Work Group 5
Clinical Safety/Performance

AHWP Meeting, Bali

Gao Jie/ Tran Quan

8th November 2011

Asian Harmonization Working Party
WORKING TOWARDS MEDICAL DEVICE HARMONIZATION IN ASIA

Contents

- Overview
- Accomplishments
- Review of 2009 Survey Results
- 2011 Survey Highlights
- Member Economies' Deep Dive
- Recommendations
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Overview

Background

WG5 set up in Q1 ’09

✓Chair& co-Chair: Jie. Gao (SFDA, China), Quan Tran (Industry, Singapore)

✓Total membership: 22 (incl. 4 regulators, 1Academia, 1 Advisor); Covers 7 member economies (China, Singapore, Hong Kong, Chinese Taipei, Malaysia, Vietnam, India)

✓3 subgroups focus (1: Comparative Study; 2: SG5 Doc. Review & Adoption; 3: Training)

Work Item

WI 1: Start up WG5 & establish work plan

WI 2: Establish WG5 representation at GHTF SG5 & participate in the development of SG5 guidance documents

WI 3: Review SG5 & other relevant guidance documents and make recommendations to AHWP member economies on the feasibility of adoption

WI 4: Comparative study of Clinical Trials regulations & related guidances on Clinical Safety/Performance in AHWP member economics

WI 5: Training to promote Good Clinical Practice, Declaration of Helsinki & ISO 14155 governing clinical investigations

WI 6: Partner with other TC Work Groups’ initiatives to provide expertise & input relating to clinical safety/performance eg. WG1 regarding CSDT’s section on clinical evidence

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Accomplishment

WI 1

- **Current membership: 20 members consisting of regulators/industry, covering 6 MEs (CHN, SIN, IND, KOR, MAL, CHN TP) + 1 Advisor (USA)**

WI 2

- **Co-Chair established membership & participation in SG5 initiatives to effectively disseminate SG5 information & guidance documents amongst WG5 & AHWP member economies & feedback to SG5 initiatives/guidance documents**

WI 3

- **Advisory Expert Panel of 6 GHTF SG5 members formed mid 2010 for greater support on training & advice on GHTF SG5 documents review & adoption Chair (MHRA, UK) & Vice Chair (Industry, CAN); 2 JPN PMDA officers; 2 Industry experts (EU & AUS)**
- **Completed studying and reviewing 5 GHTF SG5 documents within WG5.**
  - ✓ AE reporting during clinical investigation (GHTF SG2-SG5)
  - ✓ Post-market Clinical Follow-up Studies (GHTF/SG5/N4:2010)
  - ✓ Clinical Investigations (GHTF/SG5/N3:2010)
  - ✓ Clinical Evidence - Key Definitions & Concepts (SG5/N1R8:2007)
  - ✓ Clinical Evaluation (SG5/N2R8:2007

Accomplishment

WI 4

- **Comparative study of Clinical Trials regulations in AHWP member economies with 2 surveys conducted.**
- ✓ Phase I completed in '09 - 10 MEs responded on CT reg. implementation in CHN, HK, SIN, S. Arabia, S. Africa, KOR, CHN TP, MAL, THA & PHI.
- ✓ Phase II F/U completed in Oct '11 – In depth review of adoption of GHTF GN doc: 1) Clinical Evidence – Key Definitions and Concepts GHTF SG5/N1R8: 2007; 2) Clinical Evaluation GHTF SG5/N2R8:2007
- ✓ Taking into considerations of CT regulation development of MEs to make recommendations to AHWP MEs on the feasibilities of adoption at AHWP meeting Nov 2011

WI 5

- **Training completed :**
- ✓ 14th AHWP meeting, HK, Nov 2009: MD reg. in JPN w/focus on CTs regulations (Speaker: Mr Azuma Kentaro, MHLW, Japan)
- ✓ 10th AHWP TC meeting, SIN, May 2010**:** Painting the Clinical Picture - CE & CEv (Speaker: Mr. Greg LeBlanc, Vice Chair GHTF SG5)
- ✓ APEC Harmonization Centre Workshop for MD, KOR, Nov 2010: Co-Chair moderated on CI Policies in major countries; Co-ordinated speakers from SG5 experts: a) Overview of GHTF/SG1 activities & GHTF/SG 5 key definitions – Atsushi Tamura, PMDA, JPN; b) Focus on CE GHTF SG5/N2R8:2007 – Greg LeBlanc, Cook, Inc.; c) Requirements and suggestions for CT Investigations – Herbert Lerner (USFDA); d) Post Market Clinical F/U Studies GHTF SG5 N4:2010 – Madoka Murakami, PMDA, JPN
- ✓ 15th AHWP meeting, S. Arabia, Nov 2010: a) ISO14155 (Speaker: Ms. Danielle Giroud, Convenor TC 194 WG4); b) Reflection on CT reg. development – A WG5 member perspective (Speaker: Prof Mi Xian Qiang); c) CT Reg. development in India (Speaker: Sumati Randeo)
- ✓ 16th AHWP meeting, Bali, Nov 2011: Key points to Evaluate Clinical Data (Speaker: Ms. Danielle Giroud. WMDO)

