計画段階から関与しており、事後的な自発報告に依存していた市販後安全性監視について、事前に有効性・安全性の評価項目を明確化したり、企業間で共有できない情報は規制当局のみが閲覧できる仕組みを確立したりすることで、有用性を高めている。CMS(Center for Medicare & Medicaid Services) は保険償還の条件としてINTERMACs参加を求めた。これにより事実上全数調査が可能になり、バイアスを最小減にとどめることが期待されている。

既に、欧州もINTERMACsに参加している。わが国でも、承認までに必要な基準と市販後の適正使用のバランスを考慮し、保険医療の枠組みを活用しつつ質の高い臨床研究を継続的に実施するために、省庁横断型プロジェクトとしてINTERMACsへの対応を進めることが期待される。

October 19, 2006 HBD Working Group 2 Meeting
Study on Postmarket Registry - VADs
Japan MHLW-PMDA/FDA/DCRI/INTERMACs/INDUSTRY

Conference Room 20B
9200 Corporate Blvd, Rockville, MD 20850, U.S.A

AGENDA

The conference room is located on the ground floor. Sign in with the security guard and then proceed to the elevator to the ground floor. Conference room 20B is through the double doors after you reach the ground floor.

Noon – 13:00 Lunch provided in Conference room 20B

13:00 – 13:30 Introductions and Welcome – Zuckerman
HBD Concept – Carey/Handler
Working Group 2 Description – Chen/Sapirstein

13:30 – 15:30 Working Group 2 General Meeting

a) Presentation on INTERMACs – UAB (Kirklin/Naftel)
b) Japanese Presentation
    Overview - LVAS for Japan: BTT? or DT? - Matsuda
    LVAS R&D Guideline in Japan - Yamane/Takatani
    Pre- and Post-approval requirements in Japan - Takae
    Post-marketing registry in Japan and impact of INTERMACs – Nakatani
        (1) Background / Mission
        (2) What is working well now?
        (3) What is not?
        (4) Short-term goal (1-3 years)
        (5) Mid- & Long-term goal (3-10 years)

---Break---

c) Industry presentation – Bostic/Frazier
d) INTERMACs: An FDA Perspective - Gross

15:30 – 17:00 Open Discussion on next steps

a) WG2 one-pager
b) Other participants
c) Roll out in Japan
d) Program for HBD West 2007
e) Other

ADJOURN

HBD Working Group #2

Most ventricular assist devices that are approved in Japan and the United States require a post-approval study to monitor the commercial use of those devices in the larger patient population. These post-approval studies are burdensome as manufacturers have to spend additional funding to perform these studies. Recently, the NHLBI mechanical circulatory support devices registry (INTERMACs) began to collect data on those patients receiving an approved ventricular assist device in the United States. INTERMACs provides a mean for designing and conducting post-marketing studies in a cost efficient and least burdensome way for manufacturers. Similarly, it also allows the governmental regulatory agencies to develop ways for manufacturers to report this post-marketing data for the review of approved ventricular assist devices. It also allows data on ventricular assist devices to be shared between governmental agencies, industry, and academic institutions. Standardized adverse event definitions have been developed with industry, clinicians, and FDA which can be used to further enhance the clinical management of ventricular assist device patients. INTERMACs is one example of a vehicle to collect post-market data on cardiovascular devices. We recognize that there are many other ways to collect data on approved cardiovascular devices and look forward to future discussions that may occur within the Harmonization by Doing Program. We believe that Japanese hospitals and manufacturers can use INTERMACs as a vehicle to collect data on those ventricular assist devices that are commercialized in Japan.

Therefore, INTERMACs provides an enhanced surveillance on ventricular assist devices that have been approved in Japan and the United States especially regarding:

- AEs, Device Malfunctions
- QOL
- Survival
- Neurological Function

Similarly, future discussions regarding the use of INTERMACs could extend to improvement and expedition of new device clinical trials by providing historical control data to serve as Objective Performance Criteria (OPC) standards. This would be interesting as it would also involve Working Groups #1 and #4.

Therefore, as part of the HBD program between Japan and the United States, FDA sent an official letter to INTERMACs encouraging them to contact our Japanese counterparts and inviting them to participate in INTERMACs. We believe that INTERMACs can be used to collect the post-market data for Japanese manufacturers and institutions. Furthermore, we believe that Japanese ventricular assist device data can assist in the continued learning of ventricular assist device management for patients on a global scale.

