# WG1 – Pre-market: General MD

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AHWP 19th TC Meeting
5 Nov 2015, Bangkok

Asian Harmonization Working Party
WORKING TOWARDS MEDICAL DEVICE HARMONIZATION IN ASIA

# Updates

- No. of WG members: 25
- Project Teams:
  - Combination Product
  - CSDT for general medical devices
  - Grouping for Pre-market registration
  - UDI (supporting team)

# Proposed Work Plan 2015 - 2017

| Priority | Work Item | Deliverables | Action Plan and Timeline |
|---|---|---|---|
| 1 | CSDT for general medical devices<br><br>Led by: Nishith Desai | Publish a finalized CSDT document from the AHWP, for adoption across member economies. | **Jun 2015:** Review of draft CSDT guidance (2006), update<br>**Dec 2015:** Finalized CSDT for general medical devices published |
| 2 | Combination products (Medical Device) guidelines<br><br>Led by: Arthur Brandwood | White paper on best practices, gap analysis & guideline in the qualification of combination products and technical requirements during pre-market submission. | **Dec 2015:** White paper & gap analysis on summary of combination products guidelines in AHWP and IMDRF jurisdictions<br>**Nov 2016:** Circulation of draft AHWP guidelines for comments<br>**Dec 2017:** Publication of guidance |
| 3 | Grouping for pre-market submission<br><br>Led by: Meshal A. Al-Amri | Guidelines for grouping of medical devices, for the purpose of pre-market MD registration in ASEAN member states. | **Dec 2016:** Identify best practices on jurisdictions & perform gap analysis of guidelines. Road map proposal to bridge the gaps<br>**Dec 2016:** Position paper<br>**Dec 2017:** Propose a guideline document |

# WG Progress Update

since last AHWP Seoul TC Meeting in 2014

| No. | Work Item | Status |
|---|---|---|
| 1 | Guidance for Preparation of a Common Submission Dossier Template Dossier for General Medical Device Product Submission | Guidance document up for endorsement Nov 2015 |
| 2 | White paper on summary of combination products guidelines in AHWP and IMDRF jurisdictions | Reference document up for endorsement Nov 2015 |
| 3 | White paper on grouping of medical devices for pre-market submission | Reference document up for endorsement **2016** |

# White Paper: Regulation of Combination Products – a Review of International Practice

- Scope of paper:
  - Addresses products which *integrally combine* a medical device with a medicine or biological (E.G. drug eluting stents, devices with antimicrobial coatings).
  - Excludes companion products which are cross labelled (e.g. companion diagnostics) or products supplied together (systems or kits).

- Objective of paper:
  - Summarize current international practices for regulation of Combination products in a selection of representative jurisdictions including members of both IMDRF and AHWP
  - Assess areas of consensus and differences in regulatory practices

# Regulatory Challenges for Combination Products

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- Aspects of regulation can vary widely between device, medicine and biologics.
- As such, challenge in regulation of combination products in that the mixture of technologies and functions may cause ambiguity as to the application of the various regulations which may cover
- Clarity needed in definition & the range of different ways in which products can be co-regulated

# Definitions for Clarity

| Product type | Examples |
|---|---|
| ***Combination Product*** | Focus of this Project |
| Products with two or more separate medicine/biologic/device/diagnostic components integrally combined | Drug eluting stent<br>Bone cement with integral antibiotic |
| Usually requires a single marketing application, although review input from multiple regulatory divisions under a single lead based on PMOA | |
| ***Companion Product*** | |
| Two separately supplied products which are co-dependent and cross-labelled | Companion Diagnostic and associated medicine.<br>Human fibrin vial and Thrombin vial to be used together as a sealant |
| Requires separate regulatory submissions for each product, although the reviews may be cross referenced or coordinated and products may be cross labelled. | |
| ***Kit or System*** | |
| Two or more separate products which are co-packaged | Hospital dressing pack containing dressing/gauze, antiseptic swabs, vial of saline, disposable dish, forceps and scissors.<br>Fibrinogen and Thrombin in vials with their Applicator |
| May require a both separate regulatory submissions for each product plus a submission for the co-packaged kit or system. | |

# Reviewed Aspects across MD Regulatory Framework

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- Definition in Regulation
- Formal Status Determination Mechanism, i.e. Qualification
- Responsible authority i.e. Separate Co-ordination body
- Conformity Assessment Process & Fees
- Manufacturing Controls
- Labelling
- Post-market Reporting
- Clinical Evaluation Requirements
- Planned Changes

| | Definition in Regulation | Formal Status Determination Mechanism | Separate Co-ordination body | Evaluation Process | Fees | Mfg Controls | Labelling | Postmarket Reporting | Clinical Trials | Clinical Data Requirement | Planned Changes |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **USA** | Y | Y | Y | P | P | P,C | C,X | P | P | P | |
| **EC** | N | Y | N | C | C | C | C,X | P | P | P | R |
| **AUS** | N | Y | N | C | S | P,C | P,X | P | P | P | |
| **JPN** | N | N | N | P | P | P | C,X | P | P | P | R+ |
| **CAN** | Y | Y | N | P | P | P,C | P,C | P | P | P | |
| **CHN** | Y | Y | Y | P | Y | C | C | Y | Y | Y | R |
| **SGP** | Y | Y | N | P | S | P | P | P | P | P | G |
| **IDN** | Y | Y | N | P | P | P | U | U | P | P | |
| **KOR** | Y | Y | N | C | P | P,C | P,X | P,X | P | P,X | |
| **HKG** | N | N | N | P | P | P | P | P | P | P | |
| **TWN** | Y* | Y* | N | P | P | C | C,X | P | P | C | G |
| **THA** | N | Y | N | P | N | U | P | P | P | P | |
| **MYS** | N | Y | N | D | D | P | U | P | C | P | R,G |
| **SAU** | Y | Y | Y | P | P | P | P | P | P | P | R |