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2009 Survey Analysis Summary

Survey Questions	Survey Analysis
-Does your Member Economy have any established regulation on clinical evaluation specifically	• China and Korea have published administrative regulation on medical device clinical trial. Chinese Taipei has guidance document. • Hong Kong, Malaysia and Thailand plan to publish in the next few years • Singapore, Saudi Arabia, South Africa no plan as yet
-Does your Member Economy require local clinical trial for pre-market approval?	• Most Member Economies surveyed accept foreign clinical data and literature • Thailand & Philippines - Local clinical trial may be required for selected products or where additional clinical data required for pre-market evaluation • China require clinical trial for domestic class II & III products, part of class III implantable products, class II & III IVD products. Accepts foreign data for non-local trial required products.
-Does your Member Economy accept GHTF guidance documents on Clinical Safety/Performance by SG5?	• China, Malaysia, Thailand did not accept GHTF guidance doc. • China, Malaysia & Chinese Taipei indicated interest in GHTF guidance doc. for future considerations • Hong Kong, Singapore, Saudi Arabia & Korea accepts GHTF guidance doc. • South Africa: NA
-Is your authority interested in a harmonized Asian countries guideline on Clinical Safety/Performance, eg. AHWP guidelines ?	• All member economies indicated interests in AHWP guideline.
-Which topic your authority would be interested in regarding to clinical training organized by AHWP?	• All member economies indicated interests in the training program

Summary of Member Economies' Medical Device & Clinical Trial Regulations

CHINA

-The State Council Decree #276, Provision of Supervision &Administration of Medical Devices, issued in Apr. 2000

SINGAPORE

-Health Product Act 2007, published in Mar. 2007
-Health Product (Medical Device) Regulation 2010, published in Aug. 2010

KOREA

-Medical Device Law, effective as of May 2004
-Medical Device Clinical Study implementation Std., July-2005
→ KFDA Order 2010-77, 2010

CHINESE TAIPEI

-Beginning registration 1973
-Re-classification 2000
-Medical Device GCP Guideline, May, 2007

HONG KONG

-Voluntary medical device registration

INDIA

-No Medical Device Regulation. Certain categories of medical device are regulated

SOUTH AFRICA

-No Medical Device Regulation. DES is regulated as drug

CHILE & EGYPT

-No Medical Device Regulation

2011 Survey Result Highlight

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Survey Questions

1. About Clinical Evidence – Key Definitions and Concepts (Below concepts and definitions extracted from GHTF SG5/N1R8: 2007)

1) Does your member economy adopt the following GHTF concepts and definitions? (You may choose more than one answer that is applicable):

☐ a) Clinical Investigation：Any systematic investigation or study in or on one or more human subjects, undertaken to assess the safety and/or performance of a medical device.

☐ b) Clinical Data： Safety and /or performance information that are generated from the clinical use of a medical device.

☐ c) Clinical evaluation：The assessment and analysis of clinical data pertaining to a medical device to verify the clinical safety and performance of the device when used as intended by the manufacturer.

☐ d) Clinical evidence：The clinical data and the clinical evaluation report pertaining to a medical device.

2) Does your member economy have any other key definition and concept beyond the four terms mentioned above in paragraph 1? Please describe:

2. About Clinical Evaluation GHTF SG5/N2R8:2007

1) Is clinical evidence required as one of the key elements in the technical document submission in your member economy?