海外出張報告書(3)

渡航者	所　属
松田　暉	兵庫医科大学
中谷　武嗣	国立循環器病センター　臓器移植部
佐瀬　一洋	順天堂大学大学院　臨床薬理学

渡航目的及び見込まれる成果

米国NIHにおいて NHLBI, CC, NLM 等の研究所を訪問し、人工心臓に代表される次世代医療機器の開発に関する最新の動向を調査し、INTERMACsについて協議する

日　程 (予定)	宿泊地	訪問先	訪問機関名 訪問者名等	訪問目的及び見込まれる成果 (個別欄)
平成18年 10月20日	ワシントンDC 郊外(ロックビル、MD)	NIH (National Institutes of Health)	NHLBI CC NLM	別添　Agenda 参照

平成18年10月19日に学術専門家として出席したHarmonization by Doing (HBD) 会議第二作業部会(WG2)における議論を踏まえ、米国における省庁横断型の臨床研究であるINTERMACsに対する研究資金提供および研究機関選定を実施したNIHを訪問し、米国における医療機器の開発に関する歴史と次世代型医療機器に関する最新の動向、およびINTERMACsをはじめとした日本との連携の可能性について協議を行った。

INTERMACs (Interagency Registry for Mechanically Assisted Circulatory Support) は、文字通り補助人工心臓の市販後レジストリという臨床研究に関する省庁横断型のプロジェクトである。

研究費はNIHの一部門であるNHLBI(National Heart, Lung, and Blood Institute)が研究契約という形で公募し、アラバマ大学バーミングハム校のカークリン教授を主任研究者とするグループが競争的資金を獲得して研究計画を立案、実施運営している。NHLBIは、1960年代から人工心臓の要素技術開発に多くの研究資金援助を行うとともに、ベンチャー企業に知的財産を供与することにより製品化という形でイノベーションが結実した。また、REMATCH試験に代表される質の高い臨床試験に研究資金援助を行っている。

研究内容については、FDAの医療機器審査部門であるCDRH(Center for Devices and Radiological Health) が計画段階から関与し、従来は各企業の自発報告に依存していた市販後安全性監視について、事前に有効性・安全性の評価項目を明確化するとともに、企業間で共有すべき情報と規制当局のみが閲覧できる情報を分けることにより信頼性や実行可能性が高い臨床研究の実施が可能となった。

研究の実施にあたっては、中止・脱落例の取り扱いやイベント(分子)に対する施行症例数(分母)の把握が重要な鍵を握るが、CMS(Center for Medicare & Medicaid Services)が保険償還の条件としてINTERMACs参加を求めたことにより、事実上全数調査が可能となった。わが国でも承認までに必要な基準を満たしつつ市販後も適正使用の中で継続的に質の高い臨床研究を進めるために医療保険の枠組みを活用することが期待される。

NIH TOUR and VISIT

Attendees

Hikaru Matsuda
Professor Emeritus, Osaka University Hospital

Takeshi Nakatani
Director of Transplant Medicine, National Cardiovascular Center

Kazuhiro Sase
Professor of Clinical Pharmacology, Juntendo University

Marissa A. Miller
Program Director, Advanced Technologies and Surgery Branch, NHLBI
301/801-6872

Patrice Desvigne-Nickens
Program Director Heart Failure and Arrhythmias Branch, NHLBI

Karen Ulisney
Clinical Trial Specialist, Advanced Technologies and Surgery Branch, NHLBI

Accessing NIH:
Visitors will be asked to show one (1) form of identification (a government-issued photo ID – driver's license, passport, green card, etc.) and to state the purpose of their visit. If coming by taxis or private vehicle, **be sure to allow extra time for this vehicle inspection procedure.**

Agenda:

10:00 Dr. Susan Shurin
Deputy Director, National Heart, Lung, and Blood Institute
Bldg.31, Room 5A48, 301/496-5166

11:00 Overview of NIH and Tour of Hatfield Clinical Research Center,
North Lobby CRC, wait behind wooden reception desk
Tour Guide – Carol Jabir
301/496-1776

12:30 Lunch

1:30 National Library of Medicine Video and Tour
NLM Visitors Center, Bldg. 38A 1st floor