**Key:**

| | | | | | |
|---|---|---|---|---|---|
| **Y** | Yes | **N** | No | **D** | Regulations in development |
| **P** | PMOA regulations or practice applied | **C** | All component regulations applied | **U** | Undefined – no regulation or guidance established |
| **X** | Cross labelling reqmts for co-dependent pdts | **R** | Changes to Regulation<br>G: Changes to Guidance | **S** | Special Fees for combination products |

# Key Conclusions

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## Similarities

- No separate regulatory pathway for CPs anywhere – not surprisingly. CPs are everywhere accommodated within existing drug and device regulations and processes.
- Most agencies involve sister divisions or agencies in regulatory assessment of secondary modes of action.
- Most agencies have some mechanism for adjudication of borderline cases and some had arrangements for coordination of activities across divisions

## Variations

- Manufacturing regulations or standards vary widely - may apply devices (ISO 13485 or equivalent) or pharmaceutical GMP or both.
- Technical Dossier formats vary widely - variants of ICH CTD, GHTF STED, local dossier formats or a combination.

  *Note: Note IMDRF plans to align STED with CTD*
- Approaches clinical trial regulation vary. Good Clinical practice (GCP) requirements varied with application of ICH GCP, ISO 14155 or a combination of both.

## Other Challenges

- Post-market requirements almost always follow PMOA - presents a possible risk of overlooking safety issues.

# Next Steps:

**Dec 2015:**

- White paper on summary of combination products guidelines in AHWP and IMDRF jurisdictions
- Commence work on draft guidance

**June 2016:** Circulation of draft AHWP guidelines for comments

**Dec 2017:** Finalized guidance for endorsement

# Guidance for Preparation of a Common Submission Dossier Template Dossier for General Medical Device Product Submission

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- Scope of paper:
  - **Applies** to all products that fall within the definition of a medical device, except for in-vitro diagnostic medical devices.
  - **Describes** the format for an AHWP member economy harmonized common submission dossier template
  - **Provides** general recommendation on the content of the formatted elements. This document does not recommend any new or additional technical documents above and beyond what should be required per the Essential Principles

- Objective of paper:
  - **Intended** to provide guidance for submission of device information to the regulatory authorities; structured in the format of one common template acceptable by all AHWP member economies regulators.

# WG1 – CSDT: Activities

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## Environment Scan:

- Collect all published CSDT guidance documents
- Collect all Country Regulation with CSDT requirements

## Assessment:

- Review current AHWP draft CSDT guidance
- Review all published CSDT guidance documents
- Review country regulation with CSDT requirements
- Identify similarity and differences

## Development:

- Draft guidance document based on the assessment
- Finalized the guidance document

# WG1 – CSDT: Activities

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Environment Scan was done, covering the following guidelines:

- AHWP Draft CSDT Guidance Document (2006)
- ASEAN CSDT Guidance Document (2010)
- ASEAN Agreement on Medical Device Directive
- ID: Medical Device Guidebook
- PH: Guideline for Registration of MD (2014)
- MY: MD Guidance Document, MDA/GD-03 (2014)
- SG: GN – 17, Guidance for Product Registration Preparation (2014)
- TZ: Guideline on Submission of MD (2009)
- KH: Requirement for MD Registration (2013)
- VN: Draft Decree on Medical Device (2015)
- SA: MDS – 65, Guidance on Marketing Authorization Procedure

# Structure of Guidance

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| | | |
|---|---|---|
| 1 | INTRODUCTION | |
| | 1.1 | Purpose |
| | 1.2 | Scope |
| | 1.3 | Definitions |
| 2 | PREPARATION OF A PRODUCT REGISTRATION SUBMISSION BASED ON THE CSDT | |
| 3 | EXECUTIVE SUMMARY | |
| 4 | ELEMENTS OF THE COMMON SUBMISSION DOSSIER TEMPLATE | |
| | 4.1 | Relevant Essential Principles and Methods Used to Demonstrate Conformity |
| | 4.2 | Device Description |
| | 4.3 | Summary of Design Verification and Validation Documents |
| | 4.4 | Device Labelling |
| | 4.5 | Risk Analysis |
| | 4.6 | Manufacturer Information |
| 5 | REF ERENCES & ANNEX | |

# Additional Guidance Notes

- Guidance drafted with possible variations across jurisdictions' regulatory controls in mind.
- Additional notes of consideration to regulatory authorities, CSDT sections to consider when adopting the guidelines:

| CSDT Section | CSDT Section Item | Regulatory Agency Considerations |
|---|---|---|
| 3(c) | Registration status in reference agencies | Are there reference agency approvals that RA recognizes? |
| 3(d) | Declaration on labelling, packaging and instructions for use | Does RA require comparison of the proposed labelling against that approved by the reference agency? |
| 4.3.1 | Pre-clinical Studies | Biological safety guidelines aligned to ISO 10993 requirements |
| Annex | Example of an Essential Principles (EP) Conformity Checklist | Subject to each jurisdiction's EP requirements |

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# Thank you