☐ a) Yes

☐ b) No

Survey Questionaire

Survey - China

Survey summary -chna

2011 Survey Result Highlight

Yes
Conditional
No
Not Applicable

Member Economy (ME)	About Clinical Evidence GHTF SG5/N1R8:2007		About Clinical Evaluation GHTF SG5/N2R8:2007					About Investigation GHTF SG5/N3:2010		
	Adopt GHTF Concepts & definitions	Other key definitions & concepts	CEv required as one of key elements in technical doc. Submission	Accept Source: Literature/ clinical exp./ CI, used in CE	Routinely requires LOCAL CI	Clin. Lit. + pre-Clin. comparable/ Predicate device suff. To dem. Conformity	Clin. data fr. Comparable/ predicate device applicable for line extension	CI necessary once data not available from other source	Adopt ISO 14155?	Impose any GCP Reqmt for MD?
China	Y	Y	Y	Y	C[1a]	C	Y	Y	Y[1b]	Y
Singapore	Y	Y	Y	Y	N	C	Y	C[2]	Y	Y
Korea	Y	Y	Y	Y	N	C	C[3]	Y	Y	Y
India	N[4a]	N[4a]	Y	Y	C[4b]	C	Y	Y	N[4]	Y
CHN Taipei	Y	N	Y	Y	N	C	Y	Y	Y	Y
S. Africa[5]	N	N	Y	Y	N	NA	Y	Y	N	N
Hong Kong[6]	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Egypt[7]	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Chile[7]	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

Note:

1. China: a. Most Class 2&3 domestic MD; certain imported Class 3 implantable MD; All Class 2&3 IVD; b. Harmonize
2. Singapore: CI not necessary for low risk products.
3. Korea: Applicable to lower risk MD
4. India: a. In development; b. new tech./ innovative MD require CI
5. South Africa : No MD regulation. Regulate DES as drug
6. Hong Kong: In process of developing statutory reg. of MDs based on GHTF principles. During process, definitions of these concepts will be delineated.
7. Egypt & Chile: No MD regulation

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CHINA

2009

- Medical Device Clinical Trial provision (SFDA No.5 Order) issued date: Jan. 17, 2004
- SFDA is interested in Adoption of GHTF /AHWP GN Doc on Clinical Safety/Performance by SG5
- Local CT for pre-market approval applies to:
  - ✓ Most Class 2&3 domestic MD;
  - ✓ Part of imported Class 3 implantable MD;
  - ✓ All Class 2&3 IVD.,

2011

Clinical Evidence (CEv)

- Adopt GHTF Concepts & definitions
  - ✓ Clinical Investigation
  - ✓ Clinical Data
- Other Key definitions defined by ME
  - ✓ Clinical Trial Report
  - ✓ Clinical Trial Data

Clinical Evaluation (CE)

- Data sources used in the CE
  - ✓ Literature source
  - ✓ Clinical Experience
  - ✓ Clinical Investigation
- CE report contain
  - ✓ Intended use
  - ✓ Clinical performance/safety claims
  - ✓ Clinical data /evaluation
  - ✓ Recognized standards

Clinical Investigation (CI)

- CI nec. when data not available from other source
- Harmonized to ISO 14155: 1996
- SFDA Order No. 5 taken as GCP GN
- GCP under drafting

SINGAPORE

2009

- No established reg. On CEv specifically
- Clinical data is required as part of product reg. for higher risk devices (Class B, C, D)
- Accept GHTF GN doc on Clinical Safety/Performance by SG5
- Interested in adoption of GHTF/ AHWP GN doc on clinical safety/performance

2011

Clinical Evidence (CEv)

•Adopt GHTF Concepts & definitions
- ✓ Clinical Investigation
- ✓ Clinical Data
- ✓ Clinical Evaluation
- ✓ Clinical Evidence

•Other key definitions defined by ME
- ✓ Clinical Trial includes clinical investigation of MD, therapeutic product & human Cell-& Tissue-base therapy

Clinical Evaluation (CE)

•Data sources used in the CE
- ✓ Literature source
- ✓ Clinical Experience
- ✓ Clinical Investigation

•CE report contain
- ✓ Intended use
- ✓ Clinical performance/safety claims
- ✓ Clinical data /evaluation
- ✓ Recognized standards
- ✓ Others: Need demonstrate compliance to EP

Clinical Investigation (CI)

•CI is not necessary for lower risk product

•Adopt ISO 14155, to be used to supplement ICH GCP standard for MD clinical trials.

Phase implementation CT Reg. Target from 2012

KOREA

2009

- MD Clinical Study implementation Std.-14-July-2005
- NOT require local clinical trial
- Accept GHTF GN doc on Clinical Safety/performance by SG5.
- Interested in GHTF/AHWP GN on clinical safety/Performance

2011

Clinical Evidence (CEv)

- Adopt GHTF Concepts & definitions
  - ✓ Clinical Investigation
  - ✓ Clinical Evidence

(Accept Clinical Data (CD)& CE as a kind of CD" in KFDA reg.)