2:30 Depart

海外出張報告書(4)

渡航者	佐瀬　一洋
所属機関名	順天堂大学大学院臨床薬理学

渡航目的及び見込まれる成果

米国Duke大学において HBD (Harmonization by Doing, 医療機器審査開発の実践と調和) 会議に参加

米国Harvard大学と医療機器開発の国際プロジェクト実践として PREDICTION 試験を企画

日　程 (予定)	出発地	到着地 (宿泊地)	訪問機関名 訪問者名等	訪問目的及び見込まれる成果 (個別欄)
平成19年 1月10日	東京(成田) NH002/NH7144	ワシントンDC 乗継 ダーラム(NC)	DCRI	HBD West 会議 1/10-1/11 別添1 Agenda 参照
1月11日	ダーラム AA4719	ニューヨーク	Courtyard Marriott JFK	PREDICTION 会議 1/12 別添2 Agenda/Minutes
1月12日	ニューヨーク JetBlue1006	ボストン	BWH	BWH 視察 1/12 別添3 BWH資料
1月13日	ボストン JetBlue1003 ニューヨーク NH009	東京(成田)		

平成19年1月10日から11日までDuke大学臨床研究センターにおいて開催された、Harmonization by Doing (HBD) 会議に学術専門家として出席した。

FDAの医療機器審査部門であるCDRHの責任者であるダニエル・シュルツ博士が開会の挨拶と趣旨説明を行い、その後、厚生労働省、医薬品医療機器総合機構、Advamed、医機連、そして日米の学術専門家により、公開でHBD会議を開催する意義について説明された。HBDの組織図、ロードマップが発表され、概略が決定した。

主要な議題は以下のとおり。

1. 薬剤溶出型ステントおよび心血管領域における医療機器の開発と審査
2. 補助人工心臓の市販後レジストリ(INTERMACs)
3. 日本における臨床研究のインフラストラクチャー
4. 日米規制当局によるハーモナイゼーション

平成19年1月12日には、Harvard大学が日本の複数医療機関と計画している新しい動脈硬化診断技術および医療機器開発(PREDICTION試験)について、協議および視察を行った。

HBD West Think Tank Meeting
10-11 January 2007
Geneen Auditorium
The R. David Thomas Executive Conference Center
Duke University, Durham, NC

Wednesday, January 10

8:15 - 9:00 Registration

9:00 - 9:30 Welcome

a. 9:00: US Academia - Mitchell Krucoff, Duke University Medical Center

b. 9:05: Japanese Academia - Kazuhiro Sase, Juntendo University Medical School

c. 9:10: FDA - Daniel Schultz, US Food and Drug Administration

d. 9:15: MHLW/PMDA - Hiroshi Maruyama, Japan Pharmaceuticals and Medical Devices Agency

e. 9:20: Japanese Industry - Kazuo Ogino, Japan Federation of Medical Devices Associations

f. 9:25: US Industry - Janet Trunzo, Advanced Medical Technology Association

9:30 -12:00 HBD Overview

a. 9:30: FDA Perspective on Global Harmonization - Daniel Schultz, US Food and Drug Administration

b. 9:45: HBD Perspective (2003 – 2006) - Mitchell Krucoff, Duke University Medical Center

c. 10:00: Benefits to Patient Care: The Potential of HBD - Kazuhiro Sase, Juntendo University Medical School

d. 10:15: HBD Principles and Structure – Toshi Tominaga, Japan Ministry of Health, Labour, and Welfare

e. HBD Working Groups: Brief Remarks by Working Group Chairs

i. 10:30: Working Group 1: Global Cardiovascular Device Trials
Mitchell Krucoff, Duke University Medical Center
Shigeru Saito, Shonan Kamakura General Hospital

9:30 -12:00 HBD Overview (cont)

ii. 10:40: Working Group 2: Post Market Registry
Eric Chen, US Food and Drug Administration
Kazuhiro Sase, Juntendo University Medical School

iii. 10:50: Working Group 3: Clinical Trial Infrastructure
John Alexander, Duke University Medical Center
Yoshihiro Arakawa, Tokyo University Hospital

iv. 11:00: Working Group 4: Regulatory Convergence & Communication
Carole Carey, US Food and Drug Administration
Shinichi Takae, Japan Ministry of Health, Labour and Welfare

f. 11:10: Anatomy of a Think Tank: Mitchell Krucoff, Duke University Medical Center

g. 11:20: Discussion Lead: Mitchell Krucoff, Duke University Medical Center

12:00 - 13:30 Lunch

13:30 - 15:00 Working Group 1: Global Cardiovascular Device Trials
Moderators:
Mitch Krucoff, Duke University Medical Center
Shigeru Saito, Shonan Kamakura General Hospital

a. 13:30 - 14:20: Single US-Japan DES protocols: are we ready? Challenges of study design

i. 13:30: Japan Regulatory view - Masahiro Takahata, Japan Federation of Medical Devices Associations

ii. 13:35: Challenges for study processes - Allison Handler, Duke Clinical Research Center

iii. 13:40: Is industry ready? - Susan Alpert, Medtronic

iv. 13:45: Will patients and doctors randomize? - Shigeru Saito, Shonan Kamakura General Hospital

v. 13:50: Issues of poolability - Taka Uchida, US Food and Drug Administration

vi. 13:55: Discussion
Initial commentator (2 min): TBD

13:30 - 15:00 Working Group 1: Global Cardiovascular Device Trials (cont)

b. 14:20 - 15:00: Integration and independence of timelines for single protocol studies

i. 14:20: Academic view - Mitch Krucoff, Duke University Medical Center

ii. 14:25: Industry view - Stephen Mascioli, Boston Scientific

iii. 14:30: US FDA view - Ashley Boam, US Food and Drug Administration

iv. 14:35: Japan Regulatory view - Koji Ikeda, Japan Pharmaceuticals and Medical Devices Agency

v. 14:40: Discussion
Initial commentator (2 min):
Patricia Garvey, Edwards Lifesciences

15:00 - 15:20 Break

15:20 - 17:00 Working Group 2: Post Market Registry: LVAD/Artificial Heart
Moderators:
Eric Chen, US Food and Drug Administration
Kazuhiro Sase, Juntendo University Medical School

a. 15:20: Are postmarket studies for LVADs/Artificial Hearts burdensome for manufacturers?

1. Pros - validity and need of "real world" usage
2. Cons – price of performing post-market studies

Industry view - Don Middlebrook, Thoratec Corporation

b. 15:35: Single post-market study protocols in US and Japan for LVADs?

1. Integration of agreed upon definitions for outcomes and adverse events
2. Sample size
3. Are manufacturers and regulatory bodies ready?

Industry View: Gwen Mayes, Abiomed, Inc.

c. 15:50: Can post-market study data be utilized for pre-marketing approval?

1. Is additional clinical evaluation data required?
2. What differences should be considered between US and Japan?
   i. 15:50: Industry view – Chiasto Nojiri, Terumo Heart, Inc.
   ii. 16:00: Academic view – David Naftel, Univeristy of Alabama at Birmingham
   iii. 16:10: Japan Regulatory view - Shinichi Takae, Japan Ministry of Health, Labour and Welfare
   iv. 16:15: US Regulatory view - FDA

15:20 - 17:00 Working Group 2: Post Market Registry: LVAD/Artificial Heart (cont)

c. 15:50: Can post-market study data be utilized for pre-marketing approval?

v. 16:20 - 17:00: Discussion:

Initial Commentator (2 min):
Eric Chen, US Food and Drug Administration
Kazuhiro Sase, Juntendo University Medical School

17:30 - 18:00: Reception

18:00 - 20:00 Plenary Session
Global Health Care: Perspective for the Future; implications for evaluation of new therapies

a. 18:00 – 18:20: Robert Califf, M.D.
Vice Chancellor for Clinical Research
Director, Duke Translational Medicine Institute
Duke University Medical Center

b. 18:20 - 18:40: Murray M. Lumpkin, M.D.,
Deputy Commissioner for International and Special Programs
United States Food and Drug Administration

c. 18:40 - 19:00: Hiroshi Maruyama
Associate Center Director
Japan Pharmaceuticals and Medical Devices Agency

HBD West Meeting: Day 2
Thursday, January 11

08:30 - 09:00 Continental Breakfast

09:00 - 10:30 Working Group 3: Clinical Trials Infrastructure
Moderators:
John Alexander, Duke University Medical Center
Yoshihiro Arakawa, Tokyo University Hospital

a. 9:00 - 9:30: Role of academic & government leadership in clinical research infrastructure.