- Other Key definitions defined by ME
  - ✓ Clinical Trial/Study
  - ✓ Clinical Trial/Study report

Clinical Evaluation (CE)

- Data sources used in the Clinical Evaluation
  - ✓ Literature source
  - ✓ Clinical Experience
  - ✓ Clinical Investigation *(Depends on the risk of MD, accept ONLY CI for certain MD)*
- CE report contain
  - ✓ Intended use
  - ✓ Clinical performance/safety claims
  - ✓ Clinical data /evaluation
  - ✓ Recognized standards
  - ✓ Others … i.e. Investigation plan, protocol, results, summary of case report Statistical Analysis plan & results, etc.
- NOT routinely require local CI data BUT could require local data if needed for safety & effectiveness evaluation
- CD fr. Comparable/predicate, applicable for low risk line extension of MD.

Clinical Investigation (CI)

- CI is necessary once data not available thru other sources
- Adopt ISO 14155
- GCP Reqmt - KFDA Order2010-77 (CT Stds & design criteria)

INDIA

2009

- Require local clinical trial for pre-market approval of certain categories of MD
- Accept GHTF GN doc on Clinical Safety/Performance by SG5.
- Interested in GHTF/AHWP GN on Clinical Safety/Performance

2011

Clinical Evidence (CEv)

•NOT adopt GHTF Concepts & definitions

Clinical Evaluation (CE)

•Data sources used in the Clinical Evaluation

- ✓ Literature source
- ✓ Clinical Experience
- ✓ Clinical Investigation

•CE report contain

- ✓ Intended use
- ✓ Clinical performance/safety claims
- ✓ Clinical data /evaluation
- ✓ Recognized standards
- ✓ Others (Per contents of Appendix II of schedule Y)
- ✓ Local CI ONLY apply where no predicate in India OR new intended use OR any change in material/ composition of approved MD

Clinical Investigation (CI)

•CI is necessary once the data not available

•NOT adopt ISO14155

•GCP GN & applied to all ongoing CE

Draft CT GN/Regulation Released on Aug 4th , 2010, Yet to implement as regulation

Chinese Taipei

2009

- May 30, 2007 Guidelines for Medical Device Good Clinical Practice
- TFDA will consider the finalized SG5 document
- TFDA is interested in adoption of GHTF/AHWP GN doc on Clinical safety/performance by SG5
- Clinical data will be required depending on the type of device (foreign data may be accepted)

2011

Clinical Evidence (CEv)

•Adopt GHTF Concepts & definitions

- ✓ Clinical Investigation
- ✓ Clinical Data
- ✓ Clinical Evaluation
- ✓ Clinical Evidence

Clinical Evaluation (CE)

•Data sources used in the CE

- ✓ Literature source
- ✓ Clinical Experience
- ✓ Clinical Investigation

•CE report contain

- ✓ Intended use
- ✓ Clinical performance/safety claims
- ✓ Clinical data /evaluation
- ✓ Recognized standards

Clinical Investigation (CI)

•CI is necessary once the data are not available thru other sources

•Adopt ISO 14155 for GCP requirement

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Recommendations

- AHWP member economies to adopt the key definitions and concepts per GHTF SG5/N1R8: 2007 in developing and/or revising relevant regulations.
- Where member economy has implemented terminologies that differs from GHTF guidance, these definitions are recommended to be harmonized to GHTF guidance.
- GHTF SG5/N2R8: 2007 on Clinical evaluation is an useful guidance. Whilst further understanding and deliberation based on member economies' regulatory system, will be required for future consideration of the adoption of the guidance, WG5 would recommend adoption of the process of the clinical evaluation per the GHTF guidance document.
- WG5 subscribe to the GHTF SG5/N3:2010 guidance in relation to when a clinical investigation should be undertaken for a medical device to demonstrate compliance with the relevant Essential Principles and the general principles of clinical investigation involving medical devices and recommend for consideration in future development of AHWP guidance document
- Further study & evaluation of ISO 14155:2011 for harmonization

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Future Opportunities

- Support Member Economies in the development /harmonization of clinical trial regulations
  - Training modules on regulatory aspects of clinical safety/performance through e-learning platform
  - Develop applicable AHWP GN
- Collaborate with (GHTF SG5) Advisory Expert Panel /International Medical Device Regulators Forum (New) to provide guidance for clinical trials regulations development in emerging member economies
- Partner with other TC work groups' initiatives to provide expertise & input relating to clinical safety/performance

AHWP

THANK YOU !

Working Towards
Medical Device
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