i. 9:00: US perspective - Robert Harrington, Duke University Medical Center

ii. 9:10: Japan Academic perspective - Yoshihiro Aarakawa, Tokyo University Hospital

iii. 9:20: Japan Government perspective - Toshi Tominaga, Japan Ministry of Health, Labour, and Welfare

09:00 - 10:30 Working Group 3: Clinical Trials Infrastructure (cont)

b. 9:30 - 10:00: Why participate in multicenter clinical trials?

i. 9:30: US Investigator - John Alexander, Duke University Medical Center

ii. 9:35: Japan Investigator - Shigeru Saito, Shonan Kamakura General Hospital

iii. 9:40 - 10:00: Discussion: Are the US & Japan Different?
Initial commentator (2 min): Neal Fearnot, Cook/MED Institute

c. 10:00 - 10:30: Targets for Enrollment

i. 10:00: US Industry - Tony Semedo, Medtronic Co., Ltd.

ii. 10:05: Japan Industry - Shigetaka Miura, Japan Federation of Medical Devices Associations

iii. 10:10 - 10:30: Discussion
Initial commentator (2min):
Taka Uchida, US Food and Drug Administration

10:30 - 10:50 Break

10:50 - 12:30 Working Group 4: Regulatory Convergence & Communication
Moderators:
Carole Carey, US Food and Drug Administration
Shinichi Takae, Japan Ministry of Health, Labour, and Welfare

a. Pre-IDE dialogue and Early Consultation: Consultation and Pre-IDE experiences to date. How do we maximize information exchange with efficiency?

i. 10:50: Industry - Gary Thompson, Abbott Vascular Devices Japan

ii. 10:55: PMDA - Yuka Suzuki, Japan Pharmaceuticals and Medical Devices Agency

iii. 11:00: FDA - Donna Lochner, US Food and Drug Administration

iv. 11:05 - 11:20: Discussion
Initial commentator (2 min):
Martin Yahiro, Medtronic Spinal & Biologics

10:50 - 12:30 Working Group 4: Regulatory Convergence & Communication (cont)

b. Comparison of medical device good clinical practices: MHLW's requirements for GCP versus FDA's IDE regulations.

1. Are the differences significant? If not, are there other challenges posed by the mandatory requirements that are burdensome?
2. How do we converge to find the best solutions and minimize the delay in timely approvals?

i. 11:20: FDA - Carole Carey, US Food and Drug Administration

ii. 11:25: Industry - Neal Fearnot, Cook/MED Institute

iii. 11:30: Academic - Allison Handler, Duke Clinical Research Institute

iv. 11:35 - 11:45: Discussion
Initial commentator (2 min):
Toshi Tominaga, Japan Ministry of Health, Labour, and Welfare

c. Convergence of PMA and Shonin application submissions

1. Use of early consultation meetings for review prior to Shonin submission, can the review process be both better and faster?
2. Use of STED formats for PMA submission: efficiency, value, concerns

i. 11:45 - 11: 50: GHTF - Michael Gropp, Medtronic

ii. 11:55 - 12:00: Industry 1 - Hiroshi Ishikawa, Japan Federation of Medical Devices Associations / Toshiba Medical

iii. 12:00 - 12:05: Industry 2 - Brad Hassock, Boston Scientific

iv. 12:05 -12:30: Discussion
Initial commentator (2min):
Ken Cavanaugh, US Food and Drug Administration

12:30 - 13:00 Summary Discussion

a. Issues, Comments, Next Steps
b. Adjournment

13:00 - 14:00 Fly Away Lunch

PREDICTION-TRI MEETING

2007 January 12
New York City
7 am – 9:30 am

Meeting Minutes

Attendees: Dr. Feldman, Dr. Prpic (via teleconference), Dr. Reitman, Dr. Saito, Dr. Sase, Dr. Stone

Action items are noted as [AI: responsibility]

TRI was presented as a well organized Non Profit Organization (NPO) that is able to contribute to the International PREDICTION Trial in collaboration with Brigham & Women's Hospital, Reitman Corporation, Summit Trials and REGISTRAT. Dr. Sase was recognized as a professional with considerable experience who is serving in a leadership role in facilitating the architecture of the Trial.

It was recognized that there needs to be a structure for the grant provided to TRI from BWH, both for TRI work, and for TRI to provide as grants to the clinical sites. **[AI: Saito-sensei to determine the nature of the granting documentation needed by TRI with Sase-sensei support; Reitman to support Saito-sensei work on this and provide information to Saito-sensei with agreement from BWH, REGISTRAT to achieve documentation; requested for completion by February 1 so initial grant funding to TRI can be provided]**

The milestone payment process was reviewed in detail so that all participants understood that monies are contingent on: EC approvals (5, then 10 more), first patient successfully evaluated at first procedure, enrollment of patients (segments up to 500 patients), completion of patients (segments up to 500 patients), and final report. It was explained that the granting completes in June 2009 so that efficient use of time is critical for success of the study.

For the within-Japan activity, the following responsibilities were recognized.

I. Summit Trials -- Site Support

- IRB approval process **[AI: Summit goal of EC approval at all 5 EC sites by February 15 to enable study start; EC approval at additional 10 sites by June 15 to enable study start]**
- Translations

- Visits to sites every 2 months to support their enrollment, data completion practice, technical transmissions and data query resolution
- It was recognized that the study has no investigational device component and as such will not have source document verification monitoring

II. TRI Trial Activities and Granting Structure

A. Through a Medical Supervisor (currently identified as Dr. Kaneda),

- After initial training in the United States, the Medical Supervisor will be responsible for visiting all clinical sites to train Investigators and Catheterization Laboratory staff in technical procedures relating to the PREDICTION Trial. These will include, but not be limited to:
    - Contrast injection techniques
    - IVUS data collection and transmittal
    - Physician-specific aspects of the Investigational Plan

[AI: Kanata training planned for third week in January at BWH]

- Review and provide input on the correctness of the Japanese version of the clinical protocol, Investigator Brochure, case report forms and technical work sheet, case report form and technical worksheet completion instructions, and informed consent template. **[AI: Kanata; completion FEB 1 requested]**
- Ongoing visits to the clinical sites until any issues relating to the abovementioned technical procedures have been resolved to the satisfaction of the Executive Committee.
- Liaising with sites and the Core Laboratories to ensure that IVUS, ECG and other technical data is of sufficient quality for analysis.
- Liaising with sites (specifically Investigators) at the request of REGISTRAT and/or STS to resolve any issues relating to clinical data.
- With STS, conduct visits to clinical sites on a regular basis to assist the sites with any trial related questions or problems, and to encourage enrollment in the PREDICTION Trial.
- Attending Executive Committee Meetings and other operational meetings.

B. Granting

- It was recognized that cash (IRB fee, Galaxy rental cost if it is incurred) and the 6-10 month IVUS equipment should be recognized in the grant. The digitizer is only on loan and does not need to be documented in this way.
  [AI: Sase-sensei to provide models of granting used by JHF if possible;
  AI: Reitman to determine that BSC-BSJ have resolved on any equipment importation tax issues prior to distribution

AI: Feldman to determine the route of the digitizer from BSC-Freemont to sites with customs considerations]

- TRI will need to effect a contract with each hospital, and support will be given from the BWH grant ongoing (on a monthly basis dependent on milestone money received) to support TRI's effort. **[AI: TRI for first contract with Kamakura Hospital so that digitizer can be provided and financial system can be established to provide grant funding;**
  AI: TRI to determine recipient taxation at private hospitals
  AI: TRI to establish grants at all 5 EC institutions with stretch goal of Feb 15 for contract, digitizer in place for all 5 EC sites and by June 15 for additional 10 EC sites]

III. Principal Investigator

Dr. Saito's role as the Principal Investigator was recognized as key to the success of the PREDICTION Trial.

- First grant with TRI to establish the process for granting
- Completion of EC process as site for first patient enrolled
- Work with Medical Supervisor to encourage completion of site readiness at all EC sites.
- Establish additional 10 sites so that all sites are enrolling by June 2007.

The group agreed that the Architecture is best effected through close ongoing communication among Sase-sensei, Prpic, and Reitman, with copies to the others attending along with Monthly teleconferences to be organized by Reitman Corporation. **[AI: Reitman for scheduling beginning in February